Cannabis on Collision Course with Science

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Cannabis Extracts and Their Sensory Experience

Unearthing the nuances that define a specific cultivar

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Letter from the Editor

December 18, 2018

I'm increasingly amazed at how much our industry has grown in my brief time at both T&T and Extraction Magazine. I get animated thinking of the volume of molecules in the cannabis plant we have discovered with medicinal properties. The tally of nearly 300 cannabinoids and terpenes contained inside what Kevin Koby calls "goodness factories" is an astounding prospect, given all the possible permutations a unique combination of these molecules can entail.

We've seen the industry migrating towards that path already. Phyto-pharmaceutical formulations are increasingly common, as researchers dissect the cannabis genotype to isolate and characterize singular molecules. Once establishing that baseline, one can complement the studied cannabinoid or terpene with an additional one, and evaluate what utility that formulation serves. We truly could be witnessing the creation of a panacea that had previously been forbidden in Western society.

This issue, like its T&T counterpart on the flip side, predominantly considers the sensory attributes of cannabis concentrates and extracts. Terpenes are usurping some of the spotlight previously held by cannabinoids, and rightfully so, given the diverse aromas and flavors alternate terpene profiles in different cultivars can offer. Manufacturers show increasing interest in preserving the native plant's chemistry, whether when making a product like hash, a full-spectrum oil, or even a topical formulation.

The sensory aspects of cannabis concentrates segue nicely into edibles. Although my home state of Pennsylvania has not yet recognized the need for vending this alternative ingestion method, the culinary artistry one can practice in their own home can be a prosperous and rewarding adventure (if the starting material is cost-effective). What's important to recognize is that creating cannabis-infused foods or beverages at home begins with an efficient extraction of the cannabinoids. Why squander what's desired? There are devices available to assist in this process beyond standard kitchenware. It's also paramount to master decarboxylation such that the full physiological effects of cannabinoid ingestion can be realized. And with terpene formulators refining their recreations of select cannabis varieties, the DIY edible designer can easily re-incorporate lost terpenes into their final product. Our friend Luis from Pastelaria 6 Sentidos in Portugal provided a wonderful infused holiday pudding recipe that we've included for you. If you make and enjoy it, let him know.

I'll leave you with a quote from AC Braddock at Eden Labs, whose article can be found in this issue too. I liked it so much, I wanted to showcase it twice:

"…We already, instinctually, know cannabis exists to heal us physically and culturally. We know it. We experience it with every sense and fiber of our humanity."

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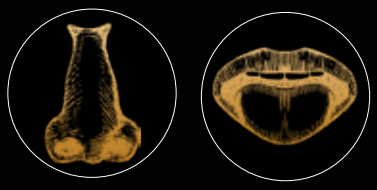
Cannabis Secondary Metabolites

By Frenchy Cannoli



Trichomes are epidermal protuberances covering the leaves, bracts, and stems of plants. The vast diversity of trichomes expressed in the plant kingdom can be loosely classified into two main types: non-glandular and glandular.

Non-glandular trichomes can best be described as the plant's hair while glandular trichomes are made of globular structures supported by stalks, which produce and store around 200,000 organic compounds, the secondary metabolites. Alkaloids, phenolic substances, and terpenes, the three major groups of secondary metabolites, are very powerful, inducing and deterring chemicals that regulate the relationship existing between plants, insects, and humans. [1]

The formation of these compounds is not related to the growth, development or reproduction of the plant; they are the chemical defensive and survival tools of the plant kingdom adapting to an everchanging environment. The plant kingdom has been producing glandular trichomes for over 300 million years [2], and while science has an understanding of the formation of terpenes, cannabinoids and other compounds found in glandular trichomes, we are still mostly guessing their various functions and roles in the plant kingdom.

In addition to phenolics and terpenes, cannabis offers humanity over a hundred unique, therapeutic and psychoactive cannabinoids produced through a series of enzymatic synthases in the glandular trichomes. Terpenoids and cannabinoids are the most influential and dominant compounds of cannabis' secondary metabolite expression. While cannabinoids are typically considered to be unique to cannabis (although product manufacturers are touting cannabidiol extracted from hops and evergreen bark), there are no known terpenes specific to cannabis.
The terpene's lipophilicity allows binding of the terpenes to the lipophilic inner core of cells, which increases permeability and facilitates the absorption of cannabinoids. [3] Additionally, this terpene property possibly facilitates the passage of terpenes across the blood-brain barrier when smoking. Furthermore, cannabis terpenes modulate the psychoactive properties of THC by acting on their receptors, and they have the ability to improve THC absorption by the lungs. [3]

Considering that terpenes facilitate the absorption of cannabinoids and modulate their interaction, it is safe to say that they are fundamental to the overall psychoactive and medicinal experience of cannabis. However, terpenes are also very potent compounds which can cause serious adverse effects; high doses of pure extracted terpenes can be extremely toxic. Such power of life and death is the reflection of the primordial hegemony of terpenes in the ecological balance of the planet. [4] Likewise, phenolic compounds have "constitutive and induced roles in toxicity and feeding deterrence in insects." [4] Phenol toxicity can be associated with the "consumption of phenolic-rich foods or beverages and various diseases, such as stroke, cardiovascular disease, and cancer and neurologic disorders such as dementia/AD." [4]

Comparatively, the 100+ cannabinoids resulting from the biosynthesis of phenols and terpenes and the terpene concentrations of cannabis plants have very little toxicity. These phytochemicals also offer greater medicinal potential when together than as individual constituents. The cannabis biosynthesis of its secondary metabolites could be

perceived as the transformation of two potentially toxic compounds into a wide array of safe medicinal compounds.

Given that cannabis plants produce something like 200 known terpenes and over 100 known cannabinoids, the possible combinations are abundant. Western medicine derived cannabis treatments of the future will not be based solely on cannabinoid medicinal characteristics. Rather, the terpene's ability to modulate a cannabinoid's medicinal and psychoactive properties can be harnessed to treat specific illnesses and will most certainly be a decisive force in the future of cannabis therapy.

However, the uniqueness and diversity of cannabis terpene profiles is certainly the most vital aspect of its psychoactive and therapeutic attributes. These profiles are made of vast terpene arrays, many at levels that are challenging to measure, making the cannabis terpene profile difficult to duplicate and as such invaluable. The preservation of the uniqueness of a terpene profile is a vital element of the quality a Hashishin seeks. Cannabis provides us with two very different and unique profiles, an amazing gift that furthers our ability to create diversity.

