AUGUST 2018 # 05

the Cannabis Scientist

Smashing the Grass Ceiling

Cannabis – a fresh opportunity for women in science?

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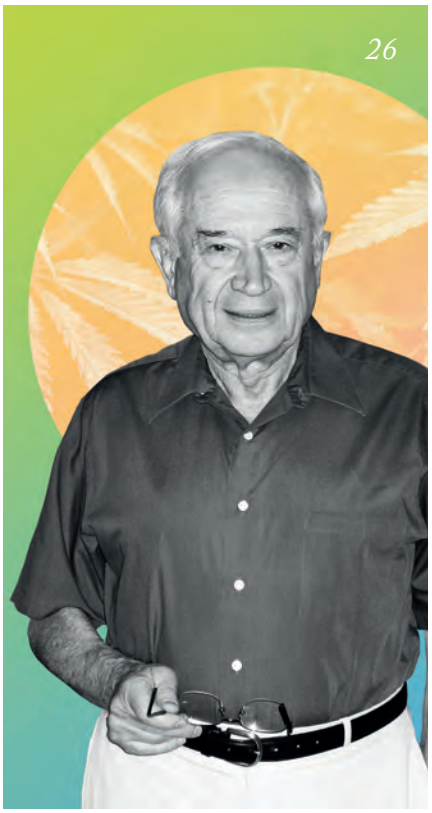


The Great Divide

If we really want to fill the cannabis research vacuum, we need to disentangle the science from the politics.

The legalization of cannabis is marching ever onwards, with Canada the latest country to join the "green rush," and several more US states slated to embrace the leaf.

The debate on legalization stirs strong emotions, and positions on both sides are entrenched. The only way to bring clarity? Rigorous, independent science, but the illegal status of cannabis and the polarized nature of discussions have made it hugely challenging for scientists. When it comes to cannabis, it appears to be impossible to entirely separate the politics from the science – after all, lawmakers have a major impact on what research can be conducted – and even how the results are interpreted.

We know that cannabis carries very little risk of immediate toxicity, but there remains surprisingly little definitive evidence on the longer-term positive or negative health effects of the drug. A 400-page report from the US National Academies of Science, Engineering, and Medicine reviewed 10,000 papers and found "conclusive or substantial evidence that cannabis or cannabinoids are effective" for only three medical conditions – chronic pain, nausea after chemotherapy and symptoms of multiple sclerosis. In terms of risk, "substantial evidence" was found in only four areas – worsening existing respiratory problems, development of psychosis, low birth weight in babies, and an increase in motor vehicle accidents. Beyond that, the evidence is "moderate" at best, and nonexistent for many purported benefits or harms.

The lack of hard facts has left a vacuum to be filled with misinformation, both positive and negative – from 1930s "Reefer Madness" propaganda to today's less-than scrupulous online retailers claiming that cannabis oil is a literal panacea.

As more territories legalize the drug, the number of studies appears to be rising – a PubMed search returns twice as many journal articles mentioning cannabis in 2017 compared with 2007 – but the number still lags far behind studies on common pharmaceutical drugs and alcohol (the most widely available recreational drug in the world).

Given that millions of people are now free to access cannabis medically or recreationally, we need more information. If we can disentangle the science from the politics, we can empower researchers with the freedom and funding to conduct major studies that fill the significant knowledge gap. As Raphael Mechoulam says on page 26, "We need data. We cannot work as though we are in the eighteenth century. Ultimately, it is governments that have the power to change things."

Charlotte Barker
Editor

Upfront

Reporting on research, personalities, policies and partnerships that are shaping cannabis science.

We welcome information on interesting collaborations or research that has really caught your eye, in a good or bad way. Email: charlotte.barker@texerepublishing.com

Take the High Road

Canadian company Molecular Science Corp has assembled a team of top equipment vendors to fit out the world's first mobile testing lab for cannabis. We speak to Brigitte Simons, VP of Labs & Strategic Operations, to find out more.

Why develop a mobile lab?

As the Canadian regulatory framework for legalized cannabis takes effect this fall, well characterized products and quality control are key to meeting the requirements for retail. Mobile laboratory services provide customers instant access to in-process data, so that they can optimize quality assurance programs tracking cultivation yields, safety, and accurate product labelling. It allows customers to access scientific advice and expertise, without having to budget for costly in-house infrastructure or recruit PhD-level scientists (a particular challenge for growers in remote rural locations).

We have launched a scientific partnership with Canopy Growth Corporation, the largest marijuana producer in Canada with 11 facilities, to help them improve their risk management and optimize product development.

How close is it to the capabilities of a fixed lab?

In some ways, it offers more versatility than a typical cannabis lot-release testing lab, designed for uninterruptable routine. Our mobile lab is a holistic service – we can do metabolite screening, assist in research and development for natural products, measure contaminants, and look at multiple inputs into the cultivation supply chain. Furthermore, if a problem comes up that we can't solve in the field, we can ship samples to our fully equipped lab in Toronto for a deeper analysis.

Is this the only lab of its kind?
This is the only mobile lab able to carry out risk assessment in line with Health Canada's stringent requirements for product lot-release testing. Mobile labs have existed in other industries such as environmental water testing and geological mining, but our lab has features specific for cannabis compliance, to allow proper record keeping for agriculture materials with narcotics handling.

What is the role of equipment vendors?
Establishing technology partnerships with the different suppliers has been a very positive experience. Working in a mobile environment is very different to a fixed lab, and we have received exceptional engineering support from Quasar Instruments (Colorado, USA) and our additional partners to make technology implementation robust and worry-free. For example, Peak Scientific (Scotland, UK) have been tremendously helpful in providing extra parts and support – without high-grade lab gas, no mass spectrometry can happen so it's vital that the gas generators stay operational.

What is the biggest challenge of going mobile?
Without a doubt, maintaining security procedures in accordance with our licence to possess cannabis products for lab testing and research. Even though the lab doesn't actually carry or store marijuana, we have to be very security conscious to protect our clients from infringing within licensed zones and work responsibly to ensure sample traceability. Confidentiality and data protection are the other major concerns for our customers, and we have systems in place to make sure that data integrity and security matches the information management of our physical lab in Toronto.

What's your take on the regulatory testing situation in Canada?
Canadian government agencies have some of best labs in the world when it comes to pest control management and environmental toxicity in consumer goods, which puts Canadian regulators in a strong position. The required pesticide reporting limits in Canada will be stricter than in the US, which is great from a consumer safety point of view but a tough challenge for the industry's product pipelines. The regulators have set the bar, and it's now up to service labs like ours to figure out how we can help our partners to meet and improve upon those standards as more cannabis products hit the market.

Perfect Partners

The mobile lab has been developed to a high specification and includes equipment from:

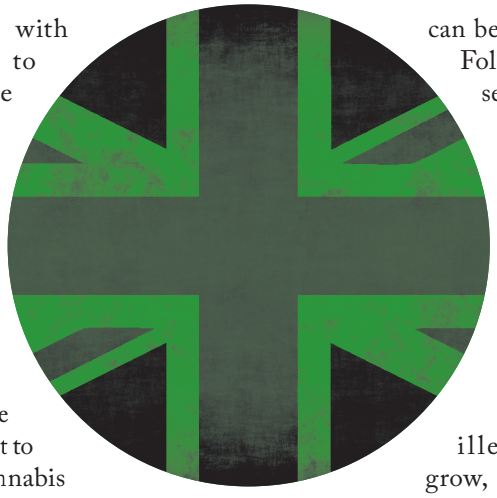
- SCIEX – mass spectrometry
- Peak Scientific – gas generators
- Hamilton Robotics – sample handling
- Phenomenex – LC columns
- VWR – lab supplies
- PerkinElmer – FT-NIR spectroscopy
- Restek – consumables
- SPEX SamplePrep – sample grinding
- Sigma – consumables
- Twister Trimmer – trimming equipment

Yes We Can(nabis)!

