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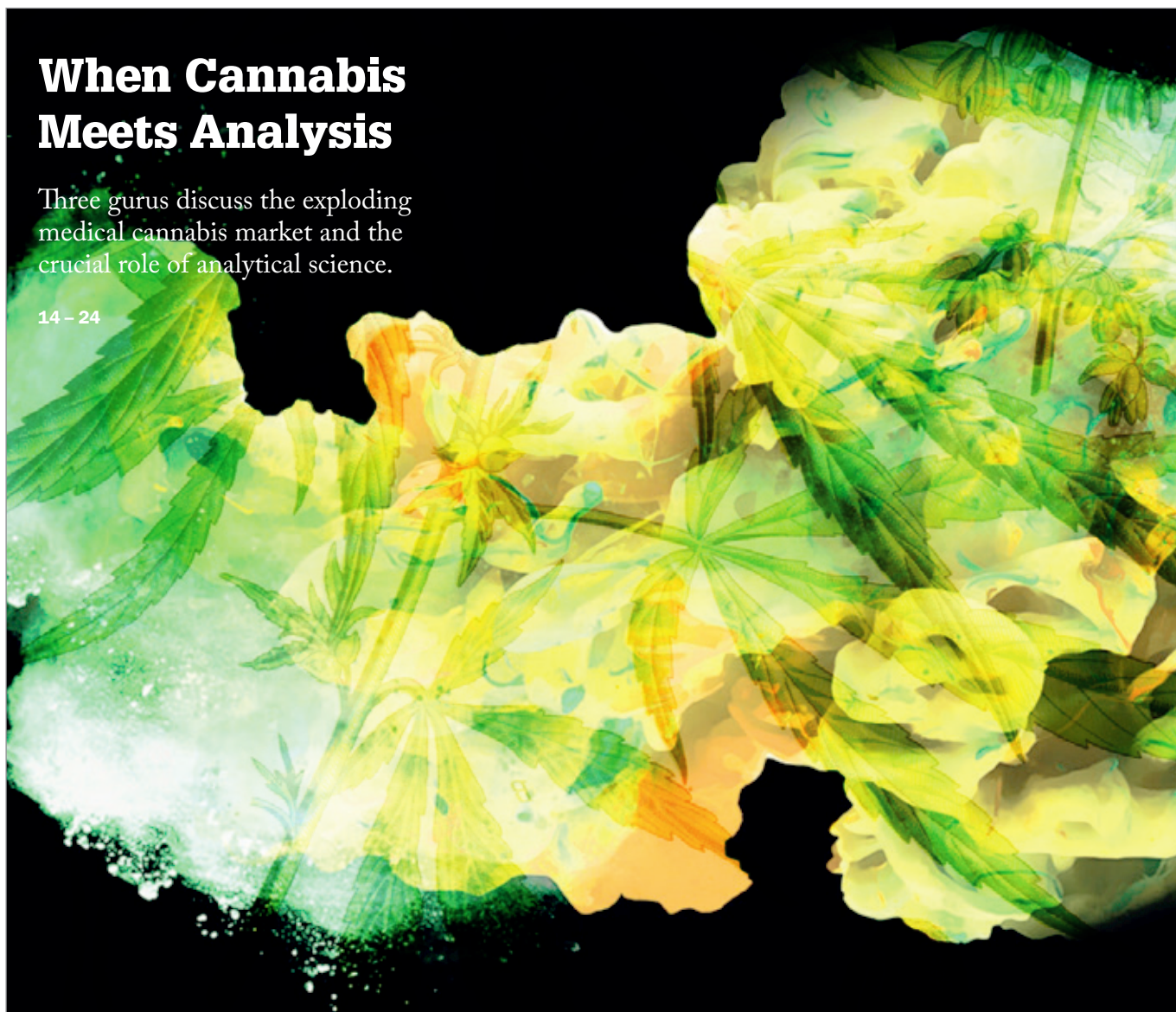
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Welcome to The Cannabis Scientist

Why we teamed up with jCanna to bring analytical scientists and the cannabis industry closer together.

Editorial



Back in the summer of 2015, Scott Kuzdzal (Shimadzu) brought to my attention a novel field of research: cannabinomics (you can read The Analytical Scientist cover story here: tas.txp.to/0916/cannabinomics). Up until that point, I must admit that I had been somewhat ignorant to the exploding medical cannabis market, but I was fascinated by both the research efforts and the analytical implications.

Fast-forward to Pittcon 2016, and the topic of medical cannabis came up again in a number of frankly absorbing conversations. In particular, Scott introduced me to the highly energetic and passionate Josh Crossney – founder of jCanna and a man on a mission: to build bridges between the analytical and medical cannabis communities (see page 10). Sitting squarely in the analytical science community, we asked what we could do to help. The result is in your hands – a ‘mini magazine’ dedicated to the world of cannabis science and in support of jCanna’s inaugural Cannabis Science Conference (www.cannabisscienceconference.com).

Over the last few months, I’ve had the pleasure of speaking with some of the people who originally inspired Josh to begin his own journey – Tracy Ryan, for example, whose daughter’s diagnosis with brain cancer spurred her to act with courage and vigor (see page 26). I’ve also spoken to other analytical chemists, like Scott (see page 14), who have already embraced the opportunity to fill analytical gaps in a therapeutic field that must endure uncertain or shifting regulations.

Two main thoughts have condensed in my mind:

i) Many people in the medical cannabis community are passionate about what they do. And they are keen to embrace analytical testing and quality control to ensure that they supply the best product possible to sometimes very sick individuals. Others are out to exploit a confused public. In either case, analytical science is key.

ii) There is still much we don’t know about the cannabinoid components of cannabis, how they affect the endocannabinoid system, or the synergistic role of other cannabis components, such as terpenes. Understanding the complex chemical composition of cannabis and fully leveraging it to address diseases, many of which we also don’t fully understand, is a huge challenge. Once again, analytical science is key.

In this inaugural edition of The Cannabis Scientist, we address both of these topics by speaking with stakeholders who are directly involved. But we realize there is much more to say. The Cannabis Science Conference will allow further debate and discussion – and I dare say another issue of The Cannabis Scientist won’t be too far behind it...

Rich Whitworth
Editor

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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: rich.whitworth@texerepublishing.com



Cannabinoids: More Research, Please!

Four researchers in health, pharma and psychology describe how cannabinoids fit in with their work – and why further research is needed to help advance treatment.

*Christian Lehmann
Adjunct Professor, Anesthesiology and
Intensive Care Medicine, Humboldt-
University, Berlin, Germany*

Research focus:

One of the current areas of research in my lab is cannabinoids and their potential effect on patients who have had strokes. On the one hand, cannabinoids may very well be a neuroprotective compound, such as in the case of Cannabinoid Receptor 2 (CB2R) activation to reduce brain damage due to strokes. On the other hand, cannabinoid pathways involved in the modulation of the immune system may be the “golden” key to pharmacologically addressing CNS injury-induced immunodepression syndrome (CIDS), a syndrome responsible for life-threatening infections in patients suffering from

strokes. In general, we have multiple ongoing studies with promising results that focus on unraveling the involvement and interplay of the immune and endocannabinoid systems in strokes.

Why further research into medicinal cannabis is necessary:

Cannabinoid-related preclinical and clinical research fields are growing with every passing day and become inclusive of more and more diseases. There are difficulties and conceptual dead-ends, just like in any other field. However, the important part is to realize that the endocannabinoid system is not yet fully understood and further research is absolutely necessary to advance this field and extract its benefits. The bottom line is this: the cannabinoid system appears to be involved in a lot of physiological processes and there is a good chance that it plays a crucial role in the development of novel therapeutic guidelines and approaches.

Irit Akirav

Senior Lecturer, Department of Psychology, University of Haifa, Israel.

Research focus:

Our research has shown for the first time that cannabinoids administered following exposure to an emotional traumatic experience can prevent trauma-related effects in rats. The effects observed are at the behavioral level (for example, preventing the effects of trauma on anxiety, startle response, extinction of fear memories) and on brain plasticity and biochemistry (for example, preventing the effects of the trauma on plasticity and cannabinoid CB1 receptors in the brain's limbic system).

Why more medicinal cannabis research is necessary:

Cannabinoids have wide therapeutic applications for a number of important medical conditions. Recently, it has been suggested that they may be efficient in treating anxiety and stress-related disorders. Yet the interest in their therapeutic applications has been restrained by the fear of potentially harmful consequences. Thus, studies should be directed at establishing whether cannabinoids have efficacy against selected symptoms that are of clinical significance and, if they do, whether the benefits outweigh the risks.

Abdulateef Isiaka Alagbonsi

Department of Physiology, University of Ibadan, Nigeria

Research focus:

Melatonin or vitamin C worsens cannabinoid-induced gonadotoxicity in vivo but ameliorates it in vitro, while their combinations are beneficial under both conditions.