Cannabis has a distinctive terpene profile at the peak of its flowering cycle which changes drastically during the drying and curing of the flowers, primarily due to the loss of highly volatile terpenes, but also to the binding of the terpene polymers into a new configuration offering its own profile uniqueness. [5] This new terpene profile will modulate the medicinal and psychoactive properties of the cultivar differently; the greater the difference between the two terpene profiles, the more diverse the experience will be.

A Hashishin is very much like a winemaker; we seek perfection within the fruit to achieve greatness. A winemaker works solely with the ripest fruits holding the most sugar in their mass, the source of the wine's characteristics and the primordial element of the transformation into wine through the fermentation process.

A Hashishin works solely with the ripest trichomes, holding the most cannabinoids and terpenes in its resin. The plant's secondary metabolite expression is the source of the hashish characteristics; and the primordial elements of the transformation process are as yet unknown.

The transformation of loose resin into a compact mass of resin through heat and pressure is a delicate yet known process.

A certain level of applied heat and time is necessary (180°F to 220°F for 30 minutes to one hour) to lose the carboxylic acid group attached to the cannabinoids, thereby unlocking the psychoactive potential of the cannabinoids. Many terpenes are extremely volatile, and while heat is mandatory to the decarboxylation process, heat is also the nemesis of terpene retention. While there is a powerful emanation of terpenes during the pressing process which indicates a loss, the resin nonetheless seems to hold an abundant amount of terpenes locked in its mass and as such is protected from degradation. The traditional hashish pressing methodology can result in a loss of the most volatile terpenes, and is also the source of transformation whereby 50+ rare compounds can be formed that are not found in fresh or cured cannabis, while their precursors are. [6]

Pressing loose trichome heads into Hashish is like transforming, through the fermentation process, crushed whole grapes harvested and selected at the peak of their maturity into the new substance that is wine. The chemical reaction triggered by pressing traditional hashish has never been studied, and while being a world apart from fermentation, it has the same power of transformation, nonetheless. The high level of corrosiveness of the terpenes has to be central to the process by dissolving the membranes, lipids and other constituents of the trichome heads into the resin mass.

Sieving and collecting whole and perfectly mature resin heads is like harvesting the ripest clusters of grapes, and most anyone, with a little knowledge and dedication, can manage. Making wine is, on the other hand, an art that requires a deep knowledge of the fermentation process and its transformative power, the cultivar's potential for transformation, the bottling as well as the aging, and the necessary conditions to enhance quality through time.

Making hashish requires as deep a knowledge, and while I have experienced the transformative power of traditional pressing all my life, the science behind the process is mandatory to perfect the pressing procedure and harnessing the potential power of the final expression of the unique natural wonder that is the cannabis plant's secondary metabolites.

Frenchy Cannoli is a consultant, educator, and writer in the cannabis industry with special focus on hash-making using traditional methods. Frenchy can be reached through his website at: www.frenchycannoli.com or seen on Instagram @frenchycannoli.

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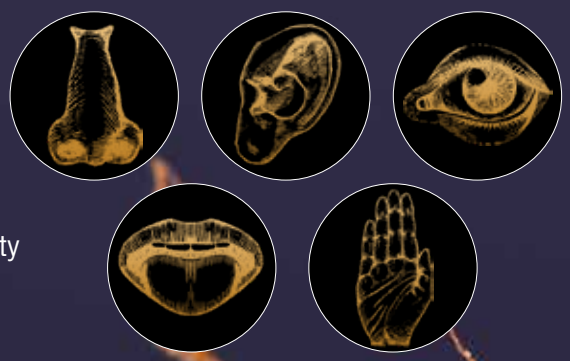
Sniffing Around Prospective Mates, Bloodletting, and Instinctually Sensing the Power of Cannabis

By A.C. Braddock, Eden Labs



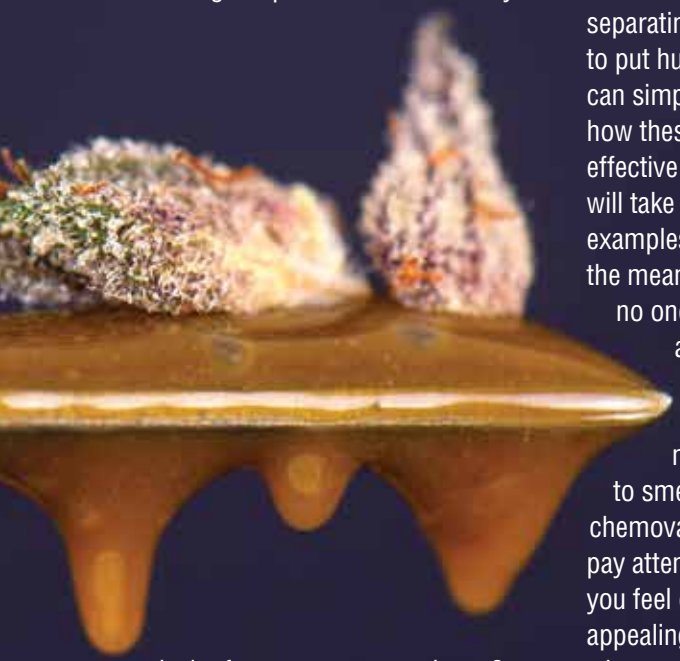
I have an exceptionally good sense of smell and I relish when I catch a whiff of something that viscerally transports me to particular place and time that has been otherwise forgotten. Boom! Suddenly I am eight-years-old again and I *feel* the moment. Our sense of smell is most similar to a sixth sense because it transports us physically, mentally and emotionally more than any other sense. Smells travel through our olfactory bulb, which is the smell analyzing portion of our brain that is closely linked to our amygdala and hippocampus regions that handle memory and emotion. Smell is emotive, but it also plays a role in selecting a mate based on our genes and immune systems. [1] Yeah, when you find someone's body odor offensive it's likely they are not a good mate; if you don't really mind their odor it's a match made in your genes. Sniffing around on prospective mates is theorized to be how we came to find our lips brushing against each other. The kiss is born.

Our endocannabinoid system (ECS) was discovered very recently in 1992 [2] and not long after that, the "entourage effect." Through cannabis research, modern science has made it more widely accepted that aromatherapy is real, and cannabis helps us create a state of homeostasis through a match between our ECS and the plant. The whole plant and nothing but the plant, naturally. It does this by attracting us with smell, taste, the beauty of its flower, and the effects we feel when we imbibe it. It relaxes us; makes us laugh; helps us feel sexy, sleepy, hungry, not hungry and escape physical and emotional pain, neurological illness and traumatic brain injury, etc. We have a long way to go to fully understand how cannabis works with our ECS and why. We are living in a time that will change how we look at human health and treat illness.