The UK government has given a green light for cannabis-derived drug prescriptions

Facing increasing public pressure on medicinal cannabis, the UK government recently announced that doctors will be able to prescribe cannabis to patients with "exceptional clinical need" by autumn 2018. The decision follows advice from the Advisory Council on the Misuse of Drugs to UK home secretary Sajid Javid that cannabis can have therapeutic benefits. However, Javid was careful to point out that the move is "in no way a first step to the legalization of cannabis for recreational use."

Debate on medical cannabis has been raging in the UK in recent months, following several high profile cases of British children with epilepsy forced to discontinue the cannabis oil that their parents claim is vital in managing their condition. Last year, Billy Caldwell, a 12-year-old with severe epilepsy, became the first UK patient to be prescribed cannabis oil. When his doctor was ordered to cancel his prescription and Billy was hospitalized with severe seizures, his mother (along with parents of other children whose epilepsy appears to be improved by the drug) began a campaign to overturn the decision. Currently, cannabis is a Schedule 1 drug in the UK, meaning that it is considered to have no medical value – although it can be used in research.



Following the home secretary's decision, cannabis-derived medical products will fall under Schedule 2, and so will be available through prescription on a case-by-case basis. Though it is illegal to possess, grow, distribute or sell cannabis in the UK without a license, a United Nations report published earlier this year revealed that the country is the world's largest producer of cannabis for medical and scientific use. The UK is home to GW Pharmaceuticals, which is licensed to grow cannabis to produce prescription drugs Sativex and Epidiolex (see page 9).

Trip Advisor

Are you under the influence? This prototype app could have the answer.

What?

A new app, currently in development, called 'Am I Stoned?' aims to tell consumers if and how they are affected by consumption of tetrahydrocannabinol (THC). The test assesses reaction time, memory and attention level to determine if users are significantly impaired.

How?

Twenty-four people were asked to take either 15mg of THC or a 7.5mg placebo and then complete a series of computer- and iPhone app-based tasks. Three out of four of the computer tasks and one of the iPhone tasks successfully detected impairment.

Why?

"One of our long-term goals is for the app to improve the safety of cannabis use by making individual users more aware of their impairment," said the team in a statement.

Who?

The app was designed and tested by a team at University of Chicago, headed by Harriet de Wit, Professor in the Department of Psychiatry and Behavioral Neuroscience. The initial results will be presented at 2018's Experimental Biology conference by doctoral student Elisa Pabon.

What next?

The effect of THC on performance can be subtle, the team acknowledge – so the next stage is to improve the sensitivity of the app-based tasks. They also hope that data gathered from use of the app will help improve future iterations. Ultimately, they hope to develop a working app that allows individuals to assess their own performance without the need for lab-based testing. However, the app is not designed to tell users whether they can drive or engage in risky activities.

Leaving Them Breathless

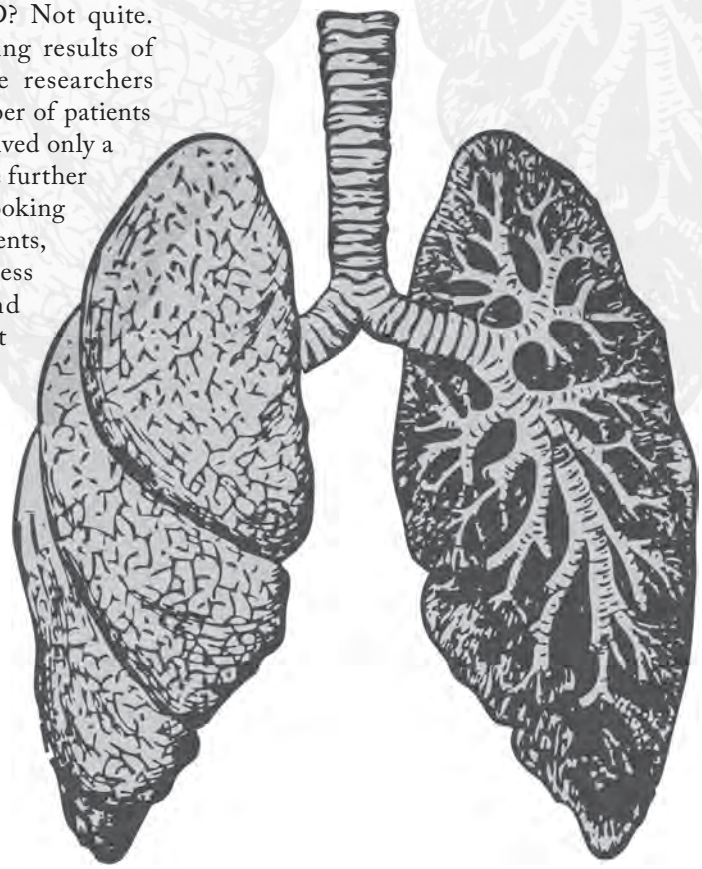
Cannabis fails to live up to promise for lung disease

Researchers at McGill University, Montreal, Canada, found that the inhalation of vaporized cannabis had no effect on the symptoms of chronic pulmonary obstructive disease (COPD), an umbrella term used to describe a variety of progressive lung diseases that cause breathing difficulties.

Smoking cannabis has obvious drawbacks for those with lung complaints, especially when mixed with tobacco. However, past studies have suggested that cannabis may help to open airways in asthmatics, and some COPD sufferers have reported reduced breathlessness with the use of medical cannabis.

The Canadian team set out to find out if cannabis vapor would have an impact on symptoms in a randomized, controlled crossover trial with 16 patients with severe COPD (1). Half of the patients were given vaporized cannabis and half a placebo, before using a stationary bike. The experiment was then repeated with the cannabis and placebo groups switched. The results revealed no significant effect of cannabis on exercise performance or breathlessness across the group.

So is this the end for cannabis as a treatment for COPD? Not quite. Despite the discouraging results of their initial study, the researchers point out that the number of patients was small and each received only a single dose. They believe further research is warranted, looking at a larger group of patients, including those with less advanced disease, and trialing several different cannabis formulations.



Reference

1. *SJ Abdallah et al. "Effect of vaporized cannabis on exertional breathlessness and exercise endurance in advanced COPD: a randomized controlled trial", Ann Am Thorac Soc, (Epub ahead of print) (2018). DOI: 10.1513/AnnalsATS.201803-198OC*

An FDA First

Does Epidiolex represent a watershed for cannabis-derived medicines in the US?

In June, Epidiolex became the first ever drug comprised of an active ingredient derived from cannabis to receive FDA approval. The drug has been found to reduce seizures in two severe childhood epilepsies – Lennox-Gastaut syndrome and Dravet syndrome. The strawberry-flavored liquid has already been used to treat 1,500 children with the conditions worldwide under a compassionate use program. With no current treatment options for Dravet syndrome, the application was fast tracked and Epidiolex was designated an orphan drug, which grants the developer tax credits and seven years of marketing exclusivity.

UK-based GW Pharmaceuticals produce the drug by extracting CBD from cannabis plants grown legally in the East of England. FDA Commissioner Scott Gottlieb said in a statement "Because of the adequate and well-controlled clinical studies that supported this approval, prescribers can have confidence in the drug's uniform strength and consistent delivery."

However, Gottlieb was quick to note that the agency will still take action against "illegal marketing of CBD-containing products with serious, unproven medical claims."