Why more medicinal cannabis research is necessary:

Further research into the medicinal uses of cannabis are necessary to explore its benefits in ameliorating conditions. In addition, more studies are needed to discover how side effects like gonadotoxicity can be managed in its users. However, research in the cannabinoid-related arena is very challenging, especially in developing countries (like Nigeria) where possession of cannabis is a criminal offense. One has no option but to obtain cannabis from the Drug Law Enforcement Agency via strenuous and rigorous processes. Apart from cannabis sativa, which can only be obtained from this agency, a researcher in this field needs to order cannabinoids from commercial dealers like Sigma Aldrich at a high cost, leaving them out-of-pocket – as of course there are no grants available anywhere.

Esther Shohami

Department of Pharmacology, Institute for Drug Research, The Hebrew University, Israel

Research focus:

Traumatic brain injury (TBI) is the leading cause of death in the young age group and the most commonly identified cause of epilepsy in adult populations older than 35 years. Following the isolation and identification of the endocannabinoid (eCB) system as acting 'on-demand', namely, in response to pathophysiological triggers, we have explored the role of this family of compounds in the brain and, in the context of TBI, focused on its potential as a neuroprotective. We found that some of these eCB-like compounds have significant neuroprotective and neuro-repair properties that can be utilized in the treatment of TBI patients. It is important to note however, that in our work we use an experimental animal model of TBI, and the family of compounds we have investigated so far are either the endogenous cannabinoids (those produced in the brain) or synthetic analogs rather than plant-derived compounds.

Why further research into medicinal cannabis is necessary:

The proportion between the main plant constituents, THC and CBD, significantly differ between the various strains. Not enough is known about the effects of these plant-derived extracts, mainly due to this diversity. Research into the effect of the individual components of marijuana, and on their combined effect, in a variety of medical conditions (such as TBI, stroke, epilepsy, pain, PTSD and psychiatric disorders) is still required in models and humans – with the proper controls – to make the use of medicinal cannabis better accepted in the clinical arena.

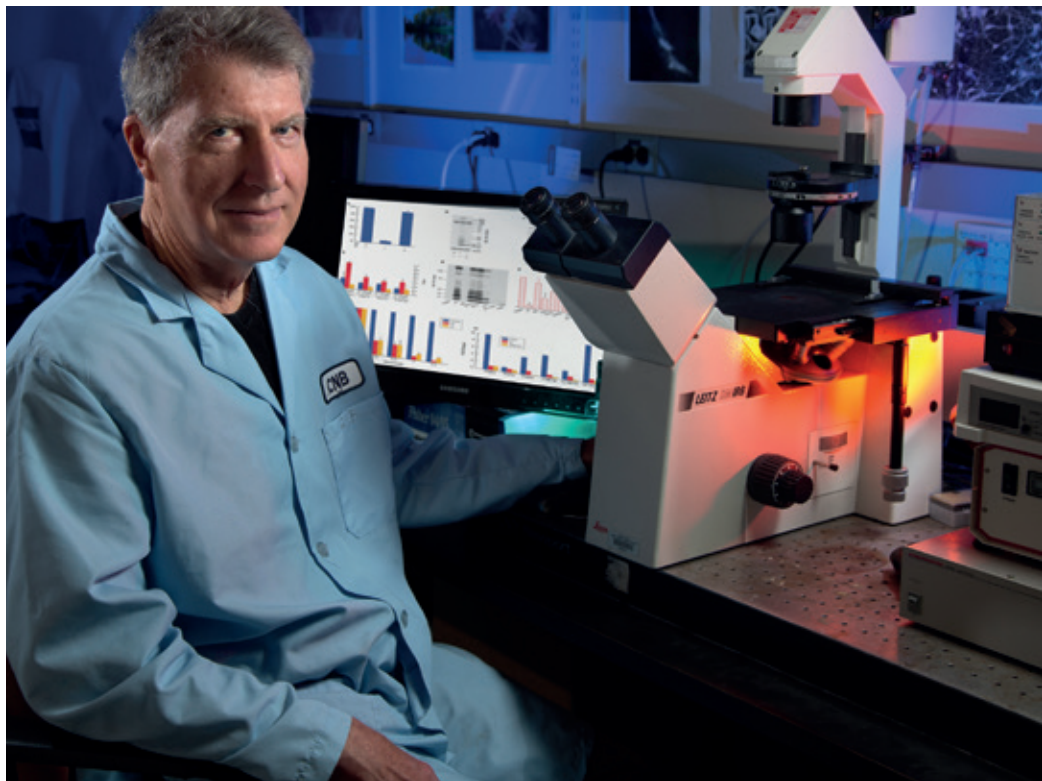
THC versus AD

Tetrahydrocannabinol may be neuroprotective against early symptoms of Alzheimer's disease

Researchers at the Cellular Neurobiology Laboratory, The Salk Institute for Biological Studies have discovered evidence that tetrahydrocannabinol (THC) may be capable of treating early stage Alzheimer's disease (AD).

David Schubert and team have been researching Alzheimer's for several years, focusing in particular on two drug candidates – J147 and CNB-001. They already knew that these potent anti-inflammatory molecules have the ability to remove the amyloid that accumulates within cultured human neurons and is thought to be involved in the development of Alzheimer's. However, they didn't know the molecular target and the signaling pathways that they activate.

While attempting to answer these questions, they first discovered that the accumulation of intracellular aggregated proteins like amyloid within human neurons caused a very potent inflammatory response, leading to cell death – but that their new AD drug candidate CNB-001 blocked both amyloid accumulation and cell death. Interestingly, the cannabis component, THC, was able to function in a similar way. “We knew that one of our drug candidates weakly bound to the CB1 cannabinoid receptor, but did not expect THC to mimic the clearance of intracellular amyloid as well as it did,” says Schubert. “We know that intraneuronal amyloid appears a long time before extracellular plaques in AD patients [...] so this suggests that they may be useful in treating early stage AD.”



Most of the work involved pharmacological studies with receptor agonists and antagonists to identify the molecular pathways. Oswald Quehenberger, collaborator at UCSD and second author, used high tech LC/MS-MS methods to identify pro and anti-inflammatory eicosanoids. Nanostring technology was used to identify changes in gene expression and Myriad RMB to measure cytokines.

Surprising as the results were, the team were more shocked by the positive reaction to the manuscript. “Unfortunately, because of the great restrictions on the efficient use of marijuana in the medical research field – because of its absurd classification as a Schedule I drug – there have been no significant clinical trials for marijuana or its component chemicals for AD. I think this is why we’ve had such enormous interest.”

Schubert says there is a need to take the

research further. “A simple experiment would be to identify the chemicals that are different between good and bad strains, synthesize or purchase them, run them through our cell culture assays for neurodegeneration and AD, and test the best in animal models of AD,” Schubert says. But, he says, even conducting such straightforward scientific research is difficult in the current climate. “Work like this is tough to do because of the regulatory requirements surrounding marijuana and the difficulty in obtaining the necessary funding. It is very curious that I can easily and legally buy medical marijuana, but cannot have a single leaf legally in the lab without an enormous amount of time and paperwork!” *JC*

Reference

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The Times They Are A-changin'

The Marijuana Policy Project is pushing for reform in cannabis legislation. Morgan Fox tells us more.

Why was there a need to establish the Marijuana Policy Project?

The MPP was established to build support, work on advocacy and communications, and fund various initiatives around marijuana laws. The harms caused by marijuana prohibition were clear to many people and mounting daily, but there were no really serious organizations lobbying to change these policies. It was time for a change.

What are the biggest legal hurdles for the medical marijuana industry?

Federal prohibition is the biggest hurdle. Despite medical cannabis being legal at the state level and the current federal policy to not target them, producers and providers can still be prosecuted under federal law, leaving them in a very unstable position. As federally illegal businesses, they cannot claim tax deductions under the 280e tax provision, and they are frequently denied access to banking and credit card systems.

How about scientific research?

Until recently, the federal government limited research in such a way that only studies looking for negative effects were approved – but that is beginning to change. We are only just scratching the surface of knowledge about the endocannabinoid system. Any and all research would help us understand more about cannabis and its potential uses.

How difficult is it for patients to enroll in medical cannabis programs?



Despite doctors being legally allowed to recommend marijuana under the First Amendment, many are unwilling to do so for a variety of reasons, including lack of education on marijuana's efficacy or the fact that it has not been approved by the FDA.

Any particular successes?

We – along with other groups – have helped make some big changes. In June this year, Ohio became the 25th state to adopt a workable medical marijuana law. The legislation was a direct response to a MPP-funded initiative and sought to qualify for the November 2016 ballot. Eventually, seriously ill patients will be able to purchase and use medical cannabis cultivated and processed in-state – without

being treated like criminals. They are not expected to for over a year, but at least they have an affirmative defense until the regulations and roll-out are complete.

What are the MPP's next steps?

We are currently involved in ballot initiative campaigns to make marijuana legal for adults and regulated like alcohol in Arizona, California, Maine, Massachusetts, and Nevada, as well as medical marijuana campaigns in Arkansas, Florida, and North Dakota. We continue to lobby Congress and state legislatures as well. In 1995, it was illegal in every state. Now, 25 have comprehensive medical marijuana laws. We need to keep going.