Modern medical science is supporting a new approach to *individualized* health based on our unique physiological, emotional and mental needs. One pill for all of humanity has not worked all that well and in the case of some drugs like opiates, it has devastated the lives of millions of people and their loved ones. [3] Do we want to keep going down this path? It's like the practice of bloodletting. Death by a thousand cuts. It's old science that has been marketed as the only solution, but we now know it's not. We *know* it. We smell cannabis and are instantly relaxed or energized. We stand in front of it and are mysteriously thrilled by the sight of it. We share it and feel deep connections. We use it and medical miracles occur. Its value is being slowly, clinically proven, but we already, instinctually, *know* cannabis exists to heal us physically and culturally. We *know* it. We experience it with every sense and fiber of our humanity.

Cannabis is also showing us what NOT to do. From trials already performed on CBD that show it has a bell curve (look it up) in efficacy over time and that utilizing the whole plant as a genetically altered, but still intact whole plant profile, increases CBD's efficacy. Taking out another powerful molecule of the plant, like THC, to treat illness has also been a flop. Yet, old medical science still wants to keep ignoring the ECS and the entourage effect while our senses are telling us that the plant is a healthy genetic match.

A single molecule of the plant does not create homeostasis nor does it have much sensory impact. Think of it this way: you are hungry, feeling like you want to treat yourself to a nice steak (I apologize, no vegan option in this illustration) dinner. The steak arrives and it has no color, it has no smell, it has no taste, no B-12, no zinc, no niacin, no selenium. It has nothing but protein. Does it satisfy your desire for a sensory experience? Does it satisfy your dietary needs? What would happen if this was the only protein you ate? You would become very ill and very unfulfilled in every sense. They can grow protein in a lab and they can grow cannabinoids in a lab, too, from yeasts. That just sounds unappealing, but amping up a particular molecule profile in a whole-plant formulation might make sense.



You know what is worrisome right now? All the hype around CBD. Not that the efficacy of CBD is hype, but there are people who do not know what the ECS is, have never seen the plant, have never smelled it, have never experienced it in any form much less in a whole-plant form. These companies are taking CBD from who knows where and putting minuscule amounts of it in products and marketing it as a health and wellness product. Guess what? It isn't going to work. Even your grandfather, who really does want to stop taking a pharmaceutical drug to treat his aches and pains, will try this pathetic representation of the plant and say "snake oil" and never try it or any other cannabis product again.

Cannabis graciously lends itself to genetic modification. Therefore, instead of separating out all of its parts and trying to put humpty dumpty back together, you can simply breed for them. Yes, studying how these specific new chemovars are effective for specific ECS deficiencies will take time, but there are plenty of examples where fast is not preferred. In the meantime, the whole plant has hurt no one and continues to wholly amaze and delight us in every way.

Try this little experiment. The next time you have an opportunity to smell three to six differing chemovars (strains are old terminology), pay attention to how that smell makes you feel or if there is something especially appealing about it. Think of it like smelling wines or perfumes. Look for the high notes (pun intended) or the woodsy, piney, fruity, sour, skunky notes. Now try each one. Does the effect relate to how it made you feel when you simply smelled it? How connected are you to the plant through your own sensory impressions? You are very connected. Your senses are there to make that connection for you.

Fortunately, there are companies now who are NOT labeling their products as "Sativa" and "Indica," but are listing the chemical profiles of the plant and what makes up that chemovar. Is your product development team looking to the future of ECS research and creating products that support the science, playing catch up or simply trying to yell the loudest about their lightly CBD-infused product? If they are still trying to get an extremely high THC content, you are missing two vast and upcoming demographics: women and people over 50. These demographics want to know what is in the product and how it was made; if it is effective, they will try other products. We are creating a new way to promote health and well-being. Now is the time to do it right or cripple the industry and our budding relationship between our ECS and cannabis.

Other than your five senses, you have common sense, your 6th sense, horse sense, intuition, gut. Whatever you want to call it, pay attention. The species survived on it and it is how you will survive and flourish in this new arena of modern medical science and is the springboard for individualized medicine.

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Skin in the Game: How Topicals Have Provided an Effective Cannabinoid Delivery System

By Steven Bennett, Prescott Logic Technologies, LLC.

The evolution of cannabis over the past five years has been nothing short of staggering. It does not seem like very long ago that we had only two options: grass or hash – the latter only if you were lucky enough to know the right people. Additionally, there were historically only two methods of consumption: combustion or ingestion. Whereas these modes of delivery are still the most popular to date, even less informed cannabis users cannot help noticing the array of products and brands at the local dispensary. Now there is much more available to consumers than simply flower and concentrates. Consumers today have a wide range of options between producers, cultivars, and extract types (BHO, CO_2, ethanol, rosin press, water hash). As impressive as this growing list of options might be, many people are against smoking anything. And we've all heard plenty of stories around the campfire of people eating too much and experiencing erratic, unpredictable intoxication. This outlook, in my opinion, does not help our cause. As much as we all might enjoy these products, it is very difficult to convince the more risk-averse patients to try cannabis. There are many people who believe that cannabis can be therapeutic but will simply never overcome the stigma associated with the smell of burning flower.

Between topicals, beverages, metered-dose inhalers, capsules, and powdered cannabis as a food additive, people are starting to see the bigger picture. That is, standardized forms of dosing have become more prevalent throughout the industry. As such, there are more products that resemble pharmaceuticals making their way to the marketplace.

Even more, companies like GW Pharmaceuticals have been researching the use of cannabinoid therapy for very specific conditions, like juvenile epilepsy, and with proven benefits. The scientific validation of the use of cannabis for specific disorders has gained momentum, to say the least, and our understanding of the pharmacology involved has been steadily improving. Whereas all this development is insightful and, in some cases statistically significant, I summon the thought of your local pharmacy. Certainly "validated medications" are available in the back of the store with a prescription, but there are myriad other products available to consumers without a doctor's consent. Many therapeutic remedies available today are over-the-counter (OTC). Some are even natural health products (NHPs). The ingredients are regarded as generally safe, and in many instances, products are "clinically proven" to eliminate instances of bad breath and headaches, for example. That is, these products are available if you want them and "work" for some folks, but not everyone agrees that ibuprofen is better than aspirin. Take a walk down the aisles past decongestants, feminine hygiene products, and baby diapers, and you will quickly discover that one particular class of products takes up a lot of real estate – skin care.