SMASHING THE GRASS CEILING

The cannabis industry is reported to have a greater than average number of women in executive level positions. But what about women working in cannabis science? With most scientific fields still struggling with equity, we wanted to shine a spotlight on the female scientists shaping this emerging sector. Here, we speak with seven inspiring women blazing a trail in pesticide testing, cultivation and classification to find out how they survive and thrive in this fast-paced and rapidly changing field.

A CLASS ACT

By Cindy Orser, Chief Science Officer, DigiPath Labs, Las Vegas, Nevada, USA.

"Cannabis is already a very challenging matrix to work with and the level of testing we do is very time-consuming and expensive."

Over the course of my career, I've worked in microbiology, genetics, biochemistry, biotechnology and cancer research. But it was while developing rapid diagnostics for biological toxins at ASDx Biosystems, a company I started in 2012 in Boulder, Colorado, that I was asked by a headhunter if I'd be interested in designing, building and staffing a medical cannabis testing lab in Las Vegas, Nevada. Today, I am the Chief Science Officer at the lab I set up – Digipath Labs. Entering the cannabis industry, I immediately saw that there was a lot of false information out there, as well as a lack of transparency at the dispensary level. My motivation is to educate cannabis users, so they can make more informed choices about what they put into their bodies. Prior to the cannabis industry, my career has been long and extremely varied, spanning various disciplines and subjects, where I have always strived to bring an innovative perspective.

The "terpene project"

Some of the most common misinformation in the cannabis industry is related to strain naming. There's no agronomic convention used in naming cannabis strains, whereby you register your cultivar and establish verification criteria. The ambiguity allows for a lot of confusion – and even fraud. Thankfully, a number of influential groups are now calling for the industry to embrace standard naming conventions for cultivars.

I wanted to see just how much diversity in cannabis strains there was, so we started doing large-scale data analytics based on the samples we are sent for testing. We are now working on "the terpene project", proposing a new classification scheme for cannabis based on terpene chemoprofiles. For one project, we looked at 2,200 individual flower samples, and across those samples there were 403 different strain names. By characterizing clusters based on their terpene chemoprofiles, we showed that there were really only three groups, and only 28 strains that could be called unique. Now, I'm working with scientists in other US states using the same in-depth data analysis.

As well as using terpenes to identify strains, I have a lot of interest in formulating terpenes, because I think they are a huge component in the "entourage effect." Also, there is more freedom to study the terpenes because they don't sit under that Schedule 1 stigma. As the cannabis industry matures and as we move towards evidence-based medicine, there is an absolute need for confidence and reproducibility in what people are growing.

Testing for transparency

I would like to streamline the required testing for cannabis – Nevada has the most rigorous testing requirements of any state, and there is some overlap in the tests we have to carry out. Cannabis is already a very challenging matrix to work with and the level of testing we do is very time-consuming and expensive. Certainly, no food product is tested to this extent in Nevada or elsewhere.

As cannabis enters the global marketplace and the path towards evidence-based medicine, standardized methods for cannabis testing are inevitable. Cannabis and cannabis-based products have to be reproducible, and I think we're going to move further away from the flower and more toward all-plant extracts. Cannabis presents many opportunities, so it's an exciting field to be in – if the federal regulations get relaxed, it's going to be amazing.

ON WOMEN IN CANNABIS

In my experience, there is a high proportion of female scientists in significant roles in the cannabis industry. Because the industry was so new, there wasn't time for male domination – it was a level playing field, and there were a lot of mature, well-educated, capable women scientists who saw the opportunity and seized it.

ON WOMEN IN CANNABIS

In the US, there is an impressive number of women in higher-level positions in cannabis – but not in cultivation. That's still male-dominated, as it is across agriculture. In other fields, such as marketing or dispensary management, there are more women compared with scientific fields. And they're doing a fantastic job!

My mom has been an incredible role model to me. She had a 200-acre tree farm, and, growing up, I watched her lead a crew of men and work really hard in a male-dominated industry. She taught me how to change a tire on a tractor; and she taught me I should aim to be on top because of my knowledge. I think she struggled at times, as she's had to deal with people who believe women are less capable. But she has always told me to keep my head up, because results speak for themselves. I've always taken that to heart.

PLANT–LIFE BALANCE

With Allison Justice, Vice President of Cultivation, OutCo, San Diego, California, USA.

After I graduated with a PhD in Plant and Environmental Science, I began producing, rearing and selling beneficial nematodes. While I was consulting with greenhouse facilities on how to use nematodes properly, I began to get calls from cannabis companies – as it turns out, they have very similar pest problems to other areas of horticulture. I started to realize how much was lacking in cannabis research and development and saw there was an out-of-this-world opportunity to adopt different methods to produce better, cleaner and faster-growing plants. I've been growing plants since I was one year old – so for me, cannabis is just a different plant.

I am now VP of cultivation at OutCo. I oversee the cultivation facilities and am responsible for the design and planning of our grow facilities. We currently have a mid-size indoor grow at our headquarters in San Diego, a small outdoor grow in Mendocino and are planning to open a large-scale indoor grow in Long Beach by the end of the year.

"I started to realize how much was lacking in cannabis research and development and saw there was an out-of-this-world opportunity to adopt different methods to produce better, cleaner and faster-growing plants"

How does your garden grow?

The science is the most rewarding part of my role. It's exciting for me to talk to industry veterans and strengthen the science behind what they've been doing up to now. Despite its obvious links to horticulture, cannabis operates as a whole different industry. Many growers have been forced to work in secret for much of their career and aren't always receptive to new ways of doing things, but I work on cultivating respect (no pun intended), and have tried to show that I just want to help.

In fact, growing cannabis – from sticking the cutting to harvest – is very similar to other plants. It needs the same 16 essential nutrients, and has a very similar range in temperature and humidity requirements as a poinsettia. Things get trickier post-harvest, when we have to figure out how to preserve the terpenes and allow time for all the enzymatic processes to happen, and yet dry the plant quickly enough to prevent the growth of destructive microbes. It's a delicate balance, yet of huge importance.

Our small San Diego facility has been used as a true R&D facility with the goal of taking our extensive updates, upgrades and optimizations to our larger expansion facilities. Some examples of these transformations are double-stacked rolling benches lit by LEDs, customized fertility programs, optimized scheduling, and a standard integrated pest management program.

Bugs with benefits

When protecting against destructive pests, growing indoors is much more difficult than growing outdoors. Outdoors, plants are exposed, so natural predators take care of some pests. Indoors, a pest may come into a protected, enclosed environment and "explode" in numbers – and there are no natural predators. Californian regulations mean that you can't spray synthetic pesticides as they will show up in the end product, so you have to come up with more creative methods. Nematodes or beneficial insects are our first line of defense. We apply different species of nematodes and predator mites. The nematodes take care of the plant roots and the predator mites protect the leaves.

Sustainable or organic cultivation is a much harder process than using chemical controls. You have to know the life cycle of the pest, and the life cycle of your beneficial – then work out how often to apply it. With a synthetic pesticide, you have the ability to be lazy – you spray and you leave it!

If applied preventively, beneficial insects are as effective as synthetic pesticides, but less so if you're trying to clean up an existing problem. A lot of these pests are microscopic, so you need to have somebody in there all the time, taking random samples. You don't want to wait until you see the damage before you begin treatment.

RISING TO THE CHALLENGE

With Julie Kowalski, Director of Science and Research, Trace Analytics, Spokane, Washington, USA.

At school, science was always a challenging subject for me. But I'm stubborn, and I decided I was going to stick with it and see if I could get better. Then, I really started to enjoy it. I ended up in analytical chemistry specifically because I've always liked to "monkey around" with equipment.

I was at chromatography company Restek, working on tools for food and environmental analysis, when we started getting calls from customers asking if we had any methods for cannabis. Around the same time my colleague, Jack Cochran, brought a magazine article about pesticides in marijuana to work. This "grass roots" pressure grew steadily, and eventually the company started to market to cannabis labs.