More information: www.mpp.org

Meet PotBot...

...your “virtual budtender”

There are several hundred strains of medicinal cannabis on the market, and with legislative barriers and misinformation, people hoping to use it to treat medical conditions could be forgiven for feeling overwhelmed. So how to choose if you choose to use? Meet PotBot.

What?

PotBot is a search engine designed to guide patients to choose the right medicinal cannabis for them. They simply input their symptoms and receive a personalized recommendation as to strain, consumption method and quantity of medical marijuana – as well as details of the nearest clinic or dispensary.

Why?

It seeks to help potential users of medicinal cannabis make informed choices between the all the strains and consumption methods on the market – as well as helping them gain physical access to supplies or practitioners.

How?

PotBot’s database has been developed using continually updated medicinal cannabis research (1) and crowdsourced reviews. They also use muscle spasm sensors and EKG devices to analyze and validate cannabinoid-based therapies.

Who?

The company behind the app is PotBotics, a technology and software design company whose aim is to “elevate the medical industry to higher medical standards by streamlining the consumer cannabis process.” They have also developed Brainbot – a wireless electroencephalography

The screenshot shows the PotBot app's onboarding process. It consists of three steps: 1. 'TELL ME ABOUT YOURSELF' with a circular gauge for 'YOUR AGE' set to 39 and a slider for 'ESTIMATED CANNABIS USE' set to 'Never' (with the note 'I have never medicated with cannabis'). 2. 'PLEASE SELECT YOUR CONDITION' with a gender selection button showing 'F' (Female) and 'M' (Male). 3. 'CREATE PROFILE' with a circular gauge for 'YOUR WEIGHT (lbs)' set to 165 and a location dropdown menu currently showing 'Oregon'.



helmet that allows GPs to analyze patients’ neural responses to cannabinoids – and NanoPot, a DNA reader that claims to help cannabis cultivators improve their growth programs.

Where?

Accessible via most electronic devices via mobile and desktop apps, patients can

access this service anywhere. There are also dedicated instore kiosks in various states throughout the US. *JC*

Visit www.potbot.com or visit Apple’s App Store.

Reference

1. <http://www.potbotics.com/#section-4>



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Atomic Spectroscopy: PerkinElmer's Atomic Spectroscopy portfolio (AA, ICP-OES, ICP-MS) is the ideal choice for meeting cannabis trace metal needs, with the ability to analyze most of the elements in the periodic table and a wide dynamic range, spanning part-per-trillion to part-per-million levels. This range means that trace contaminants as well as nutritionally significant elements can be measured during the same analysis.



In My View

In this opinion section, experts from across the world share a single strongly-held view or key idea.

Submissions are welcome. Articles should be short, focused, personal and passionate, and may deal with any aspect of cannabis science.

They can be up to 700 words in length and written in the first person.

Contact the editors at edit@texerepublishing.com

The Importance of Building Bridges

Pulling the medical cannabis and analytical science communities together has been challenging – but oh-so rewarding. Now, with a conference dedicated to the cause and colleagues who have become friends, I believe we can achieve great things.



By Joshua Crossney, President & Founder, jCanna, Inc. & Cannabis Science Conference, with Sophie Ryan (SavingSophie.org).

As I reflect on the past year, it truly amazes me to see what we have achieved in the run up to the inaugural Cannabis Science Conference. When I set out to create jCanna and start the Cannabis Science Conference, my primary goal was bridging the gap between the analytical science industry and the cannabis community. Our intention is that our organization and conferences will help to advance cannabis science and research. The road has not always been easy, and now, looking at the over 60 sponsors and exhibitors, it gives me great pleasure to see such well-respected companies supporting us at our first conference. During my campaigning, I've recognized that these sponsors and exhibitors are also pioneers of this exciting and emerging industry – and the reason that the Cannabis Science Conference will be a great success!

Looking back, I never imagined the show would grow so quickly. In addition to fantastic commercial support, we are proud to feature over 30 expert presenters from the fields of analytical science, medical cannabis, cultivation, lab operation, and more. Moreover, we've achieved global reach, hosting attendees from all around the world, including guests from Israel, Italy, Germany, Canada, Colombia, Puerto Rico, Australia, and Nigeria.

Over the last year, I have had the pleasure to work with some incredibly talented and passionate people, many of whom I can now count as true friends. One of these amazing people is Tracy Ryan, CEO & Founder of CannaKids & Saving Sophie and the Cannabis Science Conference's first plenary speaker. Her story and personal connection to this industry is truly inspiring (see page 26 for a full interview). Sophie – Tracy and Josh Ryan's daughter – was diagnosed with brain cancer at only 8.5 months old. Throughout this roller-coaster journey,

“Moreover we have achieved global reach, hosting attendees from all around the world, including Israel, Italy, Germany, Canada, Colombia, Puerto Rico, Australia and Nigeria.”

Tracy learned that cannabis, as medicine, might be able to help her daughter. Once Sophie beat every obstacle that doctors put in front of her and the Ryans saw a tumor shrink despite the fact it “wasn’t supposed to shrink”, Tracy knew that she had to share the story far and wide. This goal led Tracy to found CannaKids & Saving Sophie. Wonderful people like Sophie, Tracy and Josh Ryan drive me to continue my work.

My organization, jCanna, is highly focused on education, helping pediatric cannabis patients, and addressing (and changing) the stigmas associated with children and medical cannabis use. Our passion for education extends to raising the profile of research into the human endocannabinoid system and the history of medical cannabis. In particular, we are concerned that many doctors are still not learning about such topics in their medical training. Uma

Dhanabalan, a medical doctor based in Natick, Massachusetts, and one of the presenters in our medical cannabis session, has a great philosophy when it comes to allowing people to take control of their own healthcare: “Educating! Embracing! Empowering!” Michele Ross, Founder of IMPACT Network, is also presenting in our medical cannabis session. A great educator on medical cannabis and its benefits, Ross is both a cannabinoid medicine researcher and a cannabis patient.

In the run up to the conference, I’ve been involved in many exciting projects that have helped pave the way – from writing articles for 1,000 Watts magazine and Medical Jane to hosting The Medical Cannabis Report. I’m pleased to say that I have also been given the opportunity to organize a full day Analytical Cannabis Symposium at Pittcon 2017, March 5-9 in Chicago.

It has been a great journey so far; I am even more excited to see what the future holds for jCanna, the Cannabis Science Conference – and the industry as a whole.

Finally, I would like to offer my sincere thanks to all of our expert presenters, sponsors and exhibitors, media partners and volunteers for helping to make the Cannabis Science Conference a reality. With the conference only weeks away, I am confident that we are accomplishing my original goal: bringing the analytical sciences and the cannabis industry together for the greater good.

For more information on our non-profit, jCanna, please join us at www.jCanna.com and to learn more about our annual Cannabis Science Conference, please visit www.CannabisScienceConference.com. We would love to see you at one of our upcoming events!

Smoke and Mirrors – and Red Tape

Knowledge lags behind practice on medical marijuana. Cutting back on excessive bureaucracy for researchers is likely to help us all catch up.



By Charlotte Barker, Editor of The Translational Scientist, Knutsford, UK.

In August 2016, the US Drug Enforcement Agency (DEA) lifted rules that restricted scientists to a single, government-run source of marijuana for medical research. For the past four decades, all cannabis for research in the US has come from a tightly controlled growing facility at the University of Mississippi. With medical marijuana legalized in 25 US states, the DEA accepts that an expanded supply and greater variety of marijuana for research is needed.

However, cannabis remains a Schedule I substance in the US, and researchers wishing to study the drug have a number of regulatory hoops to jump through, as well as tight controls on storage and handling. The knock-on effect is that funders and review boards are very wary of research involving marijuana, creating a somewhat contradictory situation – patients can access marijuana in many states, while medical researchers wishing

to carry out clinical trials cannot. The drug remains Schedule I in part because there is a lack of evidence to justify medical use, but classification makes it an uphill slog for researchers to generate such evidence – classic catch-22. New pharmaceuticals can only be prescribed after extensive clinical trials have proven them to be safe and effective, but marijuana researchers are often restricted to small, open-label studies by funding and approval issues.

Despite the hurdles, there is evidence to suggest that cannabis and its active ingredients are effective in a number of therapeutic areas. The two FDA-approved cannabinoid drugs (Marinol and Syndros) are man-made versions of one of the main psychoactive ingredients of marijuana – tetrahydrocannabinol (THC) – and primarily used to stimulate appetite in AIDs or cancer patients (1, 2). Sativex, approved in Canada, New Zealand and several European countries to treat

multiple-sclerosis-related spasticity, is directly derived from the cannabis plant, and contains mainly THC and non-psychoactive cannabidiol (CBD) (3). The addition of CBD is thought to mitigate the “high” and other side effects of THC, as well as enhancing efficacy of the drug. CBD is also showing promise in some hard-to-treat epilepsies (4).