Whether you contracted poison ivy or just need to cleanse your pores and moisturize, the pharmacies are loaded up on products destined for contact with the skin – the topicals. The skin, or integumentary system, is the largest organ in (rather "on") the human body. Although it serves as a barrier to the outside world of dirt, bacteria, and chemicals, it is an

intricate system of cells that is designed to be at equilibrium with the environment. Consider the effectiveness of a plastic bag to protect you from the rain; there is no exchange of air or moisture, and the individual is immediately overheated and wet from perspiration. This fault is why the skin has evolved over time to exchange heat, moisture, and is even involved in the photosynthesis of vitamin D3 (cholecalciferol). Somewhat contrary to the skin's function as a protective barrier, it also allows for the bidirectional flow of certain molecules– an aspect that lends even further to the therapeutic use of cannabis bioactives.

It's important to distinguish first between "transdermal" and "topical" as these words have very different meanings. That said, this author suggests that the words represent two ends on the continuum of "things applied to the skin," as some of the products available arguably contain elements of both. Whereas full descriptions of the science involved here might fall beyond the scope of this particular article, it is important that patients are cognizant of the broader strokes involved with these applications of cannabis. Simply, a transdermal product -- be it a lotion or patch -- contains other compounds termed "penetrants" that can actually permeabilize the cells of the skin and carry molecules, which would otherwise sit on the skin surface, deeper into the surrounding tissues and even all the way into the bloodstream. Although the precise mechanisms of action are more involved and, in some cases, still hotly debated by the scientific community, the fact is that pharmaceutical and nutraceutical companies have been utilizing these technologies for decades to sell products to consumers. As such, some products, like fentanyl, can be (in theory) slowly titrated into the bloodstream rather than through more abusive-prone oral delivery. The latter method carries the added challenge of "hepatic first pass" or upwards of 90% destruction of active pharmaceutical ingredient (API) by liver enzymes. Topicals, however, are liberally applied to the skin with varying degrees of penetration. Long-chain fatty acids, for example, like oleic acid, have been used to provide a "natural" means of achieving some level of penetration for alleviation of arthritis pain. A compound like dimethyl sulfoxide (DMSO), a classic "proof of principle" skin penetrant, would slide the product from the topical to the transdermal side of the spectrum. Conversely, compounds like lanolin and aloe vera are topical moisturizers with little to no penetrating ability.

Cannabis producers have been prolific in offering products that can be used to treat skin disorders like psoriasis, localized pain in muscles or joints, as well as systemic delivery to distal regions of the body, including the brain, where cannabinoids have been shown conclusively to interact with mu opiate receptors. Moreover, users of topical products often attest to the efficacy of non-activated

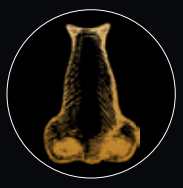
or non-decarboxylated or carboxylated cannabinoids – that is, the cannabinoid acids like THCa, which have been reported to have limited psychoactivity due to three-dimensional (steric) hinderance of the carboxylic acid (COOH) moiety, or group both at the level of the blood-brain barrier (BBB) and on individual receptors. Notwithstanding, the acid forms of the cannabinoids – those produced naturally by the plant – also exhibit physiological effects that we are only beginning to understand scientifically.

This understanding brings us to an interesting message about cannabis, let alone products in general: they appeal to different people. The topicals, and even the transdermals, offer consumers options that are destigmatized and less associated with intoxication or abuse than some of the more conspicuous means of consumption, but they *still* carry great therapeutic benefit. For instance, states like Colorado and California are identifying the "over 65" individuals as being some of the most avid proponents of topicals today. Transdermal patches, through mechanisms that we need to clearly define, are proving to be very effective for certain forms of chronic pain. Topicals include products like lotions, salves, gels, ointments, massage oils, and even sexual lubricants, which really drive the product development game for producers. Additionally, the topicals market allows groups to take advantage of existing over-the-counter formulations when combined with existing NHPs. Some of the best-selling salves, as a prime example, contain other natural remedies that were already deemed "effective." Whereas some regulatory bodies may take issue with this "piggyback" approach on approved compounds, they will be hard-pressed to determine that the product is somehow harmful with the addition of cannabis, even if the cannabis industry is restricted from advertising that it is *better.*

Despite the perceived lack of true medical application in the use of say, a lotion, this method does highlight one very salient aspect of medical philosophy: medicine is the interface of hard scientific data with patient feedback. As such, if someone claims relief from the use of a topical product – even one without activated cannabinoids or a naturally-derived penetrant – who is going to argue with them? As important as the mechanistic science may be to some, the fact that more people are claiming relief through cannabis use is unequivocal. Patients should not need to wait for the labors of the scientific community to tell them what they can take to treat their ailment; these patients should instead tell producers what works while the science catches up. In the meantime, if someone tells me that a cannabis-infused bath relieves their back pain, I believe them implicitly. The responsibility lies on science to explain the how's and why's, but not while depriving people of relief along the way as we have for over 80 years of cannabis prohibition (outlawed in 1937-stricter laws since 1977).

Cannabis Extracts and Their Sensory Experiences

By Kevin Koby, Abstrax Tech



There's nothing quite like walking through a field of flowering cannabis. The stunning experience, while quite pleasant for the type reading this magazine, can overwhelm people unaccustomed to aromas of such depth. For those uninitiated, it's the feeling of deeply breathing in a freshly-stocked flower shop, but times a thousand. The thing is, just like the floral diversity visible within that store, cannabis also has variations. There are a wide range of cultivars, each in possession of their own unique smell. Depending on the plant in question, the scent of a ripe pot grow can vary from a citric tang to the fermentation notable in hard-rind cheeses, or even the smell of human feet after a gym session. Relative to the unique characteristics inherent to a specific type of cannabis, those who enjoy it will encounter a spectrum of sensory experience, which is explored below.

A sensory experience is created through our perception of physical stimuli. But, while perception can differ from person-to-person, that external stimulus is constant. So, if the same thing happens to two different people, they might experience it differently, e.g., smoking from a dab rig for the first time. However, virtually everyone can agree upon the sensations related to consistent physical stimulus like heat, cold, etc. The primary stimulus of cannabis is the magnitude of its smell. It's that impact associated with smelling heavy, musky bud or the lack thereof when sniffing a faintly grassy nug. These differences, both in scent and potency, are determined by a plant's terpene profile. The chemicals we call terpenes are manufactured by the plant in a goodness factory called the trichome. These trichomes are predominantly located on cannabis flowers, where they volatize terpenes. The larger and more frequent the trichome, the more plentiful the terpenes.

