SEPTEMBER 2021 # 16

the Cannabis Scientist™

Upfront
Caution swimmers: marijuana's impact on male fertility
06

In My View
Making the case for automated testing systems
10

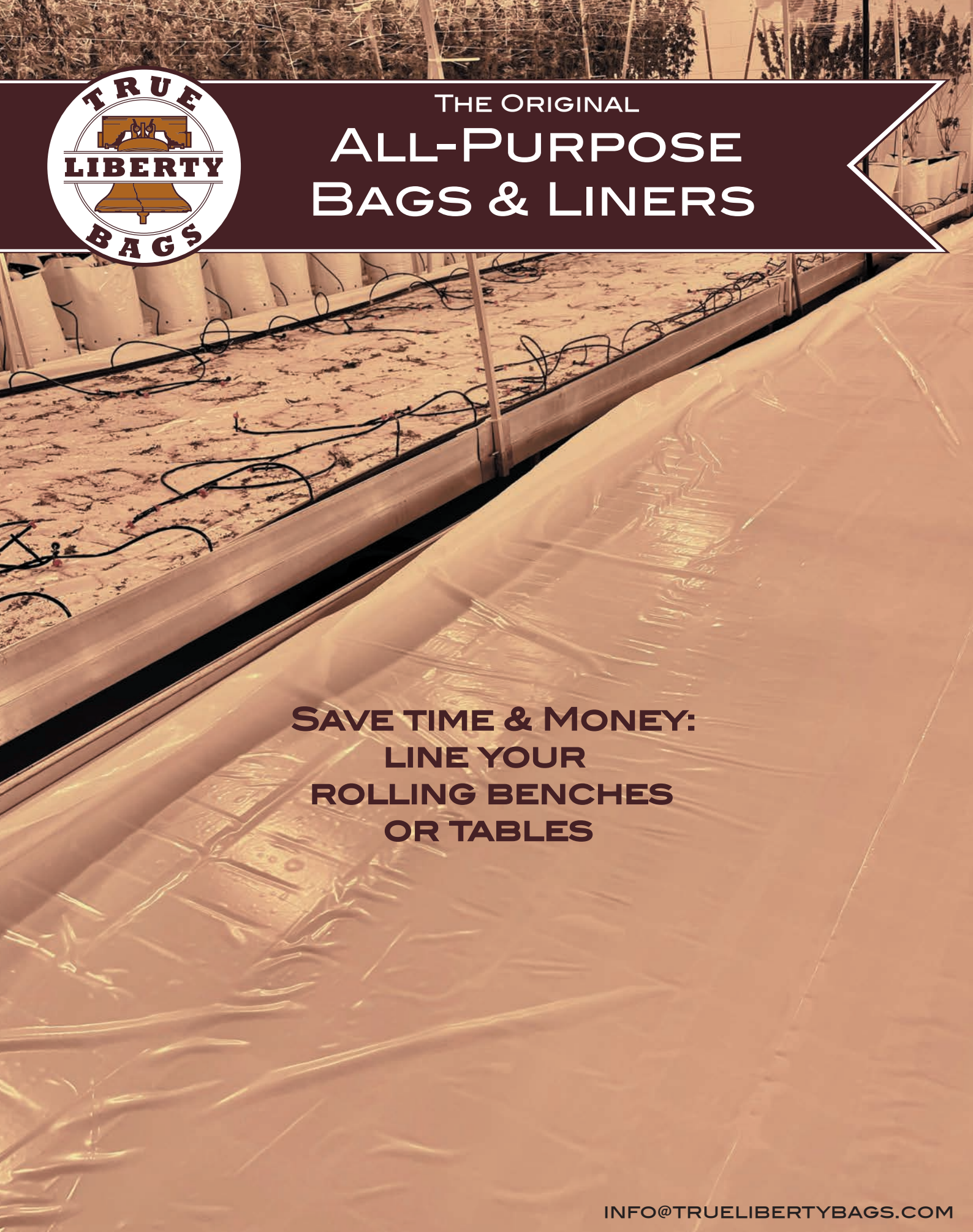
In My View
Foreign investors move in on African resources
12

Sitting Down With
Academic clinician, Mikael Sodergren
34 – 35

The Cannabis Carbon Bomb

How indoor cultivation became a luxury we can no longer afford

16 – 28



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Wake Me Up When September Ends

The most tempestuous of seasons is already making its mark on cannabis – for better and worse

September has always felt like a new start to me. Maybe because it marks the beginning of the academic year; the memory of sharpened pencils and starched uniforms. Perhaps it's the change in the seasons; the promise of crisp Autumn mornings, with their colorful flurries of leaves. Or maybe it just the feeling that with only four months to go, the year is racing by and I'm running out of chances to catch it.

Whatever your feelings, September is undeniably a time for change – and I can already see it happening politically. Just this week, Italy decriminalized the cultivation of cannabis plants for personal use, within days of Panama legalizing medical cannabis thanks to the tireless efforts of advocates like Sandra Carrillo. It is rumored that Mexico will follow suit in the weeks to come.

But not all change is good. Cannabis cultivators in Colorado are being told to prepare for what could be another year of unseasonable cold spells – snowstorms and freezes – as their counterparts on the West Coast paradoxically struggle to protect their crops against drought and wildfires. (Last year, California's historic fire season saw 4.2 million acres burn.)

Climate change is causing more extreme, unpredictable weather – and outdoor cultivators are bearing the burden. But where does cannabis as a whole fit into the sustainability debate? Are we doing enough as an industry to meet the demands of our rapidly changing world? As our feature (The Cannabis Carbon Bomb, page 16) on the emissions associated with indoor cultivation shows, the answer (for now, at least) is no. Indoor-grown cannabis is many things, but "green" it is not.

Of course, the conversation surrounding sustainability – particularly in regards to cultivation, with all the policies and politics that govern it – is too nuanced to be condensed into any single feature, and certainly any editorial. We plan on continuing this discussion in the future, so if you have anything to say, please reach out – we want to hear from you.

Until then, let's focus on the positive. Every day cannabis makes new strides in science, medicine, and politics, advancing our understanding and opening access to this most wonderful of plants. As for the rest? If we know anything, it's that change is going to come, whether you like it or not – all you can do is be ready.

Phoebe Harkin
Deputy Editor

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Contents

03 **Editorial**
Wake Me Up When September Ends, by Phoebe Harkin

Upfront

06 The latest news, views and research – from marijuana's impact on oral health to the rising number of people using cannabis as an alternative to prescription drugs.

In My View

10 **Green Machine**
Could automated testing technologies take the cannabis market to the next level? Toby Astill investigates.

11 **Where Corporate Interest Meets Community**
Louisa Mojela gives her take on the possibility of Africa being short-changed of its own resources by foreign cannabis companies.

12 **Rose Tinted Glasses**
Pharmacist Sukvinder Kaur Bhamra explores the complicated history of non-traditional medicines in the West.

Feature

16 **The Cannabis Carbon Bomb**
Why America's friendly neighborhood grow is not so green after all

Sitting Down With

34 **Mikael Sodergren,** Principal Investigator, Medical Cannabis Research Group; Imperial College London, UK.

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ISSUE 16 - SEPTEMBER 2021

Feel free to contact any one of us:
first.lastname@texerepublishing.com

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Commercial Team
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Change of address info@thecannabisscientist.com
Hayley Atiz, The Cannabis Scientist, Texere Publishing Inc, 175 Varick St, New York, NY 10014.

General enquiries
www.texerepublishing.com | info@thecannabisscientist.com
+44 (0) 1565 745 200 | sales@texerepublishing.com

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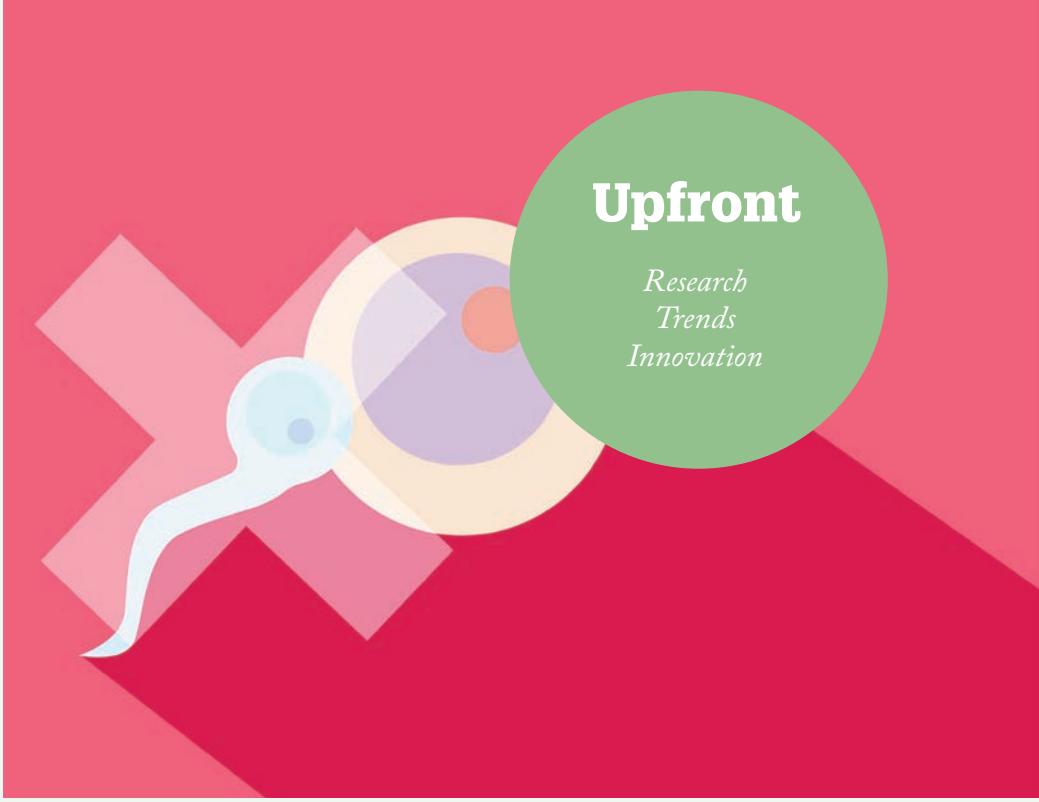


Swimmers at Risk

Marijuana appears to have detrimental effect on semen quality

Marijuana is good for many things but, as it turns out, maintaining fertility isn't one of them. Researchers have noticed that marijuana use is common among men presenting for fertility evaluation and may have a detrimental effect on semen quality, particularly morphology and volume. Confusingly, though, it may also be protective against abnormal sperm motility. So what are we to believe? In a daring evaluation, researchers have taken a closer look at this at-risk population by assessing the semen of 409 current, past, and "never-users" (1).