I soon realized how many challenges the industry was facing – and my stubbornness came into play once more. I felt there were better methods out there; why shouldn't I get involved in developing them? Trace Analytics were (and still are) engaged in early-stage development, which was really attractive to me.

I would say I'm the "technical person" at Trace Analytics. Scientific Director is, a lot of the time, an "on-paper" job… But I still love being hands on in the lab, and this job gives me that balance. I'm in the lab almost every day, developing methods, and helping out with client samples. In a broader sense, we're trying to refine our methods and keep elevating our standards. That's a major focus for me – to ensure we continue to do really solid work.

I did feel slightly nervous about making the move into cannabis – the fact that it's still federally illegal in the US means there is an obvious lack of stability compared with more established markets. I have had to learn to "roll with the punches" a little bit more than I would naturally. Also, there's a lot of "on-the-fly" developing; any product you can think of, people are trying to put cannabis extract into it. We get flowers, cannabis plant material, extracts, edibles, personal care products... And on one memorable occasion we were asked to analyze cannabis-containing personal lubricants!

Value-added tests

Our clients are also very different to those you might deal with in established markets, such as food or environment. For the average client in cannabis, testing is something that they're still wrapping their head around. Some find it hard to understand the importance of testing, but we are always respectful, and talk through any issues.

In the lab, much of what we do is compliance testing – potency testing or testing cannabinoid content. We also do residual solvents, extracts, and so on, using GC-MS. We do terpene analysis – not required by Washington State – via headspace GC-MS. We do pesticides by LC-triple-

quad MS, as well as water activity, moisture content and microbiological testing.

The plant itself is challenging, but trace level determination of pesticides can be particularly complex.

You meet these challenges by developing methods that are specific to the issues. For example, I have been spending a lot of time working with scientists at other labs on sample preparation so we can take a more targeted approach. We bounce ideas off each other and work with vendors on custom products. It's good to have a community that is willing to help out.

Historically, cannabis labs have been very secretive about their methods, but that is not how science works. If we're all doing the same methods in private, my fear is that in 20 years there'll only be repetition, and no advancement. But we are turning a corner; I've been reaching out and have found people that are of a more collaborative mindset.

In a few years' time, if I can help get the analytical testing to a really robust level – on a par with other industries – I would be totally satisfied. I know there is a better sample preparation method out there for doing pesticides in cannabis. And being the stubborn person I am, I'm determined to find it!

ON WOMEN IN CANNABIS

Women are quite well represented in cannabis science right now – but my personal feeling is that as the industry as a whole matures, and more established "traditional" companies come into play, the percentage of women will drop to the levels seen in other analytical markets: environmental, food, pharmaceutical.

Despite having really good direct managers and mentors, I have still had to be more assertive than men in the same position to make sure I'm listened to. As a woman, you're taken more seriously as you get older, so now in my early 40s I don't have to fight for a voice as much as I used to.

The advantage in the cannabis industry is that everyone is hungry for knowledge – they are more concerned about acquiring the information than who the information comes from. It doesn't matter if you're a man or woman, as long as you know something helpful.

ON THE GRAPEVINE

With Jaclyn Thomson, Director of R&D; Katie Maloney, Senior Scientist; and Clare Maloney, Scientist, Northern Vine Labs, Langley, Canada.

How did you come to work in cannabis science?

Jaclyn Thomson: My fascination with science began at a young age, but I became interested in the cannabis industry as legalization for medical use became a reality. I researched the unique properties and characteristics of the plant while working as the Quality Assurance Manager at a natural health product manufacturer, where I acquired a great deal of knowledge of licensing, regulatory affairs, and various manufacturing processes. I then joined Northern Vine in time to begin the process of outfitting the lab and developing testing methods.

Katie Maloney: A friend of a friend involved in the cannabis industry was looking for chemists, and I was interested in a new challenge! I joined Northern Vine at a time when we were pursuing our controlled substances license for the purpose of conducting quality control testing of legal cannabis in Canada.

Clare Maloney: My analytical chemistry career has led me to work in a wide variety of industries, but I was invited to join the company originally because of my experience in pharmaceutical analysis, specifically some of the generalized testing that is applied to all pharmaceuticals, and which I could adapt to cannabis. It was also an opportunity to continue collaborating with my cousin, Katie Maloney, who is a great chemist!

What is your role?

JT: As the Director of Research and Development, I oversee all laboratory testing, test method development, and validation as well as all R&D, quality management, and any scientific processes in general. I love to solve problems and educate myself, but I also enjoy teaching others to help them understand new and exciting things. My role really gives me the best of both worlds.

KM: I am the Senior Scientist in the chemistry lab. I am currently responsible for developing and validating our testing methods, as well as conducting some R&D. I love working in the lab and solving research problems.

CM: As Scientist, I work on method development, validation, and laboratory operations. I have had extensive experience in operations, and my experiences in other areas of analytical chemistry offer a bed of practical knowledge for method development.

What interests you about the cannabis field?

JT: We are all excited at the wide variety of research that remains to be done on a plant that has been a part of the human experience for so many thousands of years. We are lucky to be part of an organization that shares in that excitement, and is supporting research not only into analytical methodology, but into many other aspects of the effects, uses, and benefits that cannabis can provide, to say nothing of the more practical side of extraction, production, and delivery systems. The unique combinations of components in the cannabis matrix, variations in cannabis strain, and variations in product type result in a sizable knowledge gap that we are looking to fill. Everything is new and that's exciting!

How has the field changed since you've been working in cannabis?

JT: Initially, testing was a service only available to Licensed Producers, but now individual patients have a means of ensuring their product's potency and safety. The demand for information about all aspects of research into cannabis continues to rise as more questions are raised about its actual therapeutic uses, and literally millions more potential consumers come into play with the legalization of recreational use in Canada. We believe that the genesis of this information gathering will lie in being able to accurately analyze the plant, and the products made from it.

What do you find most rewarding about your role?

JT: The opportunity to be involved with establishing a testing facility from the ground up has been a very challenging, but educational and rewarding experience. I enjoy being able to use my skills and knowledge to move the process forward as

efficiently as possible. I also enjoy educating others, both at the corporate and operational level, about the science behind the testing and all things cannabis science! I work with a fantastic group of people and that really gets me excited to come to work every day.

KM: I really enjoy our work environment and culture, too. We are supportive, encouraging, and united in our goals to produce high-quality work, and address problems and research questions. To have a workplace that fosters problem-solving is very gratifying.

CM: We work in a very dynamic environment, and encounter many challenges, questions, and new avenues of enquiry every day. We have a pretty collaborative approach, and I feel like I can bring to bear not only the technical expertise that I've gained through my career, but also some practical knowledge when it comes to problem solving.

How does it compare with other industries you have worked in?

CM: The cannabis industry seems a lot more competitive, a lot more dynamic, and has a much more diverse personality type than most other industries. It's ever-changing and running at a million miles a minute.

Should we still be talking about women in (cannabis) science?

JT: The discussion of the role of women in science-based industry is definitely still relevant. The emerging cannabis industry has huge potential for growth, and women have a unique opportunity to make a significant contribution. Women continue to be somewhat under-represented in science, but increasing numbers are confidently pursuing advanced education and taking on higher profile leadership roles in a variety of industries. We have all had the pleasure of working with knowledgeable, experienced and talented women over the course of our careers. As women in science, we are looking forward to a more inclusive future, and hope to act as positive role models for girls and young women considering a career in science.

How important have your female role models been?

"I really enjoy our work environment and culture. We are supportive, encouraging, and united in our goals to produce high-quality work, and address problems and research questions."