Terpenes grow, accumulate, and many disperse through the air in a molecular cocktail containing a multitude of other compounds. At this point in the industry, the term "terpene profile" is almost cliché, because cannabis' sensory experience is now understood to be influenced by compounds other than terpene, such as esters, ketones, alcohols, and polyfunctional thiols. While terpenes do make up the bulk of the weight of a terpene profile's molecular cocktail, research suggests there are small compounds that have a massive effect. The relationship of these molecules to larger sensory perception effects is currently unknown. This is the principle mission of Abstrax Tech: to identify and replicate exactly what gives Tangie its Tanginess, how OG's stank is formulated, and why Sour Diesel smells like a skunk.

In a perfect world, the flavor of flower and extracts of the same cultivar would be identical. But this just isn't the case. As the raw cannabis used in extraction undergoes filtration processes, all molecules save THC are stripped away, including those original, flavorful terpenes. Recreating the precise terpene profile of individual cultivars is the core mission of some concentrate manufacturers. However, sensory experiences do differ significantly between concentrates and the more diluted molecular doses of conventional flower. Extracts are characterized as having heightened sensory experience compared to flower precisely because they are concentrated. This may be why some products are described as being "loud." It's not difficult to identify these superior products, as the effects noticeable from a simple whiff are a good indicator. The pungency of various sensory experiences that cannabis naturally gives us can vary from earthy, to herbal, sweet, and so on. We know that terpenes are largely (in terms of molecular mass) responsible for these sensory experiences. Each terpene possesses a unique smell and effect. For example, while walking through a coniferous forest, one would be immersed in a gaseous sea of pinene, the dominant terpene found in pine trees and giving them their characteristic aroma. Breathing this terpene would result in a person feeling slightly more alert, and a bit better focused. [1] Similar events occur when the humulene and myrcene of hoppy beer make someone sleepy or how the linalool in lavender soothes and eases. Fortunately,

these plants were not banned from research, so we understand them and the physiological effects of their independent molecules and derivatives well. All of the molecules mentioned above, and many more, are naturally found in cannabis.

Not unlike many other floras in modern agriculture, cannabis has been selectively bred for many years. A key factor is that a generation of cannabis plants can be ready to harvest in just a few months. This speed, plus the ease of growing, has resulted in the wide cultivar assortments visible in any self-respecting dispensary. Additionally, this developmental variety breeds more diversity, paving the road for the creation of more unique terpene profiles that we haven't even identified yet. With the rise of new terpenes that have unknown physiological effects, it's an exciting opportunity to learn more. What we do know is that these terpene blends have synergistic effects with cannabinoids, which are themselves modified terpenoids. These interact with our endocannabinoid system in a compounding combination of terpenes and cannabinoids called the entourage effect. Depending on the terpenes, cannabinoids, and concentration of each, a spectrum of interactions can occur inside the body.

Lots of terpenes exist throughout nature. Scientists have identified over one hundred within cannabis. [2] Many of these are drawing a lot of attention, so it's become common for laboratories to test samples for the content levels of 15-30 terpenes. Abstrax Labs, a licensed type-7 manufacturing lab in Long Beach, will soon test cannabis for hundreds of specific molecules, including terpenes, cannabinoids, and their derivatives in an effort to further understand cannabis. We are excited to uncover the nuances of the cannabis sensory experience and look forward to publishing our findings when we discover those subtle differences that make this plant as miraculous as it is.

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Value of Origin: Sourcing and Cultivation for Elite Extractions