Compared with never-users, current and past users had a significantly higher likelihood of abnormal sperm strict morphology (33.1 percent versus 50.7 and 53.4 percent, respectively). However, sperm motility was more likely to be below average in never-users than in current and past-users (38.3 percent versus 21.1 and 27.2 percent). Upon analyses, current use was associated with increased odds of abnormal strict morphology and semen volume less than WHO reference value, whereas below-average sperm motility was reduced.

We asked lead author Omer Raheem, Assistant Professor of Urology at Tulane University School of Medicine, USA, if he was surprised there wasn't a bigger difference between current and past users. "One would expect and hope that past smokers would have better sperm morphology since discontinuation of marijuana smoking; however, it remains unknown how long it takes to recover sperm morphology after discontinuation of marijuana smoking."

Interestingly, despite most sperm parameters' being affected by marijuana use (potentially signaling the negative impact of spermatogenesis and testicular function overall), Raheem would not advise men against cannabis if they want a child – but he does offer a word of caution. "Although marijuana use can be helpful in some medical conditions, such as chronic pain, it has a negative impact on men's reproductive ability and may render them infertile for a long time. Having said this, given the paucity of quality data investigating the full effect of marijuana on men's health, a larger study is urgently needed to evaluate these findings." So now you know. Stay safe out there, guys.

Reference

1. *M Hehemann et al., Ther Adv Urol, 13 (2021). PMID: 34367341*

INFOGRAPHIC

This or That

Global policy shifts have seen a rise in the number of cannabis as medicine (CaM) users globally. Here's what we know so far.

SUBSTITUTION users are more likely to be **women** and to use CaM in the treatment of **CHRONIC PAIN** and other somatic conditions (1).

Pain medication *(67.2 percent)*, **antidepressants** *(24.5 percent)*, and **arthritis medication** *(20.7 percent)* are the most common types of drugs replaced with CaM.

BUSINESS IN BRIEF

The latest industry news – in 60 words or less

- Grow Group has raised £3.4 million in Europe's largest-ever medical cannabis crowdfunding venture following the acquisition of a production facility in Andalusia, Spain. The fundraiser – the highest amount raised by any cannabis firm on the Seedrs platform – will be used to expand operations throughout Europe and propel R&D programs.
- The Nevada Cannabis Compliance Board issued a summary suspension of cultivation license for Green Cross of America. Board members voted unanimously to suspend the firm after agents found more than 400 plants not tracked in the state's seed-to-sale system, citing present threat to public health and safety.
- Alabama's medical cannabis program might roll out slower than expected. The state's agriculture department suggests that cultivation licenses will be issued no earlier than September 2022. Taking into account marijuana's cultivation cycle, this means licensed product won't be ready for sale until the following year.

- A Massachusetts firm has been ordered to pay US$300,000 for inadequately compensating employees for working Sundays and holidays – a stark reminder that cannabis operators must abide by nuances of states' hourly wage provisions. In this case, labor law states that "premium pay" is 1.2 times the usual rate. The company put the issue down to "inadvertent payroll errors."
- The smokable hemp ban has been removed from California's contentious AB-45 bill, which heads to final vote next week. If passed, ingestible CBD products will be legal, as will the addition of cannabinoids and other hemp extracts to dietary supplements, food, beverages, cosmetics, and pet food – all currently prohibited.

References are available online

Do No Harm

Could CBD reduce common cannabis side effects?

A novel study has examined the differential effects of various THC:CBD ratios, using widely available chemovars (1). The team assessed 159 regular cannabis users before, immediately after, and one hour after ad libitum administration of one of three randomly assigned cannabis flower chemovars: THC-dominant (24% THC, 1% CBD), THC+CBD (9% THC, 10% CBD), and CBD-dominant (1% THC, 23% CBD). Plasma cannabinoids, as well as positive (high, elation) and negative (paranoia and anxiety) subjective effects were measured at each time point.

As expected, researchers found that participants who used the CBD-dominant and THC + CBD chemovars had significantly less THC and more CBD in plasma samples than participants who used the THC-dominant chemovar. More interestingly, the THC + CBD chemovar group was associated with similar levels of positive subjective effects as the THC-dominant chemovar – but, crucially, with significantly less paranoia and anxiety.

References

1. *L Gibson et al., Addict Biol (2021). Online ahead of print. Available at: https://bit.ly/3kWe2Cd*

Among substitution users, **38.1 percent** report termination of prescription drug use, and **45.9 percent** a substantial **decrease in prescription drug use.**

Promisingly, **65.8 percent** find CaM much **more effective than prescription drugs**, with **85.5 percent** claiming the side effects associated with prescription drug use are **much worse** than those associated with cannabis use.

Reference

1. *S Kvamme et al., Harm Reduct J, 18, 72 (2021). PMID: 34246279*

Warning: Risk of Residue

Researchers investigate a potential link between pesticide residue and neurological disease

Despite more and more attention given to the toxicology of cannabis contaminants, there is still no federal regulation to standardize testing or residue limits. With countless products recalled for reports of questionable pesticide levels, the question remains: how safe is medical cannabis? To find out if cannabis represents a potential route of pesticide exposure to susceptible populations, US researchers compared a number of qualifying neurological conditions against cannabis pesticide testing requirements in 33 states and Washington DC.

The team found that movement disorders (including epilepsy, multiple sclerosis, and Parkinson's Disease) are the most common neurological category of qualifying conditions in the country. They also discovered that the number and action levels of regulated pesticides in cannabis varied significantly across the US; for example, six states imposed the strictest residue limits for food commodities on up to 400 pesticidal active ingredients in cannabis, while three states (worryingly) considered pesticides testing "optional." Of all the pesticides examined, dimethomorph, a fungicide effective against various pathogens in vines and other crops, showed the largest variation in action levels, ranging from 0.1 to 60 ppm in five states. So, what impact do these fluctuations have – if any – on a functional level?

The team used the Comparative Toxicogenomics Database to identify any possible connections with insecticides, cannabinoids, and seizure, and found that 22 insecticides, two cannabinoids, and 63 genes were associated with 674 "computationally generated chemical-gene-phenotype-disease tetramer constructs." Cholinergic, dopaminergic, and retrograde endocannabinoid signaling pathways were linked to 10 genetic variants of epilepsy patients.

The study authors conclude that medical use of cannabis could unintentionally expose susceptible patients to harmful pesticides, contaminants, and cannabinoids that disrupt the same signaling pathways that have links with seizure disorders. The team has called for further research to fully establish any potential hazards, with the hope of informing a national standard for acceptable cannabis pesticide limits. Considering the implications for an already vulnerable population, let's hope they are successful.

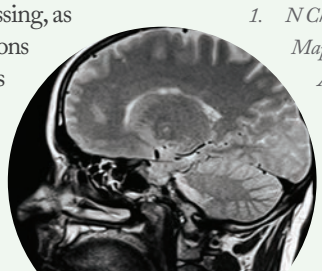
Reference

1. *D Pinkhasova et al., Curr Res Toxicol, 2, 140, PMID: 34308371*

New Hope for HIV

Cannabis has normalizing effect on pre-stimulus gamma activity in PWH

It is well reported that people with HIV (PWH) use cannabis at a higher rate than the general population, but relatively little is known about its influence on neural activity in PWH. Researchers set out to quantify the impact of chronic cannabis use on brain and cognitive function through magnetoencephalographic brain imaging data. The study split 81 participants across four demographically matched groups (PWH using cannabis, controls using cannabis, non-using PWH, and non-using controls) and asked them to complete a visuospatial processing task. They found PWH exhibited significant behavioral deficits in visuospatial processing, as well as reduced theta oscillations and elevated pre-stimulus gamma activity in visual cortices. Strikingly, chronic cannabis use was associated with a significant reduction in pre-stimulus gamma activity in the visual cortices – so much so that PWH no longer statistically differed from controls, providing evidence that cannabis use may normalize some neural aberrations in PWH.



Reference

1. *N Christopher-Hayes et al., Hum Brain Mapp (2021). Online ahead of print. Available at: https://bit.ly/38MmGgU*

IMAGE OF THE MONTH

Up In Smoke

More than 650 million dollar's worth of drugs, including heroin, cannabis, methamphetamine, and ketamine, were burned by Myanmar's military authorities in a hardline attempt to stop industrial production. The haul was set ablaze on the United Nations International Day against Drug Abuse and Illicit Trafficking.

Credit: Associated Press

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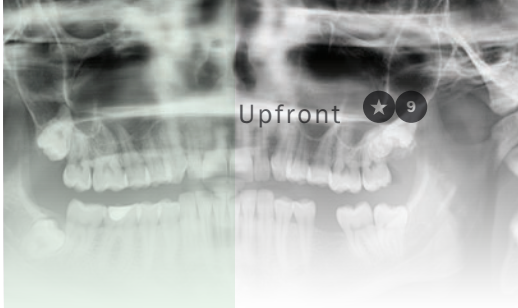
QUOTE of the month

"The cultivation of hemp at home is essential for patients who have to make therapeutic use of it and who often do not find it available, as well as [combating its] sale and consequent criminal undergrowth."

Mario Perantoni

President of Italy's Chamber's Justice Commission, as Italy votes to decriminalize small-scale cultivation of cannabis plants.



Grin and Bear It

PATH study associates cannabis use with increased risk of poor oral health

Cannabis use is increasing among adults, but though evidence connects cannabis use to poor periodontal health, few prospective studies exist in the US to prove it. A recent investigation examined associations between cannabis use and self-reported adverse oral health conditions among almost 19,000 participants as part of a nationwide Population Assessment of Tobacco and Health (PATH) Study. Reported cannabis use was positively and prospectively associated with multiple measures of poor oral health, including a number of conditions (gum bleeding, loose teeth, alveolar bone loss and gum disease) indicative of periodontitis.

The study's authors acknowledged that limited information on frequency and modality of cannabis use, but nevertheless came to a strong conclusion. Compared with participants who had never used cannabis, those who consistently reported recent cannabis use over a three-year period had nearly double the odds of subsequently reporting poor or fair overall oral health, gum bleeding and loose teeth, even after statistical adjustment for sociodemographic, socioeconomic, and behavioral risk factors, such as tobacco smoking.

Reference

1. *B Chaffee, J Calif Dent Associ, 49, 493 (2021). PMID: 8415*705

In My View

Experts from across the world share a single strongly held opinion or key idea

Green Machine

Why automated testing technologies could take the cannabis market to the next level

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

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

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

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

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

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

"Automated testing provides streamlined sample prep, increased throughput, and decreased cost per sample for all stages of the workflow."