However, by far the most common reason patients request a medical marijuana prescription is pain relief. And new painkillers are desperately needed for chronic pain; with more than 650,000 prescriptions for opioids dispensed daily in the US alone – and nonmedical use exploding – an ever-increasing number of people are becoming addicted, with tragic results. Seventy-nine Americans die every day as a result of opioid overdose (5), and opioid abuse is a problem worldwide. Like cannabinoids, opioids are derived from a plant, and have a long history of medical and recreational use.

Cannabis is not a replacement for opioids, which have unbeatable efficacy for acute pain and many types of cancer pain, but it is thought to be effective mainly for neuropathic pain, which is notoriously hard to control with existing therapies. Any therapy that can cut opioid prescriptions merits serious consideration, particularly one with a solid safety profile; the chances

of dying from a marijuana overdose are vanishingly small. A JAMA meta-analysis concluded that there was moderate evidence to support the use of medical marijuana to treat pain (6), while pain patients receiving medical marijuana have reported that they were able to reduce or stop opioid painkillers (7). Researchers want to find out whether better pain control could account for the finding that states legalizing medical use of marijuana had an average of 25 percent fewer deaths from opioid overdose (8). However, that research is being held back by the polarized nature of the debate.

Though some of those in favor of legalization like to present the drug as a 100-percent-safe ‘cure all,’ cannabis – as with all drugs – is not without side effects (9, 10), which makes it all the more important that unbiased, controlled studies are conducted. Only rigorous research can clarify the benefit and harm of medical marijuana – and allow doctors, patients and governments to make informed decisions.

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Modernizing the Cannabis Industry

Genomics tools have the potential to transform Cannabis cultivation – but collaboration between science and industry is essential for success.



By Daniela Vergara, Postdoctoral Researcher, University of Colorado Boulder, Founder and President, Agricultural Genomics Foundation and Co-founder Cannabis Genomic Research Initiative; and Reggie Gaudino, VP of Scientific Operations, Director

of Genetics, Director of Intellectual Property, Steep Hill Labs Inc.

Genomics has become increasingly important in multiple areas of biology. By understanding the genome – the whole collection of genes from an organism – instead of focusing on isolated genes, we can reach stronger conclusions about the location of particular genes within the genome, the importance of interactions between genes, the evolution of genes, and the potential for particular gene

combinations in organisms. Perhaps most importantly, genomic studies allow genes to be associated with physical characteristics – a powerful way to improve breeding and to develop crops with combinations of desired traits.

Genomic tools (for example, genetic maps) have been developed to improve breeding for multiple crops, such as corn, rice, soy, and wheat. However, for the genus *Cannabis* (despite its long history with humans, and the fact that it is the most widely used recreational drug in the world), such tools are in their relative infancy.

Right now, we have the technology to improve *Cannabis* cultivation and progress is being made despite a stringent legal environment. As with many areas of science, innovation is not always immediate and requires some patience; we hope that the cannabis industry can begin to fully support scientific investigations and understand that we are all working towards the same goal.

It is fair to say that there is some reluctance to accept (and disseminate) new genomic information on *Cannabis*. After all, the cannabis industry is an old one, with some individual breeders and growers having worked on *Cannabis* cultivation for decades. Some view scientists as outsiders who want to harm the plant that they have protected and nurtured through so many hard years of governmental and social disapproval. But the reality is that, over time, distortion and misinterpretations of the plant's biology have contributed to a pseudoscience of cannabis that may be hard to break – and it's compounded by a lack of access to (or understanding of) peer-reviewed scientific information. The upshot is that some scientists may feel hesitant to share new evidence that appears to be contradictory to current thinking – which is actually not a unique problem to cannabis science! For example, recent genomic studies have shown that the 'indica' and 'sativa' groupings might not be factual. There are also examples of people

grouping non-related varieties as 'sativa' or 'indica' or giving two unrelated cultivars the same name. Whether or not the industry recognizes this evidence at some point in the future remains to be seen...

“Right now, we have the technology to improve Cannabis cultivation – and progress is being made despite a stringent legal environment.”

Fortunately, despite some hesitancy from both the scientific and industry sides, some important cooperative relationships between cannabis scientists have been established between museums, advocacy groups, botanical gardens, and even some dispensaries, breeders and growers. Such collaborators are brought together by evidence that genetic tools produce precise, direct, fast and economic results for *Cannabis* breeding, allowing the community to move away from a sole reliance on good fortune and physical plant characteristics.

It goes without saying that scientific research, especially genomic investigation, is time consuming and requires intensive labor and expertise from specialists. In other words, it's expensive. But with just a little economic support from both the private

and public sectors, interesting and useful results are already being produced. Indeed, the projects proposed by current cannabis research groups have direct significance for industry, medicine and agriculture. A better understanding of the genetic differences between the various varieties will be crucial for breeders, making the process of crossing divergent lineages more efficient and predictable. The genomic tools will also be important for hemp production, as large-scale agricultural production is only permitted for reliably low- or zero-THC plants. Conversely, medical applications, for which it is vital that plants produce highly consistent levels of biologically-active compounds, will also benefit from more accurate information.

As an important side note, we think it's important that scientific findings are made publically available, where possible. If cannabis scientists are encouraged to publish genomic (and other) studies, we can prevent important data disappearing into the vaults of just a few corporations who wish to dominate the industry (and who likely recognize that good science can drive down costs by boosting efficiency). Open information also allows the general public to make more informed decisions. Supporting scientists who want to make their results available to a non-scientific public will go along way to ensuring ongoing and strong collaborations between the scientific community and the cannabis industry.

In conclusion, we believe that genomics will revolutionize *Cannabis* breeding. How fast? Well, that will depend on how well we all work together.

Disclaimer

The views and opinions expressed in this article are those of the authors with their own experiences, and do not necessarily reflect the position of any company or institution.

Acknowledgements

We would like to thank Alisha Holloway for her useful comments and suggestions.



THREE GURUS OF CANNABIS ANALYSIS

What's holding the medical cannabis industry back? How can we keep it on the straight and narrow? And – most importantly – how can we ensure that consumers have access to high-quality, contaminant free products? Here, we ask three speakers from the 2016 Cannabis Science Conference – Scott Kuzdzal (Shimadzu Scientific Instruments), Julie Kowalski (Restek), and Sytze Elzinga (The Werc Shop) – to discuss how the worlds of analytical science and medical cannabis are colliding for the greater good.

Medical cannabis is an exploding market – what is your reaction to this phenomenon?

SK: I credit several groups of people, the true 'gurus' of the cannabis testing market, with the recent explosion in cannabis analytical testing. Firstly, there is an amazing group of pioneering cannabis testing lab directors that have embraced this market head-on, despite an unclear and ever-changing regulatory and legal landscape. Secondly, Shimadzu sales people, technical support specialists and applications scientists eagerly supported these laboratory visionaries by helping to develop more reliable and accurate methods for cannabis quality control testing.

About four years ago we saw a spike in instrument sales due to this new market, and Shimadzu staff began applying their vast experience in more established markets like environmental,

food safety, clinical research and pharmaceuticals to help improve cannabis testing methods. At this time, only a handful of companies like Shimadzu, Fritsch Milling, SPEX SamplePrep, Restek, Golden West Biologicals and Advion stepped forward in support of improving instrumentation and testing methods to improve the safety of cannabis products. These products must be accurately labeled in terms of cannabinoid concentration, but they must also be free from contaminants such as pesticides, metals and solvents. It is this increased need for quality, safety and accurate labeling that drives our participation in the cannabis market.

Whether you are pro- or anti-cannabis, it is a complex plant that contains over 500 compounds that simply cannot be found anywhere else in nature. We must ensure safety to consumers, but we must also broaden our knowledge base regarding cannabis medicine and science.

JK: It is an exciting time for medical cannabis and cannabis in general. Ultimately for the benefit of everyone, cannabis – like other natural products – should be investigated for medicinal benefits. I am looking forward to seeing what we can learn as different scientific disciplines take on cannabis. We have gained invaluable experience already by collaborating with labs, institutions and conferences, and we hope to continue helping chemists and being part of the cannabis testing community.

SE: I think that broader access to information has played an enormous role in the legalization of medical cannabis. People don't just have to believe what they are told anymore, but can now directly look up facts online and form their own opinion on the topic. Many of the legalization actions have included mechanisms for further informing the public, driving the research needed. The comparison of risks between alcohol and cannabis use has been especially effective at opening minds.

The fact that cannabis is still federally illegal is both a blessing and curse. It is very challenging not having access to banking or better research understanding, but on the other side it has kept big monopolistic players out and prevented consolidation, where a few giant corporations control the industry. It is great to see so many small companies be successful and grow organically. Our efforts at The Werc Shop aim to help scientific backend cannabis entrepreneurs deliver top quality products to the market.

What are your opinions on the scientific value of cannabis?