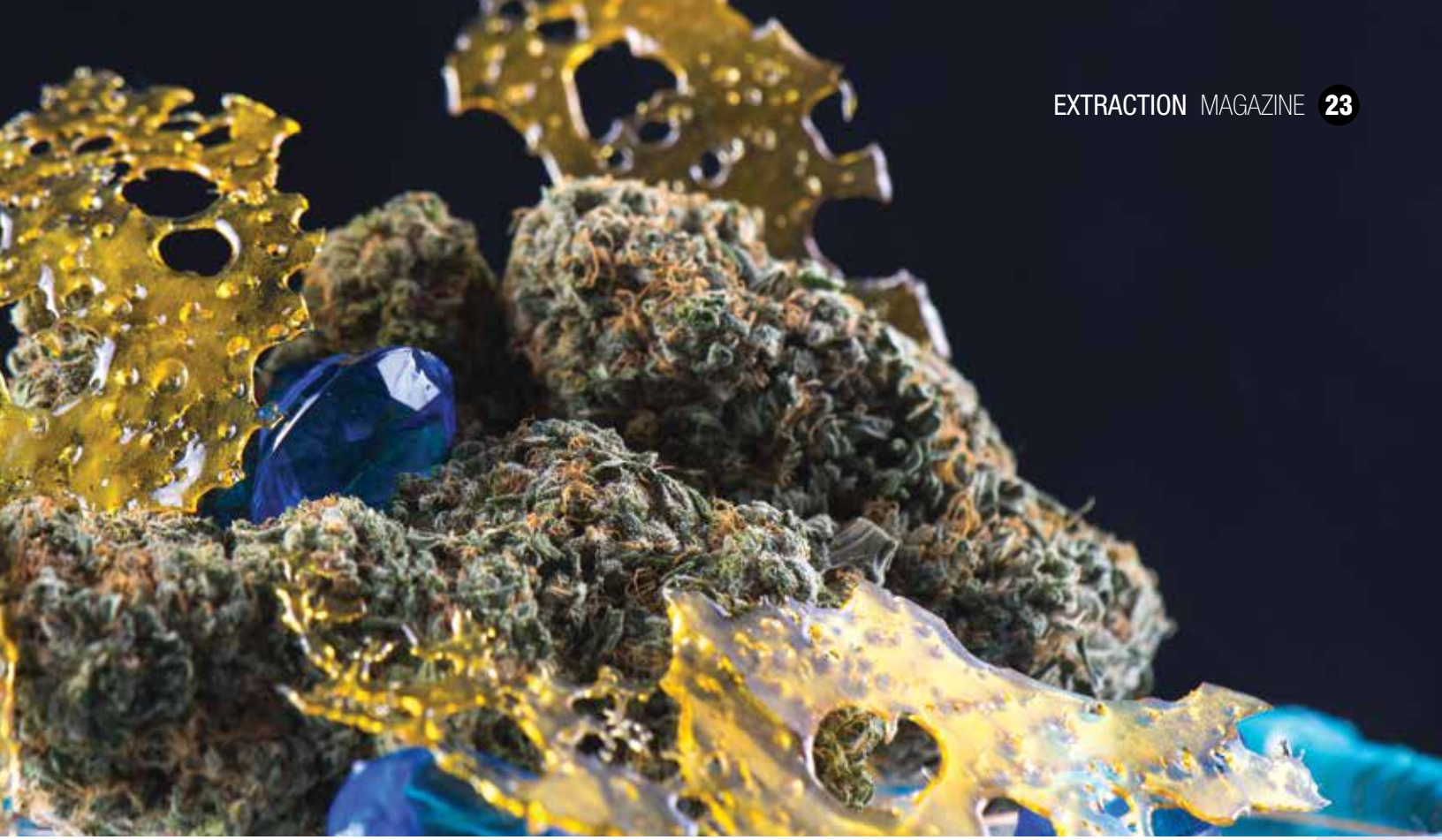
By Dave Malone, Green Dot Labs

I will never forget the first time I did a dab. I was 25 and already a knowledgeable cannabis connoisseur. I took one hit of an extract provided by a friend of mine, and it brought me back to the first time I ever tried good cannabis. I knew without a doubt that concentrates were the future of cannabis.
That realization led my wife and me to launch the cannabis extract company, Green Dot Labs, in Boulder, Colorado, in late 2012. At the time, we were trailblazers. There were no ready-made extraction machines, set regulations, technologies, or operating procedures. So, we built on what we knew, which was how to grow great cannabis plants. I'd always loved growing – tracking down exotic seeds, carefully tending to the maturing plants, savoring the joy of a bountiful harvest. We figured the best way to produce extracts would be to make sure we were developing and growing quality plants.

First, we built a cultivation platform for high-quality indoor cannabis, and then we reverse-engineered it step-by-step, utilizing the very unique data gleaned from dedicating our entire harvests to light hydrocarbon extraction to make the highest quality extract possible. One element of the breeding and cultivation process would be tweaked at a time – slightly shifting genetics, altering grow nutrients, adjusting the humidity, fine-tuning lighting schematics – followed by the fanatical tracking of the results in the final product, the essential oils of cannabis. This process was repeated until the procedures were adequately refined for every one of our cultivars. The result was an obsessively meticulous extract production process from seed through live resin. The secret to elite extractions wasn't simply focusing on the latest and greatest extraction techniques. Rather, the secret resided in starting with the best and most diverse raw materials possible: seed.

These days, however, many concentrate companies take the opposite route: processing any sort of plant material they can get their hands on, whether it's high-quality flower, commodity-level plants and trim, or even contaminated buds. On one hand, that's understandable. Concentrates are one of the fastest-growing segments of the legal cannabis industry. Consumers are clamoring for extracts of all kinds, from smokable dabs to oils for their vape pens. So, it makes sense that many operators are focused on low-quality inputs and maximum production, producing concentrates as cheaply and efficiently as possible with the assumption that clever retail branding or flashy vape pen designs will help their products stand out from the crowd.

This approach is shortsighted, though. When you are producing commodity-level concentrates, you are at the mercy of the commodity market. So as cannabis prices continue to plummet, the revenue of these operators will follow suit. And when you have little or no control over the quality of the plant materials you are using for extractions, all it takes is one bad batch of plants for your brand to end up in the dump. Most importantly, producing extracts with little regard



for the genetics and plants you're working with jeopardizes the inherent value of cannabis extracts. Concentrates are the purest expression of cannabis, a true reflection of the plant's vivid sensory profile. When you're dealing with shoddy raw materials, you're losing the vibrant aromas, tastes, and wellness benefits that make the cannabis plant and her essential oils so exciting.

Sourcing and Genetics

To understand the secret to selecting and breeding great plants for extracts, let's start with a geography lesson. *Cannabis indica* hash plants can be traced back to the Hindu Kush mountains in what is now Afghanistan and Pakistan. To withstand the harsh mountain temperatures and high-altitude UV light, these plants evolved naturally to secrete more resin, which acts as a natural sunscreen and thermal control for the plant. These plants also use their terpenes as a pest deterrent, meaning they're prone to skunky, unappetizing aromas that humans and cannabis aficionados find so intriguing and enjoyable. Indigenous tribes selected the best-yielding hash plants, which were ultimately pillaged and used for international trade. If you look up the family tree of any of the most potent, sought-after varieties available today, the common denominator is these hash plants, which pass down their genetic markers for resin production to their progeny. The flip side is that these plants are short and stocky to withstand their native environment, meaning they're not going to provide an abundant harvest, and their resin isn't particularly appealing.

On the other hand, *Cannabis sativa* plants from milder equatorial climates evolved to be taller and bushier, and their terpenes developed to evoke sweet berries and other enticing aromas, in order to convince animals to take a bite and disseminate their seeds far and wide. But since these plants didn't need so much protection from the sun and weather, their resin production was comparatively minimal.

To produce excellent plants for extracts, you need the best of both worlds. You want to hybridize Kushy hash plants with equatorial sativas. The result is big, bushy plants with excellent resin production and a rich variety of terpenes. We coined these beauties our "21st century hash plants" – modern, artificially-selected descendants of the age-old hash plants.

That's the sort of plant you want to focus on for top-shelf extracts. But sourcing and developing such plants isn't easy. The 21st century hash plants that populate our grow facilities are the result of years of hard work – tracking down promising seeds, carefully crossing and breeding interesting varieties. And it doesn't matter if a plant is as beautiful, fragrant, or resinous as they come. If the resulting extracts aren't up to snuff, we have no use for it.