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

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

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

Where Corporate Interest Meets Community

Is Africa getting short-changed on its own resources by foreign cannabis companies?

By Louisa Mojela, Chairman of the Halo Collective and Founder of Bophelo Bioscience, Lesotho

Cheap labour + cheap materials = low costs and high profit margins. It's the equation that every business strives to master. The problem is that those profit margins often come at a cost to emerging markets that are seeking growth and investment. For the cannabis industry, it makes sense to produce products in Africa, where the growing conditions are ideal and production and labor costs are lower. But that opportunity should be matched by a certain amount of responsibility. And that's something we know all too well at Halo Collective.

We're a US-based company that specializes in modern cannabis extraction techniques and cannabinoid isolation. Owner of the largest grow sites in North America, Halo uses proprietary techniques and leading-edge technology to develop innovative products. And with the cannabis industry booming, the time is ripe to expand both vertically and into new markets… But we also understand the active role cannabis can play in transforming the economies of developing nations.

We acquired Bophelo Bioscience and Wellness in Lesotho in 2020. Bophelo is currently operating in a five-hectare facility – with access to an additional 200 hectares – and it will soon be the largest cultivation site in the world. The conditions are close to perfect for a cannabis business: the environment is pristine, there is plenty of water and sunshine, energy costs are low, and labor is competitively priced. All that is needed is foreign investment and the technical and business skills to maximize this opportunity for the country.

My family is from the Mafeteng district of Lesotho, where Bophelo Bioscience is situated, so I know well the struggles that Lesotho faces. About 40 percent of the country's population live below the poverty line, with many just getting by on subsistence farming. Unemployment has left many with no choice but to leave and find work in South Africa. As a country, the challenges faced are manifold, but we continue to work towards growth and development.

Lesotho was the first country in Africa to legalize the cultivation and manufacture of medical cannabis. In fact, cannabis has been used as medicine by the local Basotho people for many years. As a result, they already have expertise in cultivating it – experience that will stand Lesotho in good stead as it enters the global cannabis market via Halo.

Halo's commitment to taking care of and developing existing resources and the community in which we operate runs deep. Our vision is to create opportunities for generations of local people, establishing a positive work environment where employees can earn more than the government-regulated minimum wage, thus raising their standard of living. We practice equal opportunity employment, with compensation based not only on labor laws, but on merit, qualifications, and individual abilities. As a local to Lesotho, I also see the importance of offering our employees career and training opportunities, teaching skill sets that can empower people on the ground to rise within our company, rather than bringing in outside hires.

When the acquisition of Bophelo was finalized, one of Halo's first priorities was to pledge 10 percent of pre-tax profits to community causes in the Tsakholo (the site of operations), as well as the greater Mafeteng area. Halo does this through the Mophuthi Matsoso Development Trust, which I founded in 2010. The Trust is

dedicated to rural community development for those in need, especially women and children, and aims to address poverty and build self-reliance.

The goals of Mophuthi Matsoso are threefold: to fund education, especially early learning; to empower women through projects and programs that develop skills, build capacity and help to generate cash; and to invest in agriculture to fight hunger and promote food security.

In line with these goals, Mophuthi Matsoso has upgraded several local schools from dilapidated old buildings, adding electricity, ablution facilities, staff offices, and libraries. The Trust has also built a learning center that is fully electrified and equipped with a science and mathematics lab, a computer center, sports facilities, and a library. These top-class learning facilities, along with well trained teachers, will equip local children for future careers that can further benefit the country.

Funds from the Trust have also been used to purchase farming equipment and plough community fields at no cost, and to set up a project where pigs are raised for food and for market. The badly eroded roads in the area are being upgraded so locals can more easily transport goods and reach towns, schools and clinics. And the newly-built All Saints Anglican Church will help anchor the community and provide for their spiritual needs.

It's my belief that the success of a company must be measured by the development of the community around it – communities (women and young people in particular) cannot be left impoverished whilst companies thrive at their exclusion. Ultimately, our goal is not just to succeed in our business in Lesotho, but also to invest in the people who contribute to that success – a blueprint we hope other companies will follow.

Rose Tinted Glasses

How a lack of training is dissuading patients – and healthcare professionals – from the benefits of traditional herbal medicine

By Sukvinder Kaur Bhamra, Lecturer in Pharmacy Clinical and Professional Practice at the Medway School of Pharmacy University of Kent, UK

Social media's impact on the popularity of "natural" products has been significant – and CBD is far from the exception to the rule. The increased demand in sales and supply of herbal remedies over the past few years is an example of how people are starting to reconsider natural products. I like to think that they are "coming back into fashion."

I recently published a paper surveying public perception of CBD globally. A wide range of responses were recorded, including some in favor and others sceptical of the use of CBD. Some participants reported a willingness to try CBD products because they were seeking a more holistic lifestyle or because of promotions they had seen on social media; others shared concerns about the lack of regulation of CBD products, especially as they were often sold as food supplements and not medicines. The need for more research and evidence to demonstrate the safety and efficacy of CBD was highlighted (1).

Naturally, we asked an important question: is lack of clinical evidence on safety and efficacy actually deterring use? For some people, the answer was yes. If there was more information to facilitate the safe use of CBD based products it would be well received. Improved clinical evidence is not only required for users/the public, but also healthcare professionals, who do not have sufficient knowledge of how herbals interact with conventional medicines so often advise against their use. On the other hand, those who are interested in natural products – based on traditional use – will not be affected by the lack of clinical evidence.

"It is important to remember that natural products were being used long before conventional medicines were developed."

It is important to remember that natural products were being used long before conventional medicines were developed. Certainly, many talented and inventive people are responsible for the advances that make up modern medicine. But, as a society, I feel we have become so driven by evidence-based medicine, guidelines, and accountability that our freedom to explore natural products has been

restricted. Where once nature provided well-known remedies, we now rely entirely on pharmaceutical intervention.

There are three reasons behind this almost complete shift away from natural products. The first is access; those products that are native to some countries are not always easy to find in others – tulsi (also known as holy basil, Ocimum tenuiflorum L.) is an example of this. Closely related to basil, tulsi has been used for various ailments, including asthma, eczema, and diabetes, in Southeast Asia. Here in the UK, tulsi is less common, but seeds are now exchanged within communities who have found ways of successfully growing this native Indian plant (2).

The second reason is cost. It is only with the introduction of the National Health Service (NHS) and free access to healthcare for all that people began seeking medical advice and with it, a prescription, as opposed to seeking a natural solution. With standardized dosing, formulations and prescribing guidelines, we have seen a transition away from nature's pharmacy and instead, a reliance upon cheaper (or free) mass-produced medicines.

The third reason is knowledge – or lack thereof. Often, healthcare professions disregard the use of natural products – even going as far as to advise patients against their use, because of unknown herb-drug interactions (3). If we don't fully understand the pharmacological effects of natural products – and if the evidence base and clinical guidelines are lacking – it's a clear problem.

As a healthcare professional, I had very limited training on natural products during my undergraduate training. Now, as an academic training the next generation of healthcare professionals, I can see the problem still exists. The answer is simple in theory, but difficult in practice. We need better education for healthcare professionals and the public, more clinical evidence, and better regulation surrounding natural products. Only by addressing all three areas will we see traditional and conventional medicines used in a safe and effective manner.

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2. *S Bhamra et al., "The Use of Traditional Herbal Medicines Amongst South Asian Diasporic Communities in the UK", Phytotherapy Research (2017). DOI: 10.1002/ptr.5911*
3. *S Bhamra et al., "Health Care Professionals' Personal and Professional Views of Herbal Medicines in the United Kingdom", Phytotherapy Research, 33, 2360 (2019). DOI: https://doi.org/10.1002/ptr.6418*

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Dead on Arrival?

Why guaranteed product shelf life may be the most critical component of cannabis research

There are plenty of anecdotes from dissatisfied patients who fail to find the same relief from one batch of cannabis to the next. There are likely even more stories of adult-use consumers questioning the provenance or identity of their purchase.

But when it comes to research – where cannabis origin and processing should (at least in theory) be guaranteed – have we placed enough emphasis on controlling what happens from the harvest to the lab?

Here, we explore how product stability is affecting patients, the industry – and, in particular, cannabis scientists who are keen to eliminate all sources of potential variation to publish the best, most reproducible research.

(Good) Practice Makes Perfect

By Andrew Samann CEO, Orion GMP Solutions

Cannabis is a living organism with complex systems designed to protect it against the environment and pathogens. When it is cut, preservation requires careful handling. Preservation directly relates to quality (see box "GMP 101"), which is dependent on some basic facts. How much time has passed between cutting and storing? How quickly was the cannabis processed? How was it dried? In short, the key to quality cannabis is adequate preservation–and that demands water activity testing.

When it comes to cannabis drying, some prefer to hang dry, others prefer to cut the buds down and dry on trays; in any scenario, measuring the rate of evaporation is critical – and this can only really be measured via water activity (the relative humidity immediately adjacent to the product vs the total moisture in the plant). Indeed, the impact of the drying process can only be understood by precisely measuring water activity in any drying case (from fastest or slowest) and relating drying rate to product quality. Product quality may be assessed by water activity, as well as, shape, odor, bud size, color, et al. These critical quality attributes (CQAs) determine if a cannabis sample is well preserved and of high quality. Optimizing CQAs for the drying process provides growers the guidelines they need to sustain the quality of their flower.

Preserve and protect

So why is preservation such a big deal? In Canada, as in many places around the world, more cannabis is grown than consumed. Overproduction results in surplus. This aged inventory may not be safe to consume, which results in companies having no choice but to destroy product. As an industry, we still haven't worked out the critical control point between packaging and long-term shelf life– but it's time we do so.

Recent global circumstances that caused retail closures and shipping delays illustrate why we must protect product throughout the supply chain. Contrary to past belief, we have little control over how long cannabis will sit on the dock or the shelf. There are no cannabis-specific guidelines for packaging and humidity control. Cannabis professionals, therefore, implement GMPs by interpreting scientific literature then relating it to the specific needs of their cultivars and extracts. Understanding how water relates to that is more fundamental than people understand.

Currently, Orion GMP is overseeing a stability study assessing the performance of salt solution-based humidity control sachets, which are designed to protect active ingredients in cannabis flower from evaporation and degradation. These saturated salt solution sachets are engineered to create a microclimate with the optimum level of humidity for sample preservation. The goal of the study is to establish cannabis shelf life guidelines for various packaging component systems.