JK: Progress in the scientific understanding of the medicinal properties of cannabis has been slow, primarily due to legal issues. Although there are peer-reviewed articles investigating various aspects of the medical use of cannabis, there is much work to be done. Understanding the relationship between natural products and the human biology – as well as disease states – is highly complex. I anticipate exponential growth of such research.

SK: Interestingly, medical cannabis dates back thousands of years. The Chinese term for “anesthesia” (麻醉) means “cannabis intoxication.” Ancient Greeks used cannabis to treat the wounds of their horses. Prior to 1937, cannabis was available for medical use in the US from hundreds of manufacturers as both dry product and tinctures.

There is an interesting campaign circulating social media where people supporting the cannabis industry are writing “#6630507” on their hands in a “talk to the 6630507 hand” campaign. US Patent #6630507, assigned to the United States of America as represented by the Department Of Health And Human Services in 2003, states:

“Cannabinoids have been found to have antioxidant properties, unrelated to NMDA receptor antagonism. This new-found property makes cannabinoids useful in the treatment and prophylaxis of wide variety of oxidation-associated diseases, such as ischemic, age-related, inflammatory and autoimmune diseases. The cannabinoids are found to have particular application as neuroprotectants, for example in limiting neurological damage following ischemic insults, such as stroke and trauma, or in the treatment of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and HIV dementia. Non-psychoactive cannabinoids, such as cannabidiol, are particularly advantageous to use because they avoid toxicity that is encountered with psychoactive cannabinoids at high doses useful in the method of the present invention.”

For an informative view of medical professionals on this topic, see the clinical decisions article “Medical Use of Marijuana” in the New England Journal of Medicine as well as the corresponding posts/comments (1). Contributor J Michael Bostwick states, “A largely anecdotal but growing literature supports its efficacy, particularly for pain or nausea that is unresponsive to mainstream treatments,” referencing “Medical marijuana: clearing away the smoke” (2).

While cannabis research has been suppressed in the US, other countries, including Israel, are investigating the medical benefits of cannabis. I do not know whether cannabis is a “wonder drug” or not, but it is certainly a natural product that contains antioxidants and neuroprotectants – and it deserves further research.

It is interesting to note that Marinol, an FDA approved drug, is actually synthesized THC. So it is confusing that the natural form is a Class I Schedule Drug with “no medicinal use”...

SE: I always like to point out that synthetic THC (generically named dronabinol) is a DEA Schedule III narcotic and has been an FDA-approved medicine in the US since the 1980s. So even the federal government acknowledges the medicinal properties of THC. It gets a little weird, however, when you look at cannabis, which is basically a diluted form of the exact same compound but is considered a Schedule I narcotic, which means it has no accepted medical use and high potential for addiction. From this it appears like the question is not so much about a single compound but perhaps more about concerns regarding the delivery method as opposed to the compounds in the plant. There is no other pharmaceutical compound that is delivered through smoking, and I think this is what has mainly held back the development of cannabis as a medicine. It is interesting to point out that whole plant cannabis as a medicine has been shown to be preferred by patients over single molecule pharmaceutical THC products (3).

The Three Gurus



Scott Kuzdzal

Scott received his PhD in analytical chemistry from the University of California at Riverside, and served as a postdoctoral fellow at the Johns Hopkins University School of Medicine, where he co-founded and directed the Johns Hopkins Center for Biomarker Discovery. Scott has a strong clinical chemistry background and has directed toxicology and therapeutic drug monitoring labs. He has co-authored several proteomics book chapters and has multiple patents. Scott currently serves as General Manager of Marketing for Shimadzu Scientific Instruments, where he continues to innovate, commercialize and market exciting new award-winning analytical platforms. Currently serving on the AOCS Cannabis Experts Panel, the Clinical Proteomics Editorial Board, and the Cannabis Science Conference's Scientific Advisory Panel, Scott also hosts the Shimadzu GrowYourLab.com microsite.



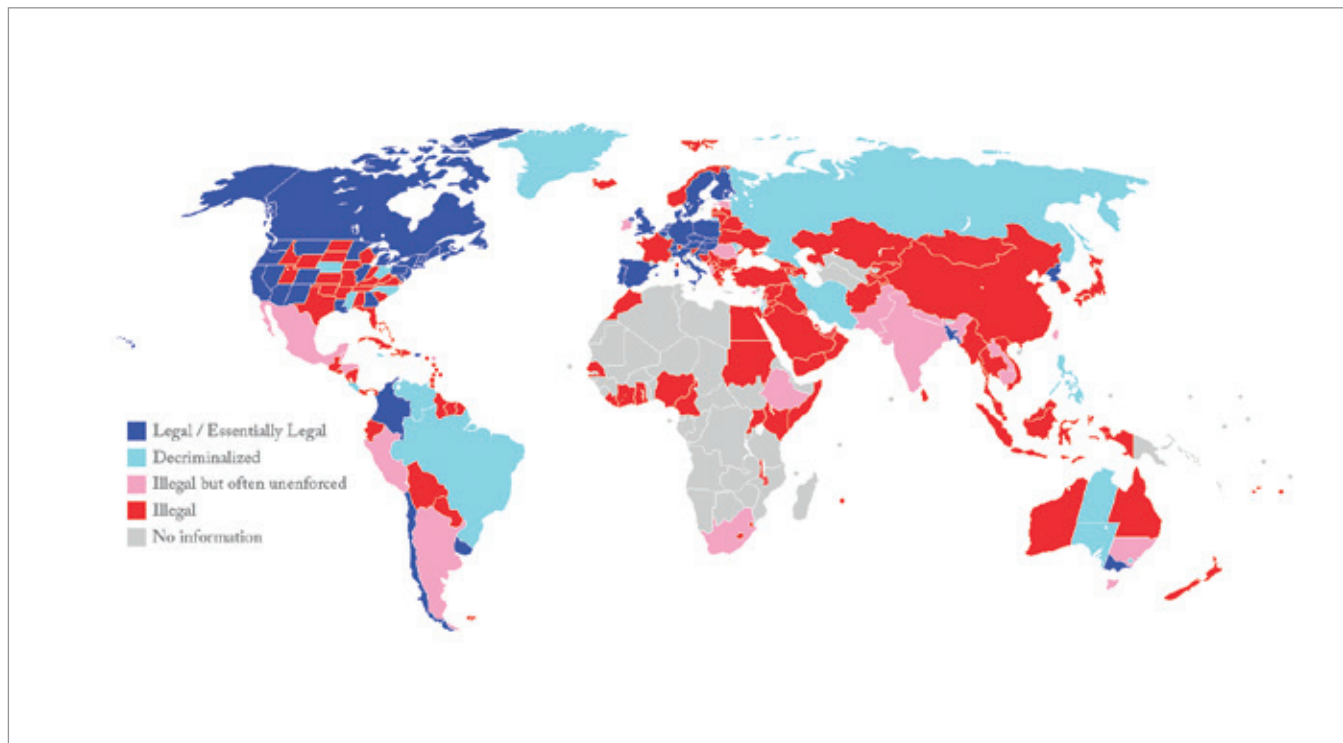
Julie Kowalski

Julie is a Senior Chemist who has been with Restek for eleven years. She has a BS in Chemistry, a PhD in Analytical Chemistry, and professional experience that includes troubleshooting and method development for GC, GC-MS, GCxGC, LC, and LC-MS/MS. Julie has served as the President of the North American Chemical Residue Workshop and serves on two AOAC Expert Review Panels. Her primary work for Restek is in food safety applications, especially pesticide residue analysis, QuEChERS and chromatography method development.



Sytze Elzinga

Before Sytze moved to the United States he worked at Farmalyse, a pharmaceutical contract laboratory that performs quality control and release of pharmaceutical products for the European market. At Farmalyse, he was responsible for the quality control of federally licensed medicinal cannabis. Research at Farmalyse was conducted on the extraction and purification of THC from medicinal cannabis – efforts that led to a spin-off company: Echo Pharmaceuticals. At Echo, Sytze produced THC under good manufacturing practices (GMP). A formulation that enhanced the bioavailability of THC was developed and, under supervision of the Dutch equivalent of the FDA, clinical trials were started. Sytze has been part of The Werc Shop team since 2011 where he oversees the development and validation of analytical methods and helps guide various R&D projects. As Chief Science Officer, he has been key to developing the intellectual property portfolio of The Werc Shop and has created customized product lines for various clients. He is the lead author of multiple papers published in scientific literature by The Werc Shop team regarding cannabis.



Courtesy of Trinitresque [CC BY-SA 3.0], via Wikimedia Commons.

Legal status of cannabis for medical use. (Accuracy not guaranteed; only for visual reference).

Could you describe the current regulatory landscape and its impact?

SE: As in any market, there are good players and bad players – and, as usual, it is more expensive to do it the ‘right’ way. From a business perspective, it is challenging to consider spending money on quality control if your competitor doesn’t need to do the same or simply isn’t doing it. While testing is required to protect your brand and make sure it is consistent, most are willing to cut this corner. And that’s why we need mandatory quality control laws and regulations. It levels the playing field and makes sure everyone puts quality first. There is no doubt that the FDA will be all over this industry once it becomes re- or de-scheduled at a federal level, so we’re doing everything we can to get ready for it.