Also, it's not about finding and developing one or two great extract plants – it's about building a library of them. Developing as wide-ranging a genetics pool as possible allows you to create something for everyone. Learn to read the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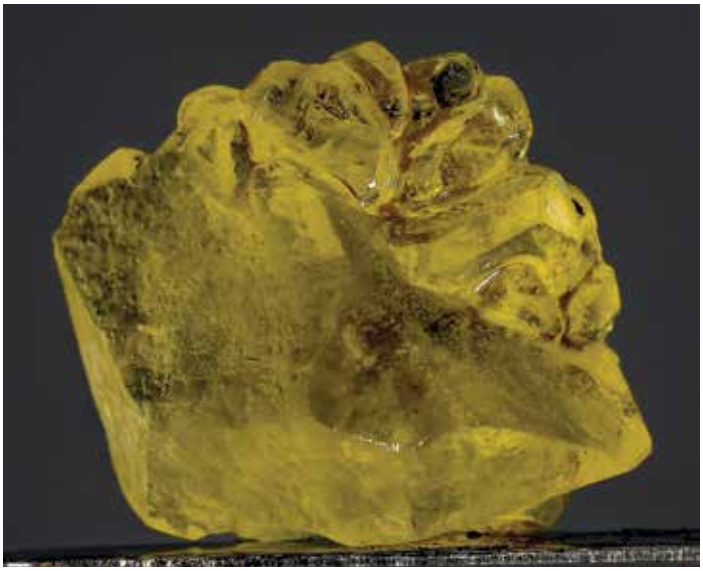

market, to breed plants to meet your customers' tastes. Here in Colorado, many people are drawn to dabs that evoke citrus fruits or crude petrol, so a good chunk of our plant diversity is devoted to varieties with those sorts of tastes and aromas. But we're also not afraid to branch out into exotic territory. Some folks thought I was crazy when I was developing a cultivar called Bottle Wash (Wookie x OZ Kush). The plant was too odd, too unique. It tasted like a mixture of lavender, grapefruit, and grapes. I was told people wouldn't go for it. But I knew I had something special – and sure enough, consumers loved it.

So, in other words, don't be afraid to experiment. The market is still young; people haven't yet solidified their preferences. It doesn't have to be sativa versus indica. Feel free to surprise them with your genetic wizardry.

Cultivation

At Green Dot Labs, we see ourselves not as cannabis extractors, but as resin farmers – with an emphasis on the farming. It's not about producing the most flower per square foot of canopy, like a typical grow operation. It's about producing the most resin, the maximum milligrams of cannabinoids and milliliters of terpenes, per square meter. Everything we do during the cultivation cycle revolves around that end result.

How do you do that? It's all about triggering the plant's natural protective mechanisms discussed earlier – i.e., its resin production. To do so, every one of our plants is thought of as an elite triathlete. Just like a triathlete, a perfect extract plant is a blend of genetics and conditioning. Just like some people aren't physically capable of handling the extreme demands of a triathlon, some plants just aren't made for the rigors of our cultivation process. But even those plants that are well-suited for our procedures still need to be trained. Like elite athletes, the plants are exposed to frequent high-nutrient meals throughout the day, versus a glut of food all at once. And they are conditioned through a strict regimen of light and heat to become lean, mean, resin-producing machines.

Similar to any elite training program worth its salt, every variable is noted that goes into the cultivation of a given plant through extensive tracking programs. Any time one of those variables is changed, whether that is an extra infusion of bone meal into the feeding process, or an HVAC system that goes on the fritz for a brief period, that's noted too. That way, exactly what changed can be known if a given harvest turns out to be particularly remarkable – or remarkably bad. Such tracking allows the isolation and control of every single variable that goes into producing each plant, from environmental controls to lighting schematics to nutritional regimens.

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The result is a head-spinning amount of data – especially since this process is replicated for every one of the 160 or so plants currently being cultivated in our two facilities. It's a daunting system, one that would surely be far easier if, say, instead of releasing new extracts each week, based on different cultivars we've developed, we focused on a half-dozen great extract varieties and devoted all energy and brainpower to them.

The Results

Clearly, we haven't chosen the easiest way to make extracts. During the 180 or so days between when we plant a seed and complete the resulting extract, there are hundreds if not thousands of elements we have to carefully control. It might seem crazy to devote so much energy and effort on plants that are just going to be processed into concentrates. But the results speak for themselves. And none of this would be possible if we didn't develop and cultivate the best possible plants.

Need more convincing that the quality of the raw materials that go into your extracts should be your top priority? Consider this: all concentrate companies use the same extraction machines and refining ovens. We all more or less employ the same extraction procedures because of the highly regulated environment. These days, there are only two ways to differentiate yourself in this industry. One is by your plant genetics, and the other is by the quality of the plants you produce. So why not double down on both? After all, as the extract market matures and stabilizes, don't you want to be among the brands that rise above the rest?

Effects of Pressure in Supercritical CO_2 Extraction of Cannabis

James E. Parco, Colorado College, Dept of Economics and Business, Colorado Springs, CO University of Cannabis Technology (UCANNTECH), Pueblo CO

Plants have long been viewed as sources of both nutritional and medicinal value. Some of the earliest recorded narratives reveal the Egyptian discoveries of coriander and castor oil providing medicinal benefits to humans. Throughout the ages, others, like Celsus [1] and Hippocrates, have produced scientific breakthroughs with plants at the source. [2] As scientific discovery of plant medicine progressed, so did the methodological protocols and techniques surrounding the extraction of desired compounds. Contemporary extraction technologies depend principally on the choice of solvent [3] and standard cost-benefit tradeoffs [4]. Azmir and colleagues provide an excellent review of extraction techniques of bioactive compounds from plant material through 2013. [5]

Supercritical fluid extraction (SFE) has emerged as a leading technology in the legal cannabis industry. Discovered at the end of the 19th Century by Hannay and Hogarth [6], SFE remained largely theoretical until Zosel received the first known recorded patent for the decaffeination of coffee. [7] Since then, technological developments have given way to a new industry aimed at manufacturing large-scale SFE systems, and very recently, the attention has turned toward cannabis. [8] However, as the science and theory mature, little data is currently available for SFE practitioners of cannabis extraction. With significant capitalization requirements for high-volume productions systems, most practitioners are reluctant to share data for fear of eroding business competitive advantages or revealing intellectual property on which individual business models are based. Thus, the purpose of this study is aimed at helping to bridge these gaps by evaluating the extraction efficacy of leading SFE technologies using CO_2 as a solvent under different pressure conditions.

Theoretical Frame

Carbon dioxide (CO_2) is one of the most widely accepted solvents used in the commercial cannabis industry for two primary reasons. First, there is a dramatic reduction in occupational health and safety risks in that it is not flammable, relatively inexpensive and commonly available at high purity levels. Second, CO_2 is chemically inert and nontoxic when consumed by humans in low levels. Contrasted to hydrocarbon-based solvents, there is a marked reduction in health risks from ingestion of residual levels that may remain post-extraction.