For pharmaceuticals, there are two main types of containers – impermeable and permeable. This stability study will go beyond those, using multiple packaging types, including impermeable, permeable and experimental containers as well as a control group. We will measure the performance of the sachets in multiple configurations of a packaging system to establish legitimate shelf-life claims.

Not only will we ascertain stability immediately after the flower is dried and cured, but how it responds over time – particularly in fluctuating environments. That means studying flower with and without a sachet through every step of the supply chain –from harvest to the point of delivery, including international distribution.

GMP 101

I am often asked: What is the value of good manufacturing practice (GMP)? A better question is: What is the cost of quality? How much does a recall or regulatory infraction cost? Then you consider the potential contracts lost as a result of any breach, the cost of quality becomes even more significant. You can put a number on the financial burden of not meeting FDA requirements, but what about the impact of a spoiled scientific sample? It's certainly less tangible but no less important for the customers of those products–researchers.

GMP essentially improves product quality through the naming of specifications. What goes into the product? Is it safe? Is the facility clean? Does it meet certain standards? Are staff sufficiently trained? Each and every aspect contributes towards a quality management system. But when it comes to cannabis flower the ultimate control points arguably happen post-harvest.

Though there are plenty of people working on stability for their own products, this will be the first time a packaging component system has been studied outside of a single company or brand. How exciting would it be to offer a universal solution, where a single sachet could offer a defined, extended shelf life to anyone, anywhere? We don't have the answer yet, but we will in time.

The cost is too great not to.

Save the Terps – Reprise!

An interview with Dr. Cindy S. Orser, CSO Clip Labs

Why are terpenes so important in our understanding of the cannabis plant?

Terpenes represent a large, diverse category of pharmacologically active chemicals made by animals, insects, microbes, and plants, including cannabis. Terpenes provide the distinguishing bouquet of the cannabis flower and can be used to phylogenetically classify cannabis strains. In fact, terpenes can make up three to five percent of the dry mass of cannabis flower.

Terpenes interact with receptors in our bodies to elicit responses, including at the neuroexcitatory dopaminergic and GABAergic receptors; beta-caryophyllene actually binds to the same CB1 receptor as THC (you may not know that cannabinoids are technically terpenoids – modified terpenes). Terpenes have shown many of the same properties associated with cannabinoids, including, analgesic, anxiolytic, anticancer, neuroprotective, and more.

Up until recently, everyone has been fixated solely on THC content. Terpenes were not only being lost during processing but also in the discussion! It's time for this to change.

How does the supply chain impact the quality of flower and therefore terpenes?

Terpenes are volatile, so their preservation in cannabis flower post-harvest can be problematic. If the environmental conditions under which the cannabis flower is cured and stored are not optimal, terpenes will be lost, which changes the original terpenoid profile of that particular lot of cannabis flower. The extraction process can further reduce or eliminate terpenes.

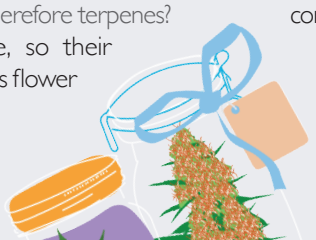
How can we make sure research materials are kept in the best possible conditions–and why should we care?

Put simply, cannabis research materials should be harvested, dried, and cured following a standard operating procedure (SOP). SOPs should also be followed after curing—cannabis flower should be stored under constant temperature and humidity conditions.

Stability of active ingredient(s) in any test material is essential. Furthermore, any active ingredient that is being studied in vitro or at the sub-clinical/clinical level must be proven to remain stable for the duration of the study at a minimum but hopefully for much longer.

What are the critical control points in cannabis research that are being overlooked?

The number one priority has been to get the DEA to allow experienced cannabis growers to produce flower destined for research, following SOPs. We have seen progress, however; in 2021, the DEA offered some flexibility on who can grow cannabis flower for research purposes. Labs such as Biopharmaceutical Research Company and other federally compliant organizations are working hard to ensure investigators are getting the best possible materials.



A Clever Primer on Quality Control

A rapid-fire interview with Andres Fajardo, President of Clever Leaves

How would accurate shelf-life claims of cannabis inflorescence benefit the industry as a whole?

Perhaps the biggest impact would be on patients and researchers, who would both have a better understanding of a critical aspect of product quality, which affects both safety and efficacy.

How critical is product stability to investigative outcomes?

The simple reality is that product characteristics can change over time. Characteristics are driven by chemical components, which can be subject to degradation. The loss of a key characteristic could result in a failure to deliver the desired effect (efficacy) or even pose a risk to the health of patients (safety). From a research perspective (for the reasons mentioned above), it is not possible to enter into an informed decision-making process without product stability knowledge. After all, instability of the product directly affects the reproducibility of the results, which harms the investigative process or the credibility of the outcome–or both.

How can we make sure research materials are kept in the best possible condition?

As with medicines destined for patients, packaging should be considered a fundamental part of product development as it guarantees the stability of research materials. An important (but often overlooked) aspect of product development is the consideration of conditions throughout the whole chain. Good packaging along with modern technology, such as conditions tracking, supports this goal.

In short, the best way to keep any material in its optimal condition is by defining the storage and handling conditions–and these are related to the production process and the packaging.

THE CANNABIS CARBON BOMB

Why America's friendly neighborhood grow is not so green after all

By Phoebe Harkin

If you'd have told Jason Quinn two years ago that he was going to publish a paper on cannabis, he'd have laughed.

Quinn is an Associate Professor in Mechanical Engineering and Director of the Sustainability Research Laboratory, Colorado State University, USA, specializing in the life cycle assessment and techno-economic assessment of emerging energy-based systems – but here he is, writing about cannabis (1).

"I'm an improv guy; I always say yes," Quinn laughs. "Someone asks 'Do you want to look at converting mining trucks to hybrid electric or hydrogen vehicles?' and I say yes. Do I know anything about it? Not a damn thing – but I'm excited to find out!"

One day, someone came to Quinn with an idea: how about running an algal-based biofuel operation with solar panels and LED lights. Quinn said it would never work. "You cannot beat the sun. Plus, the sun is free – and free is good." It doesn't take an energy specialist to work out that converting light into electricity and back into light has all the hallmarks of inefficiency. But the very radical notion got Quinn thinking about indoor cannabis grows. How could converting coal power into photons and delivering that to a plant with an efficiency of 2 percent at best be anything but bad for the environment? "The impact has to be huge – and that's where the idea for the study came from. Evan Mills had already shown it wasn't good and we wanted to see if we could take it to the next level."

Quinn, along with two of his PhD students, Hailey Summers and Evan Sproul, analyzed the energy and materials required to grow cannabis indoors and quantified the corresponding greenhouse gas (GHG) emissions using life cycle assessment methodology for a cradle-to-gate system boundary. Their analysis accounted for geographic variations and electrical grid emissions data.

A $13.6 billion industry – and, as it turns out, a whole lot of emissions. Depending on location, GHG emissions ranged by as much as 200 percent, with cannabis grown in Southern California having the lowest emissions, at 143 pounds of carbon dioxide equivalent per ounce, while eastern O'ahu, Hawaii, had the highest at 324 pounds of carbon dioxide equivalent per ounce – the equivalent of burning 16 gallons of gasoline.

Across all locations, the biggest contributors to GHG emissions were heating, ventilation, and air conditioning (HVAC) systems required to maintain indoor temperature and humidity, as well as high-intensity grow lights and the supply of CO_2, which accounts for 11–25 percent of facilities' greenhouse gas emissions alone.

The results of the study confirm – perhaps unsurprisingly – that cultivating cannabis indoors leads to considerable GHG emissions – no matter where it is grown in the country. The work gets complicated quickly. CO_2 is used in grow facilities and a lot of it is wasted. "This work assumes the cannabis facility takes the burden of emissions associated with waste CO_2 procurement but not the emission of the actual CO_2. Any CO_2 that doesn't get used is not attributed to the cannabis facility, it's attributed to the ammonia facility – but the emissions associated with getting it from A to B are atrocious," explains Quinn.

You smoked how much? Let's talk servings

Quinn and his team make the conscious decision to expand the published work to include emissions based on individual serving size – one tenth of a gram. "When reports say between two and five tons of CO_2 equivalent per kilogram of dried flower you are too concerned about who in their right mind is consuming a kilogram of dried flower to focus on what that actually means. Showing emissions based on single serving grounds everybody."

With servings in mind, indoor cannabis cultivation comes out worse – between 0.73 and 1.66 pounds of CO_2 per serving (in this case, the 10 mg of THC delivered to the user) – than beer (0.63 per 12 oz), wine (0.54 per 5 oz), coffee (0.2 per 8 oz cup), spirits (0.08 per 1.5 oz), and cigarettes, ironically, come out best (0.02 per cigarette) in terms of GHG emissions.

Quinn offers an aside: "When I show this to my students I have to say, 'Please don't go home and tell your parents that your professor said you should smoke cigarettes. That's not what I'm saying here.'" He stresses the data is an average and does not account for a 70-year-old who smokes two packs of cigarettes a day and is being treated for lung problems in hospital, with all the associated emissions...

> "MOVING OUTDOORS REDUCES GHG EMISSIONS BY ROUGHLY 80 PERCENT. MAKE THAT A GREENHOUSE – EVEN WITH LIGHTS – AND EMISSIONS STILL GO DOWN BY 75 PERCENT."

In any case, herein lies the problem in granular detail. The solution, however, has not changed since Evan Mills published his first paper in 2021. Grow outdoors. Quinn and his team calculate that moving outdoors reduces GHG emissions by roughly 80 percent. Make that a greenhouse – even with lights – and emissions still go down by 75 percent. "People say 'Well, there are security issues with that' but there are security issues with indoor grow facilities as well."

Has the work been met with any other criticism? "Many people have asked why we aren't considering illegal cannabis cultivation – either the people growing cannabis in their basements or the larger networks of facilities," says Quinn. "The truth is there is really no way for us to quantify the GHG emissions associated with that. But let's be real, the amount of land used for illegal cannabis cultivation systems cannot be equivalent to more mainstream agricultural systems. Interestingly, one of the biggest challenges we had with this study is understanding how much legal cannabis is actually being cultivated inside, because there isn't even a lot of good data on that." The next step is getting data on outdoor greenhouse facilities and outdoor grow facilities to establish a precise figure on energy reduction. "We want to be able to say: here are the emissions from an indoor facility, here are the emissions from an outdoor grow facility. Please, make good choices."