JK: If cannabis is to be marketed and regulated as a medicine, it is critical that the highest standards of safety be applied. I anticipate stricter regulations will develop in the future, which will result in a safer product – especially important for those suffering from illness. A rapidly expanding recreational market will draw investment from private industry, requiring more government resources and less focus on medical cannabis.

Consumer education will be required since less expensive recreational products may be purchased by patients instead of prescribed cannabis. For vendors, the industry is complicated by the fact that each state has a different set of testing requirements – and these requirements are rapidly changing.

SK: State laws and regulations, as well as qualifying conditions for medical cannabis patients, are extremely diverse. Cannabis is still illegal on a federal level, which complicates matters further.

What is the role of analytical science in the current world of medical cannabis – and how can analytical scientists help?

SK: Analytical scientists play a key role in ensuring that safe cannabis products are hitting the shelves. Some people argue that this is a plant, and so testing is not needed. But there are many forms of cannabis products – from “dry product” (or flower) to oils, topicals and edibles. Processing of cannabis material, and techniques like extractions, require analytical testing to ensure accurate labeling, as well as to detect contaminants.

Analytical scientists and engineers also play an important role in improving cannabis testing (and research) platforms. We need analyzers that are simple to operate, yet deliver accuracy and reliability. At the 2016 Cannabis Science Conference, we are previewing the Shimadzu Cannabis Analyzer for Potency Analysis,, which is a touchscreen analyzer (with all consumables required) that greatly simplifies and streamlines potency testing. This new platform was developed by brilliant engineers in the Shimadzu Scientific Instruments Innovation Center in Columbia, MD.

Quality control is paramount in many established markets, and we can and should apply quality control/assurance requirements and systems, proficiency testing, as well as good manufacturing processes to cannabis testing. Even in states like Washington that have established testing requirements, labs like Trace Analytics (Spokane, Washington) have gone above and beyond these requirements to develop additional quality standards and expanded testing panels, including pesticides.

JK: Many scientific disciplines will be needed to bring medical cannabis analysis to maturity – and analytical science will be critical to ensure effective and safe products. If we simply consider cannabis as a natural product, we can borrow methodologies used to test other natural products. The pharmaceutical industry is aware of the benefits of natural products and understands how to identify the biologically active components. Dietary supplements and food testing deals with matrices akin to cannabis on a regular basis, including everything from determination of active components, to authenticity and contaminants testing.

SE: Many states now have mandatory quality control requirements. Most often the level of various cannabinoids needs to be on the product label and various states have introduced requirements regarding microbiological and pesticide contamination. Natural products, like cannabis, are an exciting and challenging field for analytical chemistry. The average plant contains hundreds if not thousands of compounds that can interfere with your analysis. The challenges are similar to trace analysis in food – and many of the techniques can be converted over to be used for cannabis.

How serious is the threat of low quality/counterfeit/falsified medical-grade cannabis?

JK: Any unsafe product that is ingested has the potential to be incredibly dangerous. There are incidences of counterfeit pharmaceuticals as well as food safety issues that have sometimes resulted in death. These incidences should be used as cautionary tales to secure the resources needed to ensure safe medical cannabis products. The use of melamine in foods is just one example.

SE: The short term effects are apparently fairly minimal, as we do not see medicinal or recreation users with serious side effects. However, we do know that a large part of the current supply has pesticides and/or microbiological contamination. It is however the long-term side effects that concern me. After many years of cannabis prohibition, we finally get the right to use this plant. If, in 20 years, cannabis users are shown to have a higher frequency of cancer or other illnesses, I for one would like to know that this is caused by the cannabis and not by the residual pesticides or other toxins that are in the product. Let's make sure we provide a clean product, so we can keep this plant legal for future generations.

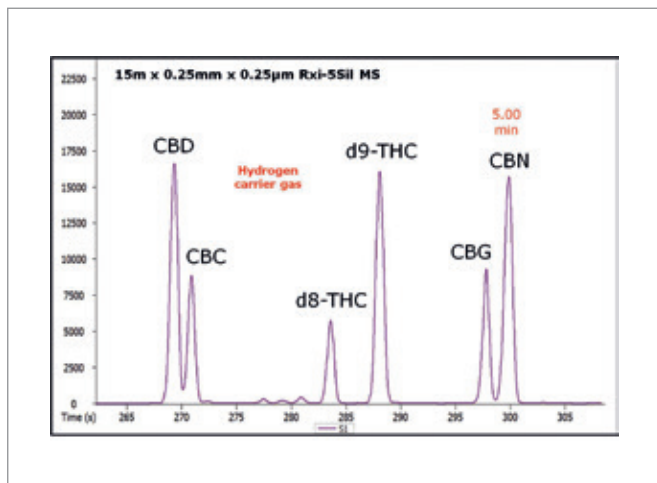
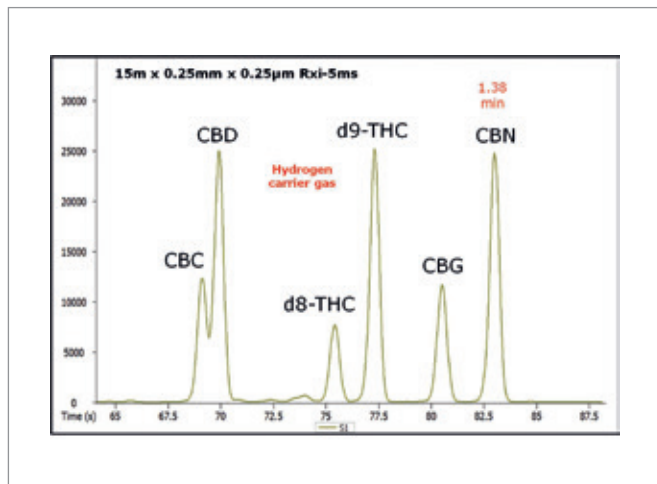
SK: Since there is no universal definition of “medical grade cannabis,” the actual quality can vary from state to state. What I see in the market now is not so much falsification or intentional deceit, but more unintentional misinformation and confusing marketing strategies regarding strain nomenclature and products. For example, the term “Charlotte’s Web” refers to a Cannabis sativa L. strain with less than 0.3 percent THC that has been widely publicized and touted as a natural therapy for treating epileptic seizures (4).

The term – “Charlotte’s Web” – however, has been widely used in the industry, including with cannabis strains that contain much higher levels of THC. Even more confusing here is that the American Academy of Neurology has published reports stating that there is no compelling data to make any conclusions regarding the safety and efficacy of cannabinoids in the treatment of epilepsy. Consumers must make their own judgments regarding the potential benefits of various strains amid many non-FDA approved claims.

One positive note here is that the cannabis community is sharing information on cannabis benefits and experiences in dispensaries, cooperatives, social media and several information-rich websites. In many ways, the community is growing and maturing because of this information sharing. Medical professionals are also learning on the fly, as details regarding the endocannabinoid system are simply not taught in medical schools.

Are medical cannabis producers taking the threat seriously enough?

SE: It depends on the producer. Some producers take their role as medicinal providers very seriously, and would never use pesticides, for example. Others are purely driven by profit – and the costs of preventative pesticide spraying are relatively small compared to the cost of a failed harvest...



Restek's Jack Cochran illustrates the impact of selectivity and GC oven programming on elution order of CBC and CBD. And notes that Rxi-35Sil MS columns perform better anyway... For the full blog and more: blog.restek.com/?p=8759

SK: As with any market, brand reputation and perception is very important. The cannabis cultivators I am aware of take great pride in their work, and also take analytical testing and accurate product labeling very seriously.

JK: I haven't had much contact with medical cannabis producers, as I live in Pennsylvania and primarily deal with labs. I am glad to see patient advocacy groups taking an active role in the cannabis industry. Consumer pressure is powerful and holding producers accountable for a safe product will shape the best behaviors. Regulation and rigorous testing will also keep producers honest, as it does in many industries.

How can high quality analytical science safeguard consumers and boost the profile of suppliers?

SK: High quality analytical testing ensures accurate dosing of cannabinoids and prevents exposure to toxic contaminants. Though analytical testing is important in both recreational and medical cannabis markets, the potential presence of pesticides, microorganisms, metals, mycotoxins, aflatoxins or solvents is especially dangerous to medical patients with compromised immune systems. Contaminants, such as metals, are known to rapidly deplete the immune system, and even induce auto-immune diseases. Mold can cause respiratory problems and flu-like symptoms, such as coughing, vomiting and diarrhea – symptoms that are exacerbated in medical patients with other health conditions or compromised immune systems. Good analytical testing is paramount in identifying such contamination and preventing these products from reaching consumers.