JT: Female role models in science are very important – I believe this has contributed to an increasing number of highly educated and skilled women assuming leadership roles. In addition to mentoring me through my research, my PhD supervisor taught me many management, supervisory and other skills, which are useful in my current role. She really inspired me to be the scientist and leader that I am today.

KM: I have been lucky enough to spend my scientific career surrounded by talented and accomplished women. They have shown me that I should have high expectations of myself, and that I can meet them day after day.

CM: My parents were both chemists and my mom was an analytical chemist, so I have followed in her footsteps. I would say I was inspired by her approach to life in general, not necessarily her choice of career. It makes me happy to see people doing what they want to do, and being appropriately compensated for it, regardless of gender.

What changes would you like to see in the field?

KM: We're looking forward to a broader knowledge base and deeper understanding of the chemical properties and therapeutic effects of cannabis. If the past year has been any indication, then we believe we'll have enough new challenges and opportunities to keep us interested for years!

PLAYING THE GAME

With Brianna Cassidy, Chief Science Officer, CDX Analytics, Boston, Massachusetts, USA.

My high school teacher, Lisa Devillez, was my first role model in chemistry. I started an advanced placement class with her, working on chemistry for a couple of hours before class – she was there at 6 am every day to tutor her students! It was a difficult subject, but I found that I could be really good at it when I worked hard. The sense of perseverance and accomplishment really drew me to chemistry, and later I was attracted to analytical chemistry by the attention to detail it required.

Cracking the cannabis code

I got into cannabis because I'm open-minded. The fact that Brian Strasnick, President and CEO of CDX Analytics, funded the entire suite of brand new instrumentation I recommended helped too! Now, CDX scientists have the greatest "toy box" for cannabis analysis in the world, which includes gas chromatographic and liquid chromatographic triple-quadrupole mass spectrometers capable of detecting pesticides in cannabis down to ten parts per billion, the lowest limit in United States cannabis regulation. We also have an inductively coupled plasma mass spectrometer to detect metals that have been found to bioaccumulate in the plants, and quantitative polymerase chain reaction technology with a robotic liquid handler on the front end for microbial analysis. These are just a few of the big players that allow us to meet the challenging testing requirements in Massachusetts.

I took two art minors while majoring in chemistry and this reinforcement of creativity really gave me an edge in the chemistry laboratory. I wasn't afraid to go outside of the protocol and try something I thought would be more efficient or accurate. It allowed me to work with difficult matrices where standard methods won't cut it – which has stood me in good stead for cannabis science. I have analyzed trace-level contaminants in fish, dirt, and groundwater, developed methods to identify degradation in reel-to-reel audio tape at the Library of Congress, and developed laboratory techniques to determine the age of bloodstains at crime scenes – but nothing I have worked with comes close to the complexity of cannabis. I like to refer to cannabis as a Rubik's Cube for chemists; it's a challenge, but I love it. There are very few peer-reviewed publications on cannabis so developing methods to make measurements in cannabis requires creative thinking and perseverance. I was allowed almost an entire year to develop and thoroughly validate our state-of-the-art testing methods before CDX opened its doors. Many things did not work, but knowing what doesn't work is just as important as knowing what does; it's all just part of the game.

ON WOMEN IN CANNABIS

As a woman, I find the cannabis field a very positive one to work in. With any other industry, you're coming into a field with older, experienced scientists that have been doing this for 40 or 50 years – a time period that has been difficult for women in science. But I feel very much equal, very much listened to and respected. We should be encouraging more women to join the industry – it's a new and fast-paced area, so you can grow together with the experts in the field.

Infinite variety

As Chief Science Officer, I'm always looking at what's out there, keeping in line with all the regulations and up-to-date with scientific papers, and talking with other scientists in the field. This way I can align research and scientific priorities to promote the success of CDX. I've got a fast-growing team of scientists in the lab and I need to make sure that everything is running smoothly for our testing in accordance with state regulations as well as for our research projects, which are designed to push the envelope in cannabis science. I also often collaborate with instrument and consumable vendors to explore the capability of new applications in the cannabis arena. Then, of course, I represent the company at regulatory meetings and at conferences, such as the American Chemical Society conference in Boston.

In Massachusetts, we have a 10 ppb limit for nine pesticides in cannabis, which is tough. CDX is the only lab in the United States that has an ISO 17025 validated method that meets this testing requirement. Challenge number two: there isn't a lot of guidance in terms of quality control for cannabis testing. We pull guidance from the FDA, EPA, AOAC, ICH, European Pharmacopeia, and the American Pharmacopeia – though it's difficult for a matrix with this much heterogeneity, which must be held to account both as a medication and a product.

Aiming high

My role has changed tremendously since I joined CDX. At first, I was in the lab 10 hours a day, evaluating instrumentation, creating testing methods, and validating methods, but later it was more about building a team. Next, we had to tell the world about what we were doing and work with regulators. Today, we are focused on identifying where we need to go scientifically to benefit cannabis as an industry. It's gratifying to feel my input is having an impact – I'm able to progress things in the industry instead of just learning from it.

THE CANNABIS SCIENTISTS OF THE YEAR 2018

In our February issue, we highlighted ten top scientists breaking new ground in chemistry, biomedical science and plant biology, as part of our annual round up of "The Year in Cannabis Science." We asked you to vote for your favourites from our list, or suggest new names.

Here are your picks for the top cannabis scientists of 2018.

1. KENT HUTCHISON, CINNAMON BIDWELL AND ANGELA BRYAN

Co-Directors, CUChange Lab, University of Colorado Boulder, USA

The three co-directors of the CUChange Lab come from the departments of Behavioural Neuroscience (Hutchison), Cognitive Science (Bidwell) and Social Psychology (Bryan). The team focus on the complex mix of psychological, physiological and genetic factors that determine our behaviour around health and risk, especially when it comes to recreational drug use. This year, Bidwell and the team were featured by publications including The Cannabis Scientist and Wired magazine with their mobile cannabis lab, housed in a converted Dodge/Mercedes Sprinter van. The team also made international headlines with a study suggesting that alcohol consumption, but not cannabis consumption, causes structural changes in the brain (1). The group will be expanding their cannabis research over the next few years, with several major new studies underway – including research on cannabis for chronic pain and recreational use of high-potency cannabis use (known as "dabbing").

"The group will be expanding their cannabis research over the next few years, with several major new studies underway."

2. CHRIS HUDALLA

Founder & Chief Scientific Officer, ProVerde Laboratories, Milford, Massachusetts, USA.

Hudalla's extensive experience as an analytical scientist, including time at instrument giant Waters Corporation, has stood him in good stead over the past five years. Since establishing ProVerde Laboratories in 2013, he has been a lynchpin in efforts to tighten up safety testing in his home state of Massachusetts, and around the US. A member of several committees helping to set standards for cannabis testing, Hudalla works with others in the field to develop realistic testing protocols that ensure consumer safety. The team at ProVerde have also benefited from Hudalla's contacts with instrument vendors, and now collaborate with a number of companies to help refine testing methods.

Hudalla says, "I'd been doing research in the industry and academia for 25 years when I left Waters to establish ProVerde. At the time, I believed the move would sever my ties with the professional scientific community. Ironically, it did exactly the opposite, and I garnered a lot of respect from my colleagues."