Ice-cold cannabis

But one issue with the cold-hard facts is that they are not one-size-fits-all. Cannabis production cannot be treated as a monolith, when geography is the biggest variable impacting emissions for better or worse. In fact, it is impossible to read the paper without thinking

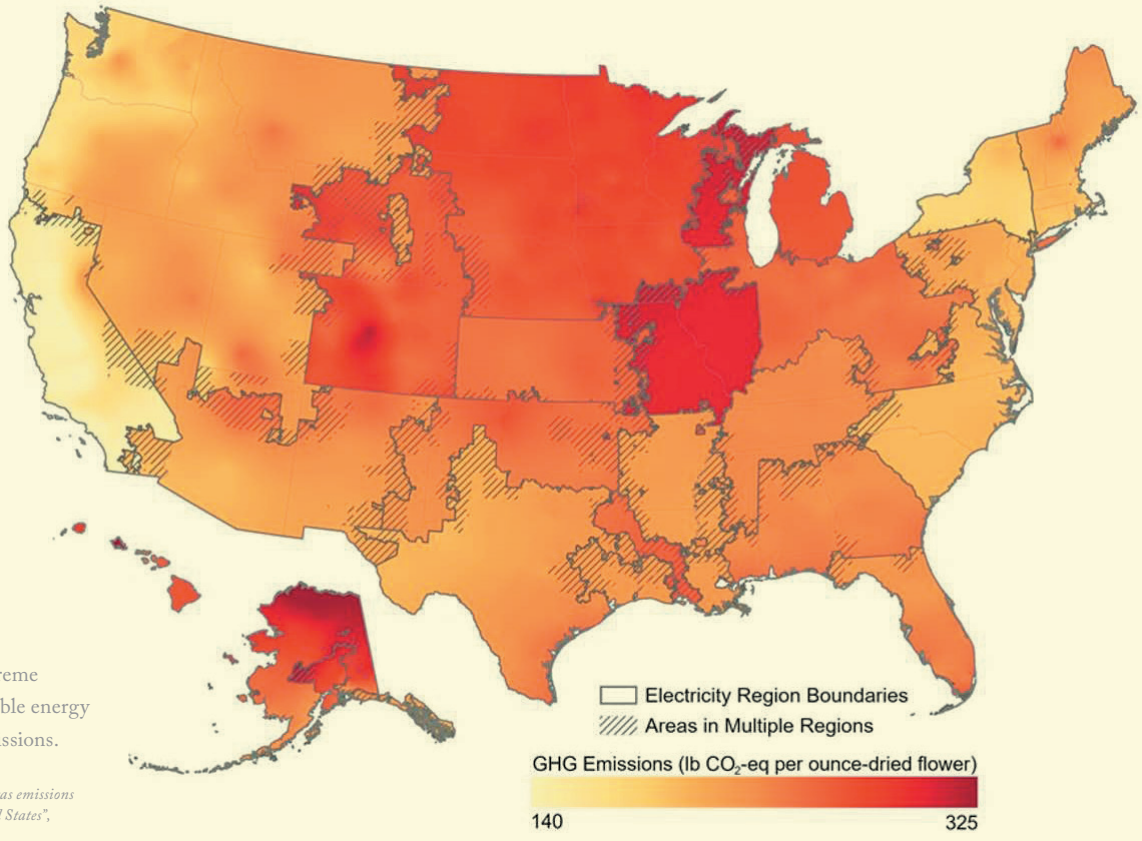


Figure 1. Places with more extreme temperatures and fewer renewable energy sources have highest GHG emissions.

Credit: H Summers et al., "The greenhouse gas emissions of indoor cannabis production in the United States", Nature Sustainability, 644–650 (2021).

that some areas shouldn't be growing cannabis at all. "Northern Minnesota is not an ideal place to grow a tropical plant indoors or outdoors. It's not rocket science," says Quinn. "Southern California, on the other hand, is perfect. It has a temperate climate that doesn't require the same indoor air controls as North Dakota. But you can't cultivate in Southern California and then transport to Minnesota because you're not allowed to cross state lines."

The elephant in the room: federal illegality. Does it matter if people make better choices on an individual level without statewide federal change? Quinn remains hopeful: "Cultivators need to start incorporating energy efficiency requirements into their grow facilities as states legalize."

But in the eagerness to legalize, there has been a whirlwind centred around the core issue, with very little thought about the energy impact and emissions. Even now, there remains little-to-no regulation on emissions from indoor cannabis grows. And perhaps it doesn't help that the first policies following legalization pushed cultivators towards indoor grow facilities. "Some of the policies were crazy," says Quinn. "In Colorado, for example, your grow facility had to be co-located with your dispensary. Where do people want to buy it? In downtown Denver – so that's where they put the indoor grow facility."

Understandably, the shift away from indoor cultivation will be simpler for some than others. But what about states that have already legalized? What can existing growers do – outside of switching to outdoor cultivation – to become more sustainable? "The answer is geographically specific," says Quinn. "In the US, we run off grid energy and some grids are cleaner than others. One way of dramatically reducing your emissions is to switch to a more renewable energy source – I even know of one company who does their own on-site power through renewables."

"I don't think that there's a silver bullet outside of switching to a cleaner energy source, which is really the lowest hanging fruit. All other suggestions will have a small positive impact but you'd need to do many of them together to get the same results you would from switching to renewable energy."

The color of money – and consumers

"The real problem here is the markup the industry has on the product – it is so large that all businesses care about is the quality of the product and they're willing to invest all their money into it, regardless of the impact. There's no pressure for them to reduce their carbon footprint because they can afford to do it."

The irony is not lost on Quinn. "The funny thing is that if you reduce the greenhouse gas emissions, you reduce your energy consumption, which means you reduce your operational costs. Now all of a sudden, your product is cheaper, but that's just lost in the noise. But consumers aren't demanding that they change either, so brands aren't trying to differentiate themselves through environmental impact either."

Enter the second most important player in the cannabis market: the "green" consumer. "I find it funny that you've got people rolling a joint, saying 'Let's save the planet, man!' and I'm like, 'If you want to save

the planet, you shouldn't be smoking indoor cannabis, you should be drinking a beer!'" quips Quinn. "People should start thinking about choices they're making in terms of the environment. The cannabis sector contributes a nontrivial percentage of a state's total greenhouse gas emissions – and consumers have an opportunity to start making personal choices that are good for the planet. Just like taking your own grocery bags to the store – it's a small thing that you can do for the planet."

Promisingly, there is already a little change in the right direction. "Life cycle assessment and carbon accounting is becoming really big, especially among start-ups. My hope is that, as the industry continues to grow, brands will look for ways to differentiate themselves by becoming low carbon." And that's a particular easy win for up-and-coming cannabis extractors who don't need to factor in the role of consumer appeal: "People think the flower needs to look this way or that – but if you're extracting THC for edibles, nobody cares what the flower looks like; that should be greenhouse or outdoor grown."

As states and countries legalize, Quinn hopes cultivators, regulators, and consumers consider some of the aspects mentioned in the paper as a part of the rollout plan: "Grow it outdoors in Southern California and ship it elsewhere. Let's not have an indoor grow facility in Fairbanks, Alaska."

But having seen what happened following the Mills paper (not very much), Quinn has his doubts. "What's frustrating for me is that, when the paper gets published, there's a whirlwind of interest, and then nothing happens," says Quinn. "I wasn't expecting the world to change overnight but I do want to see some impact of our work." He pauses, "I suppose it's the same as investing money; you've got to give it a year to see the dividends. Will anybody actually make a change?"

Let's give it a year and see.

Reference

1. *H Summers et al., "The greenhouse gas emissions of indoor cannabis production in the United States", Nature Sustainability, 644–650 (2021).*

AN INCONVENIENT TRUTH

Evan Mills has been writing about climate change for 40 years. He participated in the work of the Nobel-Prize-winning Intergovernmental Panel on Climate Change and is a former Senior Scientist at the US Department of Energy's Lawrence Berkeley National Laboratory, where he is now an affiliate. His specialty? Energy analysis – specifically the efficiency of energy use as the number-one strategy for addressing climate change.

In 2012, he conducted a study that aimed to quantify a previously undocumented component of energy demand in the US – and to establish baseline impacts in terms of energy use, costs, and greenhouse-gas emissions in the cannabis industry. Mills observed, as is the case in many other areas of the economy, that many reversible inefficiencies are embedded in current practices. The ultimate area of inefficiency? Indoor cultivation.

Indoor facilities contain lighting as intense as that found in an operating room (500-times more than needed for reading), six-times the air-change rate of a biotech laboratory and 60-times that of a home. In short, it requires the electric power intensity of a data center. He writes that "large-scale industrialized and highly energy-intensive indoor cultivation of cannabis is driven by criminalization, pursuit of security, and the desire for greater process control and yields. The practice occurs across the United States and in many other countries."

With the yearly greenhouse-gas pollution from the electricity, plus associated transportation fuels, equaling that of 3 million cars, its annual energy bill was close to $6 billion at the time of the original study. In his latest article for Medium (one of hundreds that Mills has written over the last decade), he calls indoor cultivation "an unaffordable luxury in a warming world."

We spoke to him to find out what's changed, what hasn't, and why not.

How did you come to study indoor cultivation?

About ten years ago, I was innocently shopping at a local nursery and noticed a row of 1000-watt lamps behind the counter, fans, ducting, CO_2 canisters, the whole shebang. I started asking questions about the technology and standard practices. I built a spreadsheet model of facility energy use and one thing led to another. The proprietor of that store, Scott Zeramby, had a healthy combination of conscience, knowledge, and curiosity and helped me understand the industry and real-world practices. He collaborated with me on our upcoming publication.

Have things gotten better or worse since the study you published in 2012?

Sadly, by most measures they have gotten far worse. There is actually little evidence of reductions in carbon-intensity (greenhouse-gas emissions per unit weight yield), despite the gradual introduction of LED lights, which people tend to regard as a panacea. I think there have been countervailing trends, such as increased illumination levels, more mechanization, more voluminous facilities, and wider aisles (requiring heating, cooling, and dehumidifying), and increased carbon dioxide injection. Meanwhile, there is far more indoor production in aggregate than previous years, so the total carbon footprint is no doubt growing. There was a lot of hope for misnamed "green" houses, but the reality is that they have incredibly energy-inefficient envelopes and still use a lot of artificial lighting, ventilation, and natural gas for heating, with the result that carbon intensity is only 25 percent lower than windowless warehouse facilities, according to published data.

Is your work being met differently now that climate breakdown is more visible?