JK: Certainly, testing has to be of good quality and frequent, especially while the market is still young. There are expenses associated with proper testing, and suppliers need to understand the true benefits of testing. In addition to avoiding actual violations, testing can prevent negative publicity by identifying noncompliant products before reaching consumers. It is hard to recover from a recall or scandal. On the flip side, suppliers can market compliance to testing standards as a benefit to consumers.

SE: It is an integrated part of any other industry so why should it be different for cannabis? Numerous stories of companies in the food industry skimping on quality control can be found – and the consequences can be devastating, not only for the consumer but also for the company. A great example is the peanut butter CEO who is facing life in prison for releasing contaminated products on the market.

It is also interesting to note that cannabis QC labs were the first to find pesticides in plant treatment products that claimed to be pesticide free (6) – another example of how analytical science can contribute to a better product for the consumers.

What are the analytical challenges associated with (medical) cannabis?

JK: I would say there are some challenges with simply physically handling cannabis because of its 'sticky' nature; it requires care and experimentation. Dry commodities like typical cannabis plant material are more challenging for trace level contaminant analysis, such as pesticide residue testing. The high percent level

of THC and other cannabinoids that have been bred into the plant makes sample preparation even more challenging. Sample preparation is critical to obtaining quality data because cannabis is complex and has a high potential of matrix interferences. The variety of cannabis-based products – for example, edibles and concentrates – requires that methods must be adjusted or developed. In addition, as Sytze notes, the changing regulations and requirements are also a challenge for testing labs. Unlike the more mature food and pharmaceutical markets, the cannabis market has yet to “standardize” regulations, requirements and acceptable testing practices.

SK: There are many unique challenges associated with medical cannabis testing for analytical solution providers. If you attend one of the larger marijuana business conferences, you are quickly amazed at the incredible variety of cannabis products on the market – from THC-infused chocolate bars to beverages and foot creams. These various sample forms require different sample preparation techniques and can create inter-laboratory variability. The only advice that I can provide here is to work with proven sample preparation technologies like Fritsch milling and sizing instruments, SPEX SamplePrep homogenizers and cryomills, and Restek chromatography columns. These companies have vast experience in food safety and environmental samples.

Shimadzu Scientific Instruments is headquartered in Columbia, MD, where we have our Customer Training and Education Center, a state-of-the-art Solutions Center and our new Innovation Center. But because of federal and state laws, we cannot have cannabis samples onsite, so we can only work on new methods and platforms in our customer labs. Since 1970, marijuana has been designated a Schedule I drug under the Controlled Substances Act, making it nearly impossible for academic labs to perform cannabis research. We simply do not have such restrictions in most markets, and therefore we have added hurdles in terms of method development, training and new product improvements.

Lastly, in addition to a bevy of sample prep options, there exists a wide variety of ionization techniques, chromatographic separations and analyzers that can be applied to cannabis samples. Even within a specific product line, like triple quadrupole mass spectrometers, it is important to select instrument models with the appropriate performance criteria (sensitivity, speed, and so on). There is great benefit in working with an industry leader like Shimadzu, as we can help deliver the exact instrumentation needed for cannabis QC testing, with proven applications and exceptional technical and service support.

SE: Actually, my feeling is that cannabis is really not that different from other products from an analytical perspective. It is mainly

“Regulation and rigorous testing will keep producers honest, as it does in many industries.”

a regulatory challenge. Dealing with changing requirements and without a full understanding of what may be needed in the future makes staying on top of our evolving field a pretty unique challenge. Furthermore, no formally accepted and broad-based methods are available, which makes how exactly you approach a particular test type very competitive and subject to new research developments. Working with a federally illegal substance comes with its own challenges; some states now have very strict requirements regarding the tracking and tracing of every gram of material, which creates additional paperwork and handling requirements. It can make research and normal business operations quite cumbersome and complicated...

What analytical tools are required and how should they be used?

JK: Potency: LC-UV currently works well for labeling requirements. If quantitation of many more cannabinoids becomes required for labeling, then better chromatographic separation or detector specificity will be needed.

Residual solvents: This is a GC analysis and can be done with FID or MS detection. Many of the residual solvents need to be tested using headspace sample introduction. There are some solvents that are not volatile enough to work by headspace and so an additional liquid injection analysis is sometimes needed. Mass spectrometry has the benefit of specificity, which adds confidence to compound identification, but it is somewhat limited in linear dynamic range. This makes the use of MS for residual solvents a bit tricky when the required limits among analytes varies by more than a few orders of magnitude. FID is linear over a wider concentration range but does not have the specificity that MS offers. The best choice depends on compounds and allowable limits.

Pesticide residue analysis of cannabis plant material is challenging and is best accomplished by using sensitive and selective detection like tandem MS (MS/MS). GC and LC MS/MS are the workhorse techniques used by the food safety industry with a move towards more sophisticated MS-based detection. In most cases, both GC and LC will be needed

because some pesticides are only reproducibly detected at low enough levels by one or the other, although many pesticides can be tested by both GC and LC.

Mycotoxins analysis is challenging right from sampling because fungal contamination can be localized in a field. Testing is challenging because of the low detection limits required, and affinity-based sample preparation with HPLC or LC-MS/MS is most often used. There are strip tests for mycotoxins, but these would have to be validated in cannabis matrices.

SE: The majority of the analyses that are performed are potency tests – usually with UHPLC. UHPLC is preferred over GC, as the cannabinoids are mainly present in their acidic form (THC = THCA, CBD = CBDA) in plant material. To distinguish the psychoactive neutral from their non-psychoactive acidic form, you need to use LC; the acidic cannabinoids convert to their neutral equivalent in GC.

Cannabis extracts (concentrates) are often analyzed for residual solvents. Headspace GC is typically used and detection is performed either with MS or FID.

Trace pesticide analysis requires high selectivity and MS/MS is typically used to counter the complex matrix. Sample preparation and cleanup is essential to minimize ion suppression.

There are various ways to test for microbiological contamination. PCR-based approaches are especially effective for proving absence of a specific organism like salmonella. Plating or rapid microbiological testing platforms are often used as well. Some states require colony forming unit counts and in those cases plating is almost unavoidable.

SK: I'll offer a more commercial answer! After all, Shimadzu has a comprehensive portfolio of solutions for cannabis testing:

- Potency/cannabinoids: Cannabis Analyzer (Integrated i-Series HPLC)
- Pesticides & Mycotoxins: LCMS-8050 Triple Quadrupole MS
- Terpene Profiling: GCMS-QP2020 (Gas Chromatograph MS)
- Metals: ICPMS-2030 (Inductively Coupled Plasma Mass Spectrometer)
- Residual Solvents: GC-2010 Plus with HS-20 (GC with headspace)
- Moisture Testing: MOC63U or MOC-120H Moisture Analyzer
- Integrated Supercritical Fluid Extraction–Chromatography Mass Spectrometry: Nexera UC, “Unified Chromatography”

What about the diagnostic angle, for law enforcement, for example?

SE: Employers and law enforcement would love a quick test to show if someone is under the influence of cannabis and impaired. The difficulty right now is that most methods were designed to test for the use of cannabis at any point in time. Such tests fail to show that the individual is high/impaired at the moment of the test because they usually measure a long-lived non-psychoactive metabolite (THC-COOH). This proves use, not impairment – two very different things. It also appears that the actual THC plasma level does not directly correlate to the experienced intoxication of the individual, and that users become tolerant to its effects. We need to make sure we have an objective way to judge intoxication – and currently that is lacking.

SK: I have been following many of these devices and technologies, but interestingly, the National Highway Traffic Safety Administration (NHTSA) report (DOT HS 812 117, published in February 2015) reported that analyses incorporating adjustments for age, gender, ethnicity, and alcohol concentration levels did not show a significant increase in levels of crash risk associated with the presence of THC. The report also stated that, “Understanding the effects of other drugs on driving is considerably more complicated than is the case for alcohol impairment.”

Additionally, several reports, including one by the Washington Post, claim that the number of highway fatalities in Colorado is down since the state legalized recreational marijuana in 2012 (“Since marijuana legalization, highway fatalities in Colorado are at near-historic lows” by Radley Balko, August 5, 2014). So much of the hysteria regarding drugged-driving concerns seems to be hype...

JK: I expect developments in this area as regulations and enforcement in the new legal landscape matures. As noted by Sytze, quick, cheap and accurate methods will need to distinguish between chronic use and immediate use, which is probably the most important challenge with respect to use at work or use while driving.

What are your views on ‘cannabinomics’?

SK: In brief, we need to screen beyond the 10-15 cannabinoids that are commonly tested for. To me, this is more research than QC testing. An interesting point here is that many of these cannabinoids are present at extremely low levels. Identifying and quantitating these more esoteric cannabinoids is fairly straightforward and a task that can be achieved using LC-

MS/MS. Such investigations will remain as research (and not QC testing) until manufacturers begin to both increase these cannabinoid concentrations (which involves more complex breeding and purification techniques) and better understand their medical benefits. Understanding synergistic effects between cannabinoids, terpenoids and flavonoids is an even greater challenge.