3. COMMITTEE ON THE HEALTH EFFECTS OF MARIJUANA, NATIONAL ACADEMIES OF SCIENCES, ENGINEERING AND MEDICINE

The committee, who published the most comprehensive review yet of the health impacts of cannabis and cannabinoids, was made up of 16 well respected scientists:

- Marie C McCormick (Chair), Sumner and Esther Feldberg Professor, Harvard T.H. Chan School of Public Health, Harvard University, Boston, Massachusetts, USA.
- Donald I Abrams, Professor of Clinical Medicine, University of California, San Francisco, And Chief of Hematology–Oncology Division, Zuckerberg San Francisco General Hospital, California, USA.
- Margarita Alegría, Professor, Departments of Medicine and Psychiatry, Harvard Medical School, and Chief, Disparities Research Unit, Massachusetts General Hospital, Boston, USA.
- William Checkley, Associate Professor of Medicine, International Health, and Biostatistics, Division of Pulmonary and Critical Care, Johns Hopkins University, Baltimore, Maryland, USA.
- R Lorraine Collins, Associate Dean for Research, School of Public Health and Health Professions and Professor, Department of Community Health and Health Behavior, State University of New York At Buffalo–South Campus, USA.
- Ziva D Cooper, Associate Professor of Clinical Neurobiology, Department of Psychiatry, Columbia University Medical Center, New York, New York, USA.
- Adre J Du Plessis, Director, Fetal Medicine Institute; Division Chief of Fetal and Transitional Medicine; and Director, Fetal Brain Program, Children's National Health System, Washington, DC, USA.
- Sarah Feldstein Ewing, Professor, Department of Child and Adolescent Psychiatry, Oregon Health & Science University, Portland, USA.
- Sean Hennessy, Professor of Epidemiology and Professor of Systems Pharmacology and

Translational Therapeutics, University of Pennsylvania Perelman School of Medicine, Philadelphia, USA.

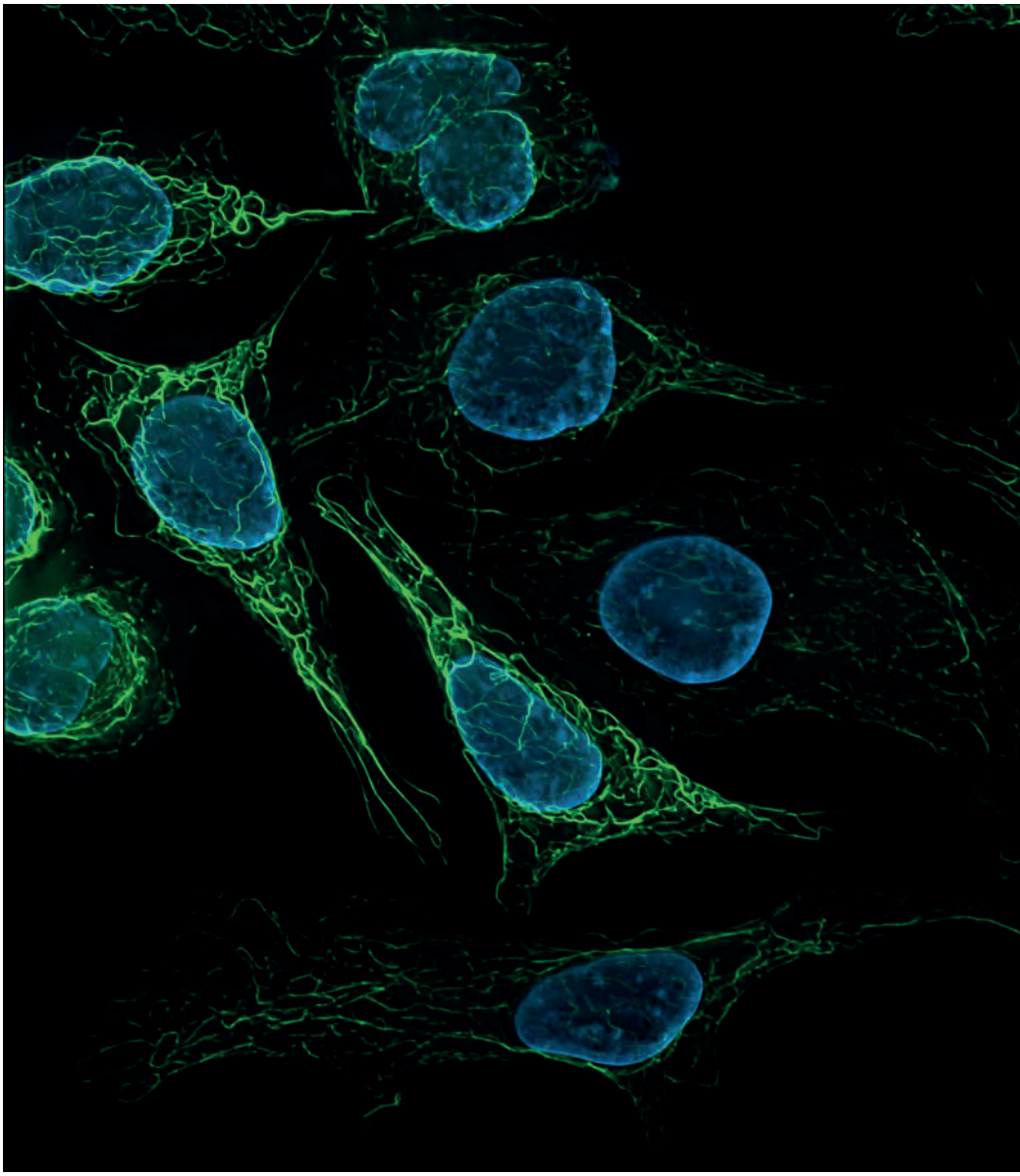
- Kent Hutchison, Professor, Department of Psychology and Neuroscience and Director of Clinical Training, University of Colorado Boulder, USA.
- Norbert E Kaminski, Professor, Pharmacology and Toxicology, and Director, Institute for Integrative Toxicology, Michigan State University, East Lansing, USA.
- Sachin Patel, Associate Professor of Psychiatry and Behavioral Sciences, and of Molecular Physiology and Biophysics, and Director of the Division of Addiction Psychiatry, Vanderbilt University Medical Center, Nashville, Tennessee, USA.
- Daniele Piomelli, Professor, Anatomy and Neurobiology, School of Medicine and Louise Turner Arnold Chair in Neurosciences, Department of Anatomy and Neurobiology, University of California, Irvine, USA.
- Stephen Sidney, Director of Research Clinics, Division of Research, Kaiser Permanente Northern California, Oakland, USA.
- Robert B Wallace, Irene Ensminger Stecher Professor of Epidemiology and Internal Medicine, Department of Epidemiology, University of Iowa Colleges of Public Health and Medicine, Iowa City, USA.
- John Wiley Williams, Professor of Medicine, Duke University Medical Center, Durham, North Carolina, USA.

Between them, the scientists reviewed 10,000 studies and compiled their findings into a report – a balanced view on the harms and potential benefits of cannabis use and misuse, entitled "The Health Effects of Cannabis and Cannabinoids: the Current State of Evidence and Recommendations for Research."

Based on their research, the members of the committee strongly recommend additional research in a number of areas. In the report, the scientists wrote, "This is a pivotal time in the world of cannabis policy and research. Shifting public sentiment, conflicting and impeded scientific research, and legislative battles have fueled the debate about what, if any, harms or benefits can be attributed to the use of cannabis or its derivatives."

Quantitation of Aflatoxins B1, B2, G1, G2 and Ochratoxin A in Cannabis Using Integrated HPLC with a Fluorescence Detector

By Craig Young, Sarah Braseth, Max Wang, Michaela Davenport



Introduction

Studies have found that many mycotoxins, including Aflatoxins G1, G2, B1, and B2, and Ochratoxin A, are immunosuppressive, carcinogenic, neurologically toxic, and hepatotoxic, and that the mold itself can cause diseases such as lung infection and aspergillosis (1,3). Due to the high level of matrix complexity of cannabis products, mycotoxin testing in cannabis is very challenging. This study focuses on developing a powerful detection method that allows cannabis testing labs to confidently report concentrations below regulatory limits – Aflatoxins B1, B2, G1 and G2 combined to 20 ppb and 20 ppb for Ochratoxin A alone.