There has been a lot of discussion and appreciation of the work since the beginning – though that, of course, is a far cry from change in actual practices. That said, a number of growers have contacted me over the years saying they've shifted operations outdoors, in part due to what they learned from my publications. There was never any serious push-back on the work. It took High Times five years to raise some questions, and it was kind of embarrassing for them, since their points were mostly erroneous (some outrageously so) or were strawman arguments attempting to shift the conversation away from the industry. They also aligned themselves with long-since-debunked misinformation from the fossil fuel industry. It was kind of like Big Tobacco saying cigarettes are healthy for you. They really missed an opportunity to take a constructive leadership posture on the issue. As I wrote to them at the time, I have no bias against the cannabis industry, safe recreational use, or legitimate medical applications of its products, but do have a strong bias against excessive avoidable energy use and associated greenhouse gases, wherever they can be found. Marijuana is hardly being singled out here. On the contrary, it has had a free ride for decades while all other energy uses have had to come into the 21st century.

"THE CANNABIS SECTOR CONTRIBUTES A NONTRIVIAL PERCENTAGE OF A STATE'S TOTAL GREENHOUSE GAS EMISSIONS – AND CONSUMERS HAVE AN OPPORTUNITY TO START MAKING PERSONAL CHOICES THAT ARE GOOD FOR THE PLANET."

Could you explain the concept of "embedded" energy use?

There is a widespread practice of quantifying the energy and carbon embedded (sometimes people say "embodied") in the making of stuff – for example, the packaging, transportation, and storage energy use associated with a quart of milk. For cannabis, this would include growing media, fertilizers, industrial CO^2 for injection into the growing space, carbon content of failed crops, and equipment manufacture. As one example, the very popular mineral-wool growing media is made by essentially melting rock (often with coal). This is a one-and-done product, with no recycling or other re-use. In our new study, we estimate that a 100ksf indoor grow would use 85,000 to 200,000 cubic feet of mineral wool per year (which goes to landfill), bumping the overall carbon footprint by 5 percent to 11 percent, depending on your assumptions.

In their recent study, Jason Quinn, Hailey Summers and Evan Sproul analyzed the impact of the energy and carbon embodied in waste, transportation, injected CO^2 and some agricultural inputs in some detail and found the inclusion of embedded energy to make a non-trivial contribution to the overall carbon footprint: it ranged almost 50 percent in milder climates to about 20 percent in more severe climates where relative energy use was greater.

There is also a parallel consideration of embedded water. Few people realize that it takes a lot of water to produce electricity. Those giant, iconic hourglass-shaped towers condense and cool a thermal power plant's exit water so that it can be safely reintroduced to the environment (rivers and oceans). Even more water per unit of energy output is evaporated from behind hydroelectric dams. Water is also needed for the routine washing of solar arrays. When considering this "hidden" use, it turns out that it takes far more water to grow cannabis indoors than outdoors. This is yet another inconvenient truth about indoor cultivation.

Why are policymakers so reluctant to address this cannabis carbon bomb?

It's an enigma, but my theories are that it is a combination of ignorance, being co-opted, and political inconvenience. Few policymakers have the patience to really understand energy systems, and, increasingly, even fewer are willing to take an unpopular position of concern about cannabis cultivation practices. I think people are wooed and/or wowed by all the bling of indoor cultivation. (The indoor industry unashamedly uses women in bathing suits to sell lighting equipment and such…) The industry is much better organized and moneyed than the sungrowers, and has a more aggressive and sophisticated lobbying presence. I think there is also a problem with local government, which is hungry for the sales-tax revenue, and the only way to get that is to keep cannabis cultivation within the city limits – which of course generally necessitates indoor cultivation because of land prices and odor-control considerations. And energy companies (often referred to as "20-percent partners" by growers who pay that proportion of their revenues for electricity) want the increased revenue, even though in other quarters they talk a good line about promoting climate solutions. I've even been (quite) disappointed with my own colleagues who are so exuberant about energy efficiency that they can't see that doing this in the particular case of cannabis is only optimizing the suboptimal. Meanwhile, environmental groups probably feel they would be in a bind by coming out against (indoor) cannabis, which many of their subscribers imbibe in and identify with in the increasingly blurred association with cannabis, nature, and green values.

At what point did cannabis and environmentalism diverge?

Cannabis was more or less synonymous with the social and intellectual movements of the 1960s: mind expansion, interconnected, the earth and its resources are finite and need to be stewarded rather than squandered. Of course, some (perhaps many) cannabis cultivators and users likely still hold those good values, but there was a divergence first when cultivation moved indoors (requiring intensive energy use) and later as the industry became "big business." It's important to say that, in parallel with this, many outdoor growers came to flaunt environmental values as well (illegal water diversions, use of illegal rodenticides, unpermitted road construction, for example). As is the case for almost all big businesses, profits and the game of skirting regulation often come before other goals. Though this is gradually improving through the environmental, social, and governance (ESG) movement, progress is slow and cannabis producers have not appeared in the vanguard. Most of the attention to sustainability among indoor producers does not get far beyond green-washing, with energy improvements limited to those that enhance profits and solar panels on the roof that look great but only meet a few percent of total energy needs.

So, who should be leading the charge: producers, investors, retailers, consumers, or policymakers?

All of the above.

Is there any other change that comes close to switching to outdoor growing in terms of environmental gains?

I'm afraid there is no viable alternative to outdoor cultivation. But the good news is that outdoor cultivation has helped people get high and healthy for 5,000 years. It's like they say: if it ain't broke, don't fix it.

It would only take 0.01 percent of US farmland to meet all US cannabis needs outdoors. The only crop requiring less land today is birdseed.

I used to think that creating "net-zero" indoor facilities--with high efficiency and all energy provided by solar panels--was the way to go. But, I later found that zeroing-out carbon emissions would require vastly more capital investment than this industry or its investors would tolerate. To provide all electricity needs for a typical grow requires around twenty times the building's land area in solar panel coverage, which is clearly a non-starter as well. I don't see that waiting decades for the grid to be clean is appropriate either, as there are many, many other electric loads that have no outdoor alternative that need to be first in line. Also, there are impacts of centralized renewable energy production and transmission, so we need to always optimize and minimize energy demand first before producing energy, be it with coal plants or wind turbines.

Do you think you'll see positive change in the cannabis industry within your lifetime?

I'm certainly hopeful, but there is no real indication that this is happening – or that the industry or policymakers are taking it seriously enough. Rather, we're seeing a lot of green-washing by this industry and willful ignorance by policymakers (local, state, and national). On the rare occasion when an indoor grower contacts me and says, "Hey, we're running our operation with no carbon emissions," I congratulate them, ask for the data, and then never hear from them again.

What has to happen for industry to take greenhouse gas emissions more seriously?

In decades of work on climate policy, we have massive evidence that free markets don't, on their own, properly value environmental costs. This is often because of market imperfections and distortions.Regulation is usually needed to resolve market failures. I think the only option for policymakers is to require that all cannabis cultivation occur outdoors (and, of course, follow sustainable practices). This makes it incumbent on them to remove disincentives (for example, subsidies to indoor growers for LED lights that just make unsubsidized sungrown less competitive)and barriers (for example, the interstate transport issue – growing indoors in Long Beach requires half the energy as growing in Anchorage). As for the industry itself, I think there needs to be an effort to dispel the mythology about the inferiority of sungrown cannabis. If best-practices are pursued, subsidies or favoritism to indoor cultivators stopped, and the tendency of indoor retailers to undermine the reputation of sungrown is curbed, the straight economics will ultimately show that outdoor can be the most profitable strategy.

WELCOME TO CALIFORNIA

How history and policy is shaping cannabis cultivation in the Golden State

The focus of the Berkeley Cannabis Research Center is cultivation; namely, understanding how cannabis is grown, the environmental consequences of these practices, and how social, economic, and regulatory forces influence grower behavior and corresponding environmental impacts. Ted Grantham is Co-Director of the Center and Assistant Cooperative Extension Specialist at UC Berkeley's Environmental Science, Policy and Management department. Here, he touches on how cannabis agriculture in California is evolving, as well as the burdens placed on growers seeking to enter California's legal market.

Has conservation always been part of the cannabis conversation?

Discussions around cannabis' environmental impact are nothing new. California has had a long history of cultivation, starting in the 1960s, but accelerating in the mid-90s with an explosion of medical marijuana farms that preceded statewide legalization. With this significant growth of cannabis in North Coast region came environmental harms. After California voters approved the Adult Use of Marijuana Act under Prop 64 in 2016, the state developed a legal framework for regulating cannabis cultivation that was oriented towards minimizing potential environmental impacts, especially to wildlife and water resources. Less attention was given to greenhouse gas emissions associated with indoor cultivation.

Is there a reason for that?

Most of California's cannabis is grown in outdoor and greenhouse settings and state regulations were focused on these types of operations, which have relatively low energy demands. Though there are certainly large indoor facilities, historically, they have been a smaller contributor to the market than in other states which do not share our climate. But one of the ironies of establishing stringent regulations around outdoor cultivation is that it may actually incentivize indoor production, which aren't subject to the same requirements. For example, indoor production often occurs in facilities that are tied into municipal water supplies, whereas outdoor cultivators tend rely on groundwater and surface water local to meet their irrigation needs. Withdrawals from these natural water sources are subject to regulations that municipal sources are not and meeting these requirements can be quite difficult and expensive. If indoor production continues to expand in California, a lot more attention should be given to greenhouse gas emissions from cannabis cultivation.

How do the environmental impacts of cannabis compare to other crops?

One of the most important distinctions is scale. The footprint of cannabis is actually very small compared to that of most other agricultural crops. The average farm size in northern California is about a quarter of an acre. In comparison to wine grapes, for example, which are grown in vineyards that often span hundreds of acres, cannabis farms are quite small. Now consider agriculture in California. Statewide, we have around 9 million acres under irrigated agricultural production – a fraction of one percent of that footprint is occupied by cannabis. But, the reason we are concerned about cannabis impacts has everything to do with where it is grown. Unlike most other agriculture in the state, which mostly occurs in large valleys, cannabis farms are concentrated in remote, upland watersheds, which is a consequence of decades of prohibition. Because of their location, cannabis farms tend to be in closer proximity to wildland areas, where impacts to fish and wildlife are more likely to occur. Though cannabis isn't a particularly thirsty crop (despite how it's portrayed in popular media coverage), we also have concerns about the water usage because supplies are naturally limited in the watersheds where farms are located. So even though water demand for a cannabis farm is low, relative to other crops, withdrawals can still have a big impact on streams and other ecologically sensitive habitats.

How is Berkeley's Cannabis Research Center engaging with these issues?

First and foremost, we are conducting research to establish a foundation of knowledge around cannabis cultivation practices and environmental impacts. Prior to legalization, it was quite difficult to conduct cannabis research and it's remarkable how few scientific studies have been conducted on cannabis agriculture. We've also been working to bring the regulatory community – the agencies responsible for issuing permits – and the grower community together, using scientific information to facilitate conversations around cannabis policy. These conversations are complicated by the fraught history between government law enforcement and growers. Understandably there is distrust on both sides. But if we want a

successful legal market for cannabis, this relationship needs to be rebuilt.