SE: Customized cannabis formulations with well-defined standardized chemical constituents are the future of cannabis. If different types of cannabis have different effects, some chemical compound or combination of chemical compounds must be responsible. Called the entourage effect, the variations are thought to largely be a result of interaction between terpenes and cannabinoids. In one of our recent papers, we have shown that strain names and even the sativa or indica designation often does not reflect what chemical constituents are present or being consumed (7). So if the chemical composition is

not consistent, how can you predict the effect of the strain? To solve this issue, we have designed a process that isolates the various major cannabinoids to high purity. We can then reintroduce specific strain properties by using our terpene-based formulation platform, allowing for standardization and careful control over product composition. Reproducible effects are critical for patients who need this medicine.

JK: As with any natural product, there is a complex web of interactions with human biology. Unraveling this web will take an enormous effort, including the need to identify activity at the molecular level – it would clearly benefit from an integrated “omics” approach. Large data sets will be needed to yield scientifically significant relationships between cannabis or active components and biological changes. And though the research needs to be extensive and time-consuming, the upside is that there are growing opportunities for researchers to work with cannabis.

Cannabis Milling & Grinding Solutions



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- Sample preparation for analysis- potency, pesticides, metals, residual solvents
- Separate & isolate stems, buds, leaves, and trichome material based on particle size
- Produce homogenous ingredients for pre packaged products
- Create uniform powder from cryo-frozen edibles



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The Cannabis
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and Pittcon 2017**

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**CONSISTENT, REPRODUCIBLE PERFORMANCE
HIGH THROUGHPUT, EASY TO CLEAN
COMMERCIAL INSTRUMENTS FOR PROFESSIONAL RESULTS**

Some analytical instrumentation vendors (and scientists) have stepped up to the challenge whereas others are holding back – why?

SK: This is a great question and one that has puzzled me. Many companies will NOT allow their logo anywhere near the words “cannabis” or “marijuana”. Instead they surreptitiously attend conferences or host symposia using the terms “hemp” and “natural products.” Some of these vendors have marching orders from the executive level, others feel like they may jeopardize existing government business. Shimadzu has embraced this market, as we see a clear need for quality control and consumer safety for the legal, medical cannabis market.

SE: Many equipment vendors have seen the pharmaceutical industry move their laboratories overseas and noticed a drop in equipment sales. They recognize the potential of our industry and see it as one of the few growing markets that can afford the expensive analytical tools they sell. Other vendors still do not feel comfortable with cannabis as it is a Schedule I substance and fear prosecution for assisting a potentially illegal business...

JK: Any new scientific challenge can be fun and exciting – and will draw attention. In addition to learning, it is great to help people who are taking on this challenge. I can only speculate as to what is holding back some vendors. There is the fear of backlash from other customers who may not agree with cannabis use. There is still a stigma associated with cannabis use. There is a stereotype that the industry is not quite legitimate and those involved aren't necessarily ‘serious’ – conjuring images of ‘hippies’. All of this is changing as the industry grows, evolves and is more easily identifiable as a proper business. Finally, there are still legitimate legal concerns as well as some perceived legal risks.

How do you feel about the future of the medical cannabis industry?

JK: Federal regulation of cannabis for medical use will change the game. It will dictate the resources needed to meet federal drug regulations as well as open the door to large pharma. Regardless, I predict a large increase in investigations probing the biological and medicinal properties of cannabis.

SE: I do not foresee federal legalization within the next presidency, but depending on who will run in 2020, it

could be a major topic. I agree with Julie, that once there is legalization on the federal level, things will change really fast. If and when cannabis moves into the jurisdiction of the FDA, it seems likely that only a couple of companies will be able to move into clinical trials and comply its requirements for drugs – probably in partnerships with existing pharmaceutical companies.

Many of the medicinal cannabis companies will switch to recreational operations where less stringent laws will most likely apply. Some major publicly traded companies will move quickly and buy up many of the current players today. The corn states will seed their fields and medium quality cannabis will be a commodity and prices will plummet. Consumers will probably keep paying high taxes and might not really see any effect of commercialization on prices. Specialized stores will disappear and it will become available either through liquor stores or pharmacies. It is interesting to note that Walgreens already has an information page on medical cannabis...

SK: Within two years I believe that all of Canada will be recreationally legal. My hope is that within five years we will be able to convince Congress that cannabis has positive economic and human health benefits, and that cannabis needs further research – but this can only be fully realized with de-scheduling.

As for the recent history of the cannabis industry, I'd like to thank pioneers like Raphael Mechoulam (Weizmann Institute of Science), Ed Rosenthal, Tracy Ryan (CannaKids), Ken Kovash (GI Grow) and Josh Crossney (jCanna, Inc.). Without these visionaries and the incredible spirit they bring to the cannabis industry, we wouldn't be where we are today.

I hope this historic new magazine – The Cannabis Scientist – helps pave the way for a new generation of cannabis science!

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Sitting Down With... Tracy Ryan, CEO and founder of CannaKids.

Could you share a little of your background?

To cut a long and quite entertaining story very short, I grew up in Tennessee, moved to Florida to be a resident DJ in a nightclub and ended up in Los Angeles, working on feature films and events management. But that didn't match the lifestyle I wanted; in particular, I wanted to have a kid, so to gain flexibility I started my own business. Just as my company and family was growing, my 8.5 month-old daughter – Sophie – was diagnosed with brain cancer and everything changed. It was the hardest period of our lives.

How did you get into the world of medical cannabis?

Ricki Lake! Two weeks after Sophie's diagnosis, I got connected to Ricki and Abby Epstein through social media. They were doing a documentary called "Weed the People" that focused on cannabis use for pediatric cancer patients. I already loved and trusted these women; I'd met Abby when I was six months' pregnant with Sophie – I waited outside where she was speaking, like a stalker, just so I could meet her. Little did I know she would end up being my friend. Many people had already told us to try cannabis – I thought they had all smoked too much! But Ricki and Abby started sending me scientific evidence and stories about kids benefiting from cannabis and so I did my own research and just couldn't find anything negative about it. I decided that we should do everything we could for our little girl.

And how did that lead to CannaKids?

I had created a Facebook group where parents could talk about cannabis use in a secret forum; for example, I was able to share all the miracles that were happening to my own daughter's body. I grew aware that there weren't many quality cannabis oil makers – and even fewer who

cared about lab testing and dosing for children. So that's how CannaKids and SavingSophie.org were born. Firstly, we wanted to help people with the extremely difficult task of navigating through all the information online. Secondly, we wanted to create a company that was run by people who understood the importance of high quality medicine.

It sounds like an emotional roller coaster...

It certainly was. About a week into Sophie's diagnosis, we felt like we were going through a death every day; we were living in a waking nightmare. Our little girl was facing toxic treatments and an uncertain prognosis; we had no idea what the future was going to hold for her. I remember sitting on the couch with my husband, grieving, when I suddenly felt a wave of peace – "I believe Sophie has a message and we are her messengers," I said. "I feel like she chose this life and she chose us – and something beautiful will come out of this." Within 72 hours we were connected to Ricki and Abby. I honestly believe that my daughter was sick so that others could be healed – and that's exactly what has happened. It has been one of the most incredibly difficult, emotionally draining but also rewarding experiences – one that you could never fathom going through.

How do you approach quality and analytical testing?

First of all, we ensure we know and trust the people we work with. For example, we know our suppliers grow their flowers in organic soil and without pesticides. But even though we've been using them for two years, we still use analytical labs to test the flowers every single time, without fail. I am not an expert in oil extraction, so we use people who fully understand the plants and the process. After the extraction, we test our products again for pesticides and various other potential contaminants, using well-respected contract analytical

*"We ensure
we know and trust
the people we
work with."*

laboratories. In fact, we work with three different labs and regularly check that they are in line with each other, so we know the results are as accurate as they can be.

Do we need more regulation and more analysis?

Absolutely. I don't think any product should be allowed into a dispensary unless it has been tested – and I know that about 85 percent of all products right now in California are not. I'm personally excited to see more regulations come into play in California in 2018, when analytical testing will be mandatory. There will also be more tracking of the grow process.

Ultimately, we would love to build cGMP facility to prepare for FDA and DEA intervention. Indeed, we are actively seeking a license to grow and stabilize the strains that have been most beneficial to diseases – no easy task! But we're passionate about taking medical cannabis to the next level – and before it's forced upon us.

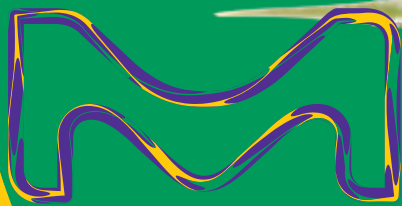
Where do you see the future of medical cannabis?

I fully believe that in the next 5–10 years we're going to see hospitals all over the world adopting medical cannabis. Truly groundbreaking scientists and doctors believe in this plant because they have seen how it helps patients get through chemotherapy and radiation therapy. I believe we're at the forefront of a medical revolution; the way we treat patients is going to change before our very eyes.

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