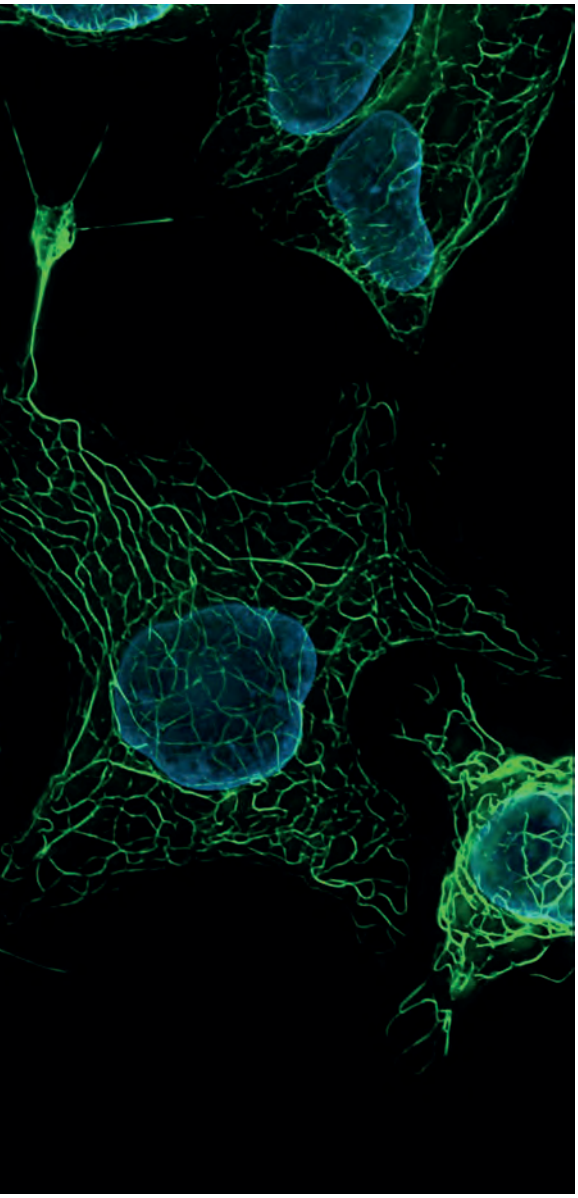
Experimental

Standards were run in triplicate at 2, 5, 10, 14, 20, and 50 ppb for the Aflatoxins and 10, 14, 20, and 50 ppb for Ochratoxin A. All standards were spiked in matrix and extracted so the actual concentrations of the injected material were 0.2, 0.5, 1.0, 1.4, 2, and 5 ppb for the Aflatoxins. The Ochratoxin A does not need as low of a detection limit because the limit is 20 ppb by itself; the Aflatoxins is 20 ppb for the sum of the four (4).

Results and Discussion

Channel 1, excitation of 365 nm and emission at 450 nm, provided the best response for all Aflatoxins and Channel 3, excitation of 330 nm and emission at 460 nm, was chosen for Ochratoxin A, though Channel 2 was also suitable. Aflatoxin G1 had the lowest response of all the Aflatoxins, but Channel 1 still provided quality data for analysis even at the lowest concentration of 2 ppm. Calibration curve R^2 values for each compound were 0.998 or greater, indicating great linearity.

Samples were spiked at 10 ppb of



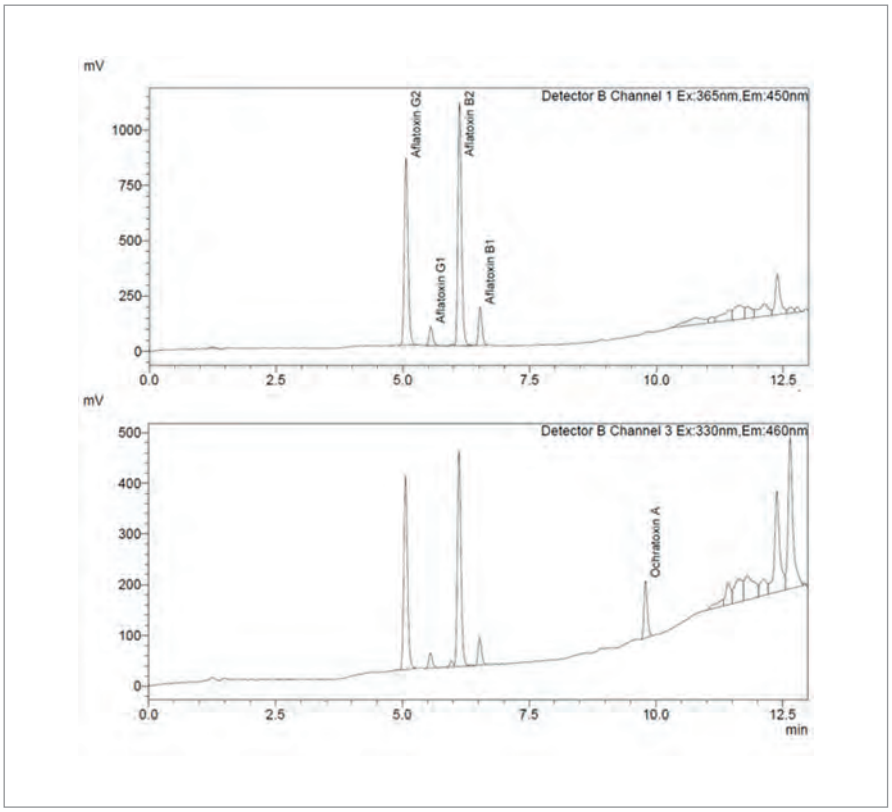


Figure 1. Full chromatogram showing Channels 1 (top) and 3 (bottom) for 10 ppb spiked sample.

Mycotoxin	*Concentration (ppb)*	*Recovery (%)*	*Concentration (ppb)*	*Recovery (%)*
Aflatoxin G2	8.022	80.22	8.380	83.80
Aflatoxin G1	8.534	85.34	8.958	89.58
Aflatoxin B2	7.901	79.01	8.363	83.63
Aflatoxin B1	7.704	77.04	8.044	80.44
Ochratoxin A	8.781	87.81	10.925	109.25

Table 1. 10 ppb spiked sample results.

mycotoxins and run as unknowns. The chromatograms are shown in Figure 1. The recovery results, indicating the high accuracy of the method, are shown in Table 1.

Conclusion

A new fluorescence method has been developed to determine Mycotoxins in cannabis. This method is sensitive and robust, and incorporates an easy sample preparation procedure.