We are particularly interested in lowering unnecessary barriers to participation in the legal system. Despite being two or three years into the legalization program, the vast majority of cannabis growers in California do not have permits. We believe legal operations represent less than a quarter of the operations that exist statewide. So we still have a long way to go in the transition into a fully-legal market. There are some growers that will inevitably remain in the black market, but there are likely many more that would otherwise enter if regulations were streamlined.

Could you explain what makes the regulatory process difficult?

The difficulty lies in the way the law is structured. Though there is a statewide framework for issuing permits, the law has a local control provision which means every county must develop a local ordinance to allow for cannabis cultivation. Currently, fewer than half the counties in the state have those ordinances, which effectively means it is still illegal to grow cannabis in half the state. So even if growers were interested in entering the legal market, they cannot until a local ordinance is established.

Another key issue is cost. To get a permit, you are required to make infrastructure upgrades, for example, by redesigning your facility to minimize the risk of sediment runoff from roads and farm operations. This can cost upwards of $100,000. The permits themselves can also be quite expensive, not to mention the administrative burden that many growers are not necessarily equipped to navigate. Because growers have long operated at the fringes of society, permitting can be a foreign and challenging bureaucratic process.

When you speak to growers, are they generally receptive to these kinds of conversations?

Growers – at least the ones we speak to – are generally very supportive of our work. They view our research as helping to legitimize cannabis as an agricultural commodity, rather than an illicit drug. The stigma against cannabis growers is still quite prevalent; many people don't consider its cultivation a legitimate economic enterprise. However, most growers see themselves as farmers – not dissimilar to a grower of wine grapes who creates a product that is extremely valuable though arguably non-essential.

Speaking of cannabis as an agricultural product; how does its cultivation standards compare with those of other crops?

Most people are not aware that California's agricultural regulations are actually much more stringent for cannabis than for other crops. There are strict standards for cannabis cultivation practices that set requirements around the use of fertilizers, pesticides and water use, and limit the size and location of farms. And then there is the extremely rigorous testing processes (for heavy metals, pesticides, and contaminants) that go far beyond what's required for other crops. As there is still uncertainty around the human health impacts of consuming trace chemicals on cannabis, the state took a very conservative approach in setting thresholds. Whether warranted or not, from a grower's perspective, the burdens are much greater for cannabis than other crops. Of course, it is important to distinguish between growers who have received permits and comply with these regulations, and the vast majority of growers, who still operate on the black market and are unlikely to follow the same practices.

What can we do to support environmentally sustainable cannabis production?

Policies need to address barriers to compliance, especially the costs for infrastructure upgrades to satisfy permit requirements. The problem is that many of the federal programs designed to support other agricultural crops, through incentives such as matching funds, aren't available to cannabis growers. These programs need to be revised or the state needs to develop analogous programs that will provide more support for growers who currently don't have access to the resources needed to make the site improvements needed to obtain permits.

The fact also remains that, as long as cannabis is federally illegal, there will continue to be strong incentives for illegal growers. And that's because the black market is primarily supported by interstate commerce (illegal product crosses state lines to places where it will get a better price). Until cannabis is legalized at the federal level – effectively undercutting the black market – the state will struggle to bring growers into compliance. And the environment will continue to suffer.

WATER TO WINE

Meet the company challenging the concept of waste with a microbe-based process that converts organic material into fertilizer

Charles Smith, co-founder and CEO of Full Circle Microbes, is a self-confessed optimist. Smith believes that people working together can overcome any challenge. And, in this case, the challenge is waste – lots of it. The agricultural industry generates nearly 24 percent of global greenhouse gas emissions (GHG) – and treats a significant portion of each crop as waste. Smith and his co-founders found a way to help farmers and the environment by turning wasted organic material that harms the planet into sustainable fertilizer that helps it. Here, he tells us how.

What is Full Circle Microbes doing to tackle the environmental impact of cannabis cultivation?

We started Full Circle Microbes to address the environmental issues associated with wasting organic matter – and in recognition that there is great value potential in things that are treated as waste. Farms often produce organic "waste" in the same location that plants need to consume nutrients, making it a very natural fit for our on-site organics recycling process. In developing microbial inoculants that turn crop-residuals into bioavailable nutrients through on-farm recycling, we allow farmers to keep valuable nutrients where they're needed, improving their financial and environmental outlook.

How can organic waste help with our indoor grow problem?

Recycling organic waste on-site allows growers to reduce their reliance on nutrients and Ag chemicals that they ship to their location, reducing emissions in three key ways.

Less fertilizer consumption: synthetic nitrogen fertilizer is commonly made through the Haber-Bosch process – an extremely energy intensive approach to artificial nitrogen fixation that often relies on natural gas feedstocks that are sourced through fracking. Recapturing the nitrogen contained in the cannabis stalk and introducing beneficial microbes offers a much more environmentally-friendly alternative.

Reduce emissions from transportation of nutrients and offsite disposal: recapturing nutrients with on-site recycling and using less fertilizer means fewer trucks are required to transport fertilizer and therefore less GHG emissions from hauling. Similarly, avoiding the need to dispose of wasted organic matter offsite eliminates transportation emissions.

Eliminate emissions from incineration and improper disposal: some growers currently incinerate their leftover plant matter, releasing GHG emissions as smoke. Others render their wasted plant matter unusable and send it to the landfill, where organic matter often breaks down anaerobically, generating methane gas which is ~28 times more potent than carbon dioxide as a greenhouse gas.

Our research partners at University of Vermont recently generated data showing that recycling cannabis biomass with our inoculant also has pathogen suppressive effects, which can help growers reduce their reliance on chemical options that can be harmful to ecological and human health.

How do you transform harmful waste into valuable nutrients?

Organic matter becomes harmful waste when it's improperly disposed of in landfills and burn piles. The key to our organics recycling process is the microbial inoculant we've developed to efficiently turn leftover plant matter into a fertilizer substitute within 3–5 weeks. Whereas traditional composting relies on input balance and ongoing maintenance (watering and turning piles) in an effort to indirectly cultivate the microbial communities needed for organics recycling, our approach directly introduces the microbial communities that we

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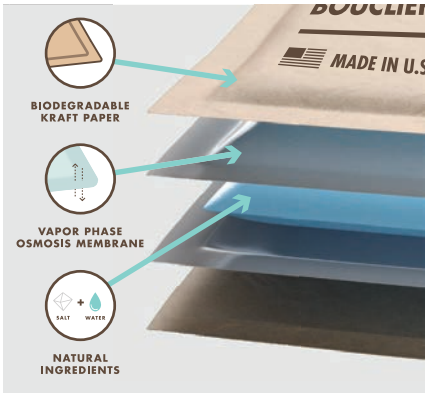

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know are most effective in recycling organic matter.

Our inoculant contains microbes that break down lignin, cellulose, and hemicellulose, the plant fibers that give the stalks its structure, but also shield the nutrients within it after the plant is harvested. Breaking through these tough polymers creates nutrient access, which is then increased by microbes that produce organic acids to further enhance nutrient bioavailability. Finally, our inoculant contains microbes that form beneficial relationships with the next generation of the plant and facilitate efficient nutrient uptake once the recycled biomass is reincorporated into the growth substrate.

Our inoculant can be applied to chipped up stalks and plant residuals either in a pile or a container – whichever works best for the individual grow.

What are your thoughts on cannabis' impact on the environment more generally?

I think the attention being paid to environmental issues with cannabis and the fact that many industry participants and consumers care very much about sustainability bodes well for positive changes in the industry. The research by Hailey M. Summers, Evan Sproul and Jason C. Quinn at Colorado State University is very important in understanding where things currently stand – and the need for action. As noted in their paper, certain regulatory and industry factors have pushed cultivation indoors, where huge amounts of energy are needed for lighting, HVAC, and other aspects of indoor cultivation. I believe many cultivators would welcome the opportunity to generate this energy through alternative energy sources, and I know of some growers that have been able to implement solar energy, Powerwalls, and geothermal power to fully supply their cultivation sites without fossil fuels. I'm hopeful that industry dynamics, regulatory updates, and consumer preferences for sustainability will all help to move the industry in a more environmentally-friendly direction.

Do you feel hopeful that the industry can and will become more sustainable?

I do feel hopeful, as I see both a need and desire for increased sustainability. The recent IPCC report shows overwhelming data that every industry needs to immediately work to reduce GHG. As a relatively young industry, I hope that cannabis will respond quickly to incorporating environmentalism into its foundation as it continues to grow. I also believe that consumers of cannabis products tend to be environmentally conscious and that consumer preferences will reward cultivators that produce a high-quality product in an environmentally-friendly way.

What needs to happen for the industry to adopt more earth-friendly processes?

Many cannabis cultivators want to be sustainable and there are several factors that can help push the industry in that direction. The first is continued innovation. Our technology allows growers to increase sellable yields, while reducing nutrient costs and becoming more sustainable. There's a myth that helping the environment means hurting your business, but this absolutely does not need to be the case. The second is consumer preference. Cannabis consumers tend to care about the environment, and I believe we'll see an increasing preference for sustainable practices as the industry matures and brand recognition increases. The third is a regulatory focus on sustainability. I am seeing regulatory entities paying more attention to the environmental impact of their policies and I'm hopeful that sustainable production can become a key tenant of future regulatory frameworks.

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HPLC Method to Differentiate Four THC Stereoisomers Formed From Δ⁹-THC Degradation

Discover a robust, chiral HPLC stationary phase method to separate Δ¹⁰-THC and Δ⁶ᵃ,¹⁰ᵃ-THC isomers produced from Δ⁹-THC degradation

By Jeffrey B. Williams, Kathleen B. Calati, Kirk W. Hering, Roxanne E. Franckowski, Weston J. Umstead and Donna M. Iula

Degradation of Δ⁹-THC to Δ¹⁰-THC and Δ⁶ᵃ,¹⁰ᵃ-THC isomers provides a challenging separation in Cannabis-derived products. The use of an immobilized cellulose chiral column under normal-phase liquid chromatography conditions provides an analytical method to fully separate these four THC isomers for identification and accurate determination of potency.