Crucial to understanding CO_2 extraction is the notion of a critical point. A critical point can be identified on a phase diagram where there exists clear delineation between various phases of the compound. [9] As identified in a generic phase diagram as Figure 1, the critical point of a compound exists as a function of temperature and pressure where there are no longer well-defined properties between the gaseous and liquid forms. Specifically, for CO_2, the critical point rests at a pressure of 1,080 psi (*Pc*) and 88°F (*Tc*). [10] Any combination of values in excess of *Pc* and *Tc* simultaneously will result in a supercritical fluid. Said differently, a supercritical fluid is essentially a fluid with gas-like densities and viscosities but it cannot be compressed, thus behaving more like a liquid. As a supercritical fluid, CO_2 makes an excellent extraction method leaving behind no harmful residues. A corollary to supercritical fluids are subcritical fluids. Subcritical CO_2 can be achieved by either lowering the pressure below *Pc* or the temperature below *Tc*. Most commercial extraction operations achieve subcritical

or supercritical extraction results by modulating temperature while maintaining constant pressure. However, because of the chemical properties of the biomass being extracted and the combination of time, temperature and pressure, different sets of parameters will attract different compounds in the starting biomass based on molecular weights. Thus, it is common for CO_2 extraction protocols to extract terpenes at subcritical parameters and cannabinoid extraction as supercritical parameters.

Research Design

This study aimed to investigate the effects of pressure on CO_2 supercritical extraction of cannabis. Specifically, we designed an experiment to test the effects of increased pressure levels above *Pc* to evaluate the extraction efficiency at low (1800psi) and high (3600 psi) pressures. We used three independent systems manufactured by Apeks Supercritical. We employed the use of an independent third-party cannabis analytical laboratory, Green Lab Solutions, to conduct all testing, pre- and post-extraction. All extraction was performed at Mesa Organics (DBA Purplebee's), a licensed supercritical CO_2 extraction facility. All activities in this study were performed under the rules of the Colorado Marijuana Enforcement Division within the state of Colorado by licensed, retail cannabis facilities.

Methodology and Data

Supercritical extraction results in more efficient extraction (faster run times) of the most desirable compounds in cannabis. Thus, for the purposes of this study to ensure maximal control over the independent variables, the extraction runs were set at fixed parameters for supercritical behavior.

The data for this experiment were collected from a series of runs of a single cannabis variety known as "Ambulance CBD" from Los Suenos Farms (LSF), the largest licensed adult-use cannabis cultivator in the United States. LSF is unique as a cultivator in that it produces very large harvest batches (hundreds of pounds per harvest batch). We chose this particular high-CBD cannabis plant with relatively balanced levels of delta(9)-tetrahydrocannabinolic acid (THCa) and cannabidiolic acid (CBDa). All biomass material was ground to 200 microns and then subjected to a partial decarboxylation process pre-extraction to convert approximately 90% of the acidic THCa and CBDa to their neutral forms, tetrahydrocannabinol (THC) and cannabidiol (CBD), pre-extraction. Because THC and CBD are more soluble in supercritical CO_2, they are also more efficiently extracted.

Table 1. Biomass Cannabinoid Levels, Pre-Extraction vs Post Extraction

PSI	Phase	THCa	THC	CBDa	CBD	CBN	CBGa	CBG	CBC	*Total*
3600	Pre	0.52	6.02	3.71	6.20	0.08	0.23	0.24	0.82	*17.31*
3600	Post	0.24	0.53	1.00	0.21	0.00	0.20	0.00	0.04	*2.06*
1800	Pre	0.73	5.43	3.89	5.14	0.07	0.24	0.25	0.70	*15.88*
1800	Post	0.67	2.04	3.83	0.44	0.05	0.26	0.10	0.13	*6.96*

Table 2. Supercritical CO_2 Extraction Efficiency

PSI	THCa	THC	CBDa	CBD	CBN	CBGa	CBG	CBC	*Efficiency*
3600	54%	91%	73%	97%	100%	14%	100%	95%	*88%*
1800	9%	62%	2%	92%	37%	NR	59%	82%	*56%*

Table 3. Final Cannabinoid Potency as a Percentage of Overall Distillate Potency

PSI	THC (early)	THC (late)	CBD (early)	CBD (late)	Total THC	Total CBD
3600	23.9	32.7	46.2	28.8	28.3	37.5
1800	22.2	28.4	50.1	28.4	25.3	39.2

The equipment used to conduct the experiment were an Apeks 5000 2oL x 20L system (aka The Beast), the Apeks 5000 40L x 20L system (aka Big Mama) and the Apeks 2000DP 20Lx20L system (aka El Jefe). Each machine was loaded with 13,608 grams of ground, decarboxylated material and run for approximately eight hours each. Although the material loaded was from a single harvest batch and homogenized, we tested a sample for each extraction vessel (top, middle and bottom) both BEFORE and AFTER each extraction run and averaged the results. The results for pre- and post-extraction levels of cannabinoid content can be seen in Table 1. Comparing the pre-extraction to the post-extraction results, the reported extraction efficiencies from the experiment can be found in Table 2.

Extraction temperature on all three systems was set at 108°F. Whereas The Beast and Big Mama were set to 3600 psi (High Pressure Condition) and El Jefe was set at 1800 psi (Low Pressure Condition). The selection of the pressures was ad hoc and not theoretically prescribed, except for the fact that both pressures exceeded *Pc* for supercritical CO_2.

Terpenes were extracted from each of the three runs during the first thirty minutes of extraction time and not considered in the data for the study. Average terpene yields were approximately 7% of the extracted biomass. Raw crude extract from each system was separated into "early" (first 25% of extraction time) and "late" final 75% of extraction time. Approximately 50% of total extract volume is produced during the first 25% of extraction time, thus the volumes for the "early" and "late" fractions were relatively equal. Once all extraction had been completed, each run was turned into cannabinoid distillate. The final potency results are listed in Table 3 separately for both Early and Late fractions for each pressure condition.

Analysis and Discussion

The average pre-extraction potency of the input biomass ranged between 5.4-6.0% for THC and 5.1-6.2% CBD (Table 1). One must remain skeptical and mindful of normal variances reported by lab instruments due to methodological variance and potential error on top of normally expected error ranges. [11] Looking across all cannabinoids pre-extraction, the biomass potency exhibited about a 1% variation between the systems. We have no way of knowing where the source of the error lies, be it the true value of material not fully homogeneous, sampling error or testing error. Thus, with such a small variance, we conceded such error levels were acceptable.

Post-extraction results (Table 2) revealed that increased pressure levels resulted in higher extraction efficiency levels

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