References

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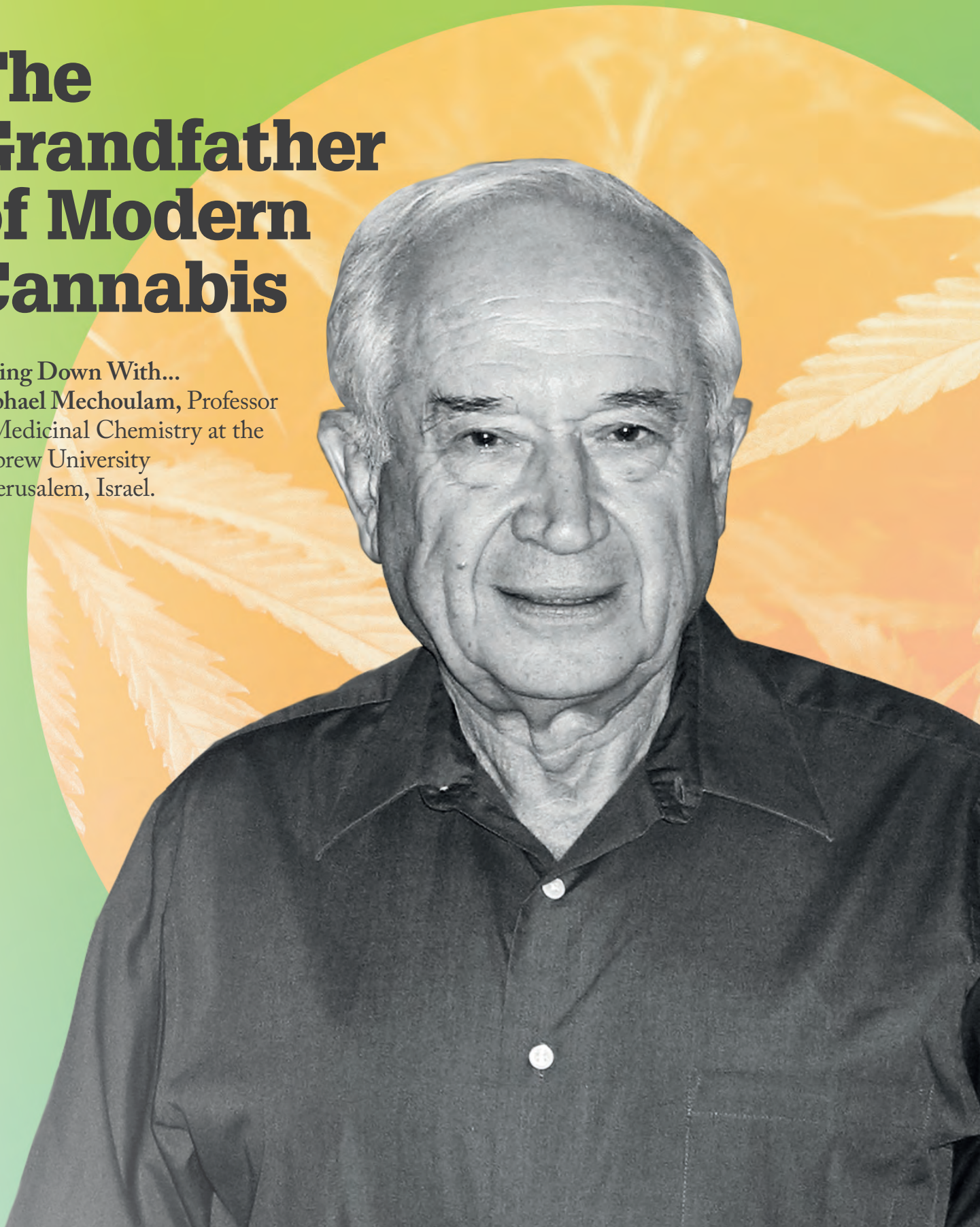
2. *GC Llewellyn, CE O'Rear, "Examination of fungal growth and aflatoxin production on marihuana", Mycopathologia, 62, 109-112 (1977).*
3. *M Sedmikova et al., "Potential hazard of simultaneous occurrence of aflatoxin B1 and ochratoxin A", Veterinary Medicine - Czech, 46, 169-174 (2001).*
4. *Full sample preparation and analytical conditions are available in Shimadzu's document: SSI-HPLC-019, Quantitation of Aflatoxins B1, B2, G1, G2 and Ochratoxin A in Cannabis by LC Using Prominence-i and the RF-20Axs Fluorescence Detector*

The Grandfather of Modern Cannabis

Sitting Down With...
Raphael Mechoulam, Professor of Medicinal Chemistry at the Hebrew University of Jerusalem, Israel.



How did you come to study cannabinoids?

My background is in the chemistry of natural products. I was surprised to find that, although morphine had been isolated from opium 100 years previously and cocaine from coca leaves 50 years previously, the chemistry of cannabis was not well known. The active constituent had never been isolated in a pure form, so it was not known whether we were dealing with one compound or with many. For pharmacology – and later on, clinical work – one has to have a well-defined compound. We first tried to define the chemistry of cannabis, and in the early 1960s, we isolated tetrahydrocannabinol (THC) in its pure form, elucidated its structure and later synthesized it. We then had to define the chemistry for additional compounds (not necessarily the psychoactive ones), so we worked on the chemistry, metabolism, structure and synthesis for the next decade.

Did it feel significant at the time?

Not really. At that time, I asked for a grant from the NIH in the US, and they told me to apply again when I was doing "something more relevant." Well, in a few years, cannabis did become relevant, and the NIH supported my work financially for nearly 45 years.

Was there any stigma?

No – scientists considered it another part of chemistry to be clarified and evaluated. My colleagues believed it to be legitimate, even voting for me to be academic head of the university. They wouldn't have done that if they'd thought I was working on something 'questionable!'

How has your work progressed since?

In the beginning, we were thinking only of the plant material, but we later found that THC mimics the activity of endogenous compounds synthesized by the mammalian body. These compounds, which we identified in the 1990s and named anandamide and 2-AG, are part of a biochemical system known today as the endocannabinoid system. This system involves at least two receptors in the brain and the periphery, as well as enzymes that both synthesize and degrade the endocannabinoids. This is a major field of biochemistry and pharmacology, and is of significant biological and clinical importance.

Do people appreciate its significance?

It has been reported by scientists at the NIH in the US that the endocannabinoid system is involved in essentially all human diseases – which is a strong (yet seemingly correct) statement. There are hundreds of groups working on all aspects of it now. We reported recently that our brain forms an endocannabinoid-like compound that fights addiction to nicotine; there is another one that fights osteoporosis, another that tries to fight brain damage.

What research is still needed?

Along with many others in Israel and elsewhere, I have worked to establish a strong understanding of the chemistry of cannabis-related compounds. What is missing, not only in Israel but in many other countries, is clinical research. To give an example: 35 years ago, we did a clinical trial showing that cannabidiol (CBD) is excellent for epilepsy; however, it's only within the last ten years that people have heard the results of our work. And now children with epilepsy are given CBD.

There isn't a single clinical trial in cancer; however, thousands of people are using cannabis medically, because they've heard it can help. But that's not how it should be done; one should know which specific cannabinoid one should use for a specific kind of cancer. We need data. We cannot work as though we are in the eighteenth century. Ultimately, it is governments that have the power to change things.

Why is there resistance to the use of CBD as a medicine?

Cannabidiol is a strange animal. It's not toxic and doesn't cause psychoactivity or side effects – so there is absolutely no reason to keep it from patients. Health, in my view, is more important than questionable legal issues. A major hurdle is that medical and recreational uses for cannabis have become mixed together. The medical aspect should be pursued according to medical rules; recreational use is a social issue, and the population of a certain area, state or country has to decide if it should be legalized. One should not say, "We want recreational cannabis because it's anti-epileptic" – it doesn't make sense.

What are the highlights of your career?

There have been three: the identification of THC in the 1960s, the identification of the endogenous cannabinoids in the 1990s, and our work now on the third phase of cannabinoid research – endogenous anandamide-like compounds of importance in numerous areas. There is so much more to study in cannabinoids, which keeps me motivated. It's what any scientist likes to do – tackle a research project of some importance and ultimately find out it has been worthwhile.

Anything you wish you'd done differently?

I may have broken the law at the beginning of my research, which I regret! But when we started, nobody was working in this field (mostly for legal reasons, I suspect). As a matter of fact, I got the cannabis from the police. If it had been in the US, we'd all have gone to prison. Thankfully, we never had any major problems working with cannabis in my lab. People knew we were using it for legitimate research.

How do you feel about being called 'the father of modern cannabis'?

I object – I'm the grandfather!