As the primary phytocannabinoid associated with psychoactive properties, Δ⁹-THC is crucial to the determination of potency for extracts, edibles, and other Cannabis-derived products. The additional processing required for providing these Cannabis products may result in their degradation, forming isomers that can be misidentified and provide invalid potency claims. Δ⁹-THC can isomerize to two diastereomers, (6aR,9S)-Δ¹⁰-THC and (6aR,9R)-Δ¹⁰-THC. These two distinct stereoisomers may undergo additional isomerization to form a pair of enantiomers, providing 9(S)-Δ⁶ᵃ,¹⁰ᵃ-THC and 9(R)-Δ⁶ᵃ,¹⁰ᵃ-THC, respectively (Figure 1).

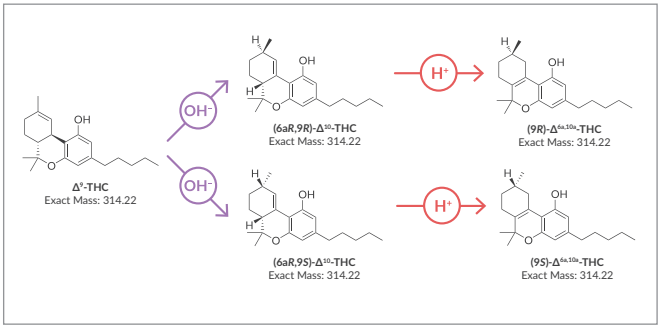
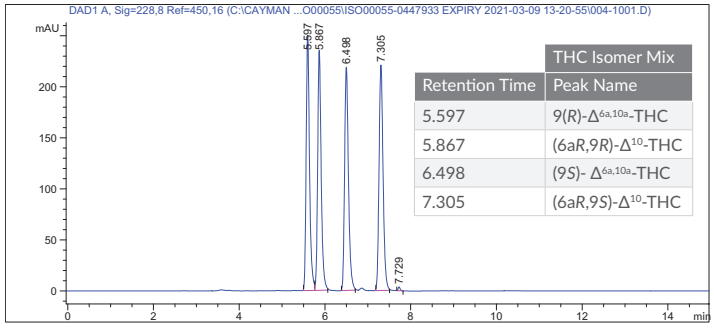


Figure 1. Isomerization of Δ⁹-THC under first basic (OH^-) and then acidic (H^+) conditions can lead to several structurally similar isomers

The stereochemical similarities between the Δ¹⁰-THC and Δ⁶ᵃ,¹⁰ᵃ-THC isomers are particularly challenging to fully resolve under typical reversed-phase liquid chromatography. Additionally, the Δ⁶ᵃ,¹⁰ᵃ-THC enantiomers are not separable without the use of a chiral stationary phase.

A chiral column under normal-phase liquid chromatography (NPLC) conditions fully separated these THC isomers (Figure 2). Chiral column CHIRALPAK® IB N-3 (250 x 4.6 mm, 3 µm) under NPLC conditions, controlled at 30°C, was used. Elution was accomplished with mobile phase 95:5 Hexane:Isopropyl Alcohol (IPA) at 0.85 ml/min for 15 minutes. A 1 µl injection of a 1 mg/ml solution in IPA was monitored at 228 nm. The neat materials were formulated into certified reference material (CRM) solutions. To provide CRMs with optimal stability, each of the solutions were prepared as a 1 mg/ml solution in acetonitrile. Although acetonitrile and hexane are immiscible, the inclusion of IPA to the mobile phase maintains the baseline resolution of the analytes despite the diluent. This method may be used to develop testing methods to resolve and accurately quantify ingredients in Cannabis products.

Normal-Phase HPLC



THC Isomer Mix	
Retention Time	Peak Name
5.597	9(*R*)-Δ⁶ᵃ,¹⁰ᵃ-THC
5.867	(6a*R*,9*R*)-Δ¹⁰-THC
6.498	(9*S*)- Δ⁶ᵃ,¹⁰ᵃ-THC
7.305	(6a*R*,9*S*)-Δ¹⁰-THC

NPLC Conditions

Instrument	Agilent 1100 Series
Column	CHIRALPAK® IB N-3 (250 x 4.6 mm, 3 µm)
Mobile Phase	A: 95:5 Hexane:Isopropyl Alcohol
Flow Rate	0.85 ml/min
Column Temp.	30°C
Wavelength	UV monitored at 228 nm

Figure 2. A co-injection of all four isomers in acetonitrile with the NPLC method

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Analysis of Pesticide Residues, Mycotoxins and Potency in Cannabis using QuEChERS Extraction

Introducing the QuEChERS method for the simultaneous analysis of cannabis for 47 pesticides, 5 mycotoxins and 3 cannabinoids. Most of the LC-MS/MS amenable compounds on the Massachusetts and Nevada monitoring lists of pesticides and mycotoxins are included within the application note. Sample purification is carried out using UCT's cleanup product SpinFiltr™, which combines the convenience of classical dispersive-SPE (dSPE) with an ultrafiltration tube containing a 0.2 µm filter membrane to simultaneously remove unwanted matrix components and filter the sample prior to LC or GC analysis. The SpinFiltr™ dSPE tube uses PSA, C18 and ChloroFiltr® sorbents for sample cleanup. ChloroFiltr® is a unique polymeric sorbent designed for the removal of chlorophyll and, unlike graphitized carbon black (GCB), does not result in the loss of planar analytes. Liquid chromatography, using a Selectra® Aqueous C18 column, coupled to tandem mass spectrometry (LC-MS/MS) is used for analysis of the pesticides, mycotoxins and cannabinoids.

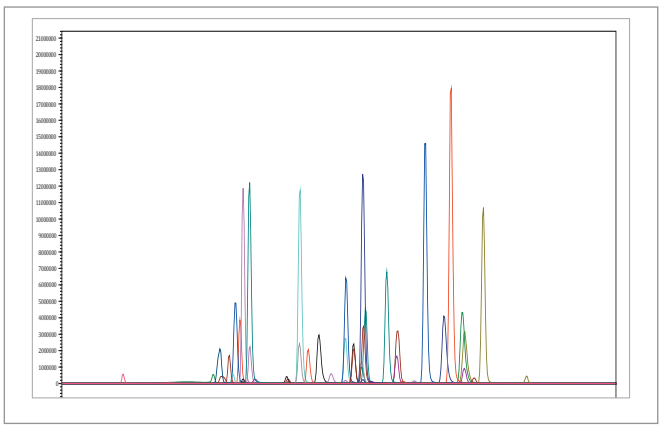

Figure 1: Chromatogram showing extracted sample of pesticides at 5ng/ml

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Dr (No) Pain

Sitting Down With… Mikael Sodergren, Managing Director & Academic Lead, Sapphire Medical Clinics, Research Director, EMMAC Life Sciences, Consultant Hepatopancreatobiliary Surgeon and Honorary Senior Clinical Lecturer, Imperial College London, UK.

What did you want to be when you were growing up?

I wanted to be a cowboy until I was six or seven. After that, a tennis professional. Then, when I was 16, I settled on being a doctor. Now, I'm pretty happy but always intrigued what life as a cowboy would be like.

So how did you end up in cannabis?

I'm a surgeon by training. One day a week, I do operations on complex cancers of the pancreas and liver. The natural extension to that clinical interest was research around (pancreatic) cancer biology. In 2018, the Nobel Prize was awarded for cancer immunotherapy and we suddenly realized we'd been barking up the wrong tree. The real prize in the treatment of cancer is to focus not on the cancer cells, but on the immune system.

After that, I became involved with looking at ways we can modulate the immune system, which is how I stumbled across CBD – a very effective anti-inflammatory. At the time, it hadn't been mapped out on a scientific level in relation to cancer biology. We could see the therapeutic benefit in combining CBD with cytotoxic chemotherapies for pancreatic cancer – we just didn't know how. It was a black box.

Eventually, we secured funding for the Imperial College Medical Cannabis Research Group, which I now lead.

As well as cancer biology, we research another of my clinical interests: pain. As a surgeon, I unfortunately cause people pain by default – a short-term disadvantage we try to address in surgery. We've been trying to move away from systemic opioids, which have negative effects on respiratory function and predispose patients to chest infections, ultimately keeping them in hospital longer. Cannabis is a promising alternative.

Where does Sapphire Medical Clinics come into this?

My colleagues and I set up Sapphire Medical Clinics around the time the law changed, almost as an extension of our research. Having established what cannabis can (and can't) do naturally leads to one of two things: either conducting clinical trials for marked authorization or prescribing medicines under certain circumstances off-label. We saw a really interesting opportunity in collecting that data so that we could help eliminate the medical cannabis knowledge gap and, ultimately, allow more people to access these medicines for free on the NHS.

Is it frustrating to know that medical cannabis is legal, but still so difficult to access?

It's heartbreaking to see patients who obviously derive great benefit from the medications, but can't access them for free like other treatments on the NHS. But at the same time, I can see how it has happened. We have a system in place in the UK in which we undertake cost-effectiveness analysis to establish whether taxpayers are prepared to foot the bill on a population level for certain medicines. I don't think cannabis should be treated any differently.

What are the barriers to getting data on this scale?

Funding is obviously key. We need everyone – policymakers, regulators, medical professionals, academics – to sing from the same hymn sheet to work out these compounds' medical uses. That requires short-term solutions. One of the positive things in the UK is that NIHR, a major funding body, has designated calls for research into cannabis-based medicinesh. Despite that, we haven't seen any large-scale randomized controlled trials, in part because they are so expensive. We need to prioritize and accelerate this, because we urgently need to resolve the mismatch between our knowledge and patients seeking treatment.

Why hasn't it happened yet?

It goes without saying that the pandemic has slowed things down. Clinical research was essentially put on hold for a year. But a group effort almost certainly requires national infrastructure. Hopefully, in this post-Brexit era, more resources at a government level will be dedicated to these kinds of initiatives between industry and academia.

Do you think the rise in popularity of CBD is helping or hindering medical cannabis advocacy efforts?

A bit of both. It's certainly not helpful to read tabloid articles claiming that CBD cures everything under the sun (because it doesn't), but it clearly highlights the fact that we need to understand CBD better. Public perception is distorted by the fact that not only can a doctor prescribe CBD, but you can also buy it on the high street. So is it a medicine or not?

Can you tell us more about your own research activities?

We're doing some really interesting work on pain, essentially trying to untangle the spaghetti of different compounds present in the plant. Right now, we're looking at three individual cannabinoids and seeing how, when combined in different proportions and doses, they create an analgesic effect (or not).

So far, we've been able to decrease the dose of THC by adding another cannabinoid without reducing the analgesic effect in vitro. I'm excited to develop that research further, and hopefully translate it to human studies soon.

If you weren't doing this, what would you be doing?

I'd be involved in drug development for cancer with immunotherapies. I still hope that I will someday cure cancer – but, although there are lots of people working on immunotherapy at the moment, there are far fewer looking to plug the gaps in our understanding of medical cannabis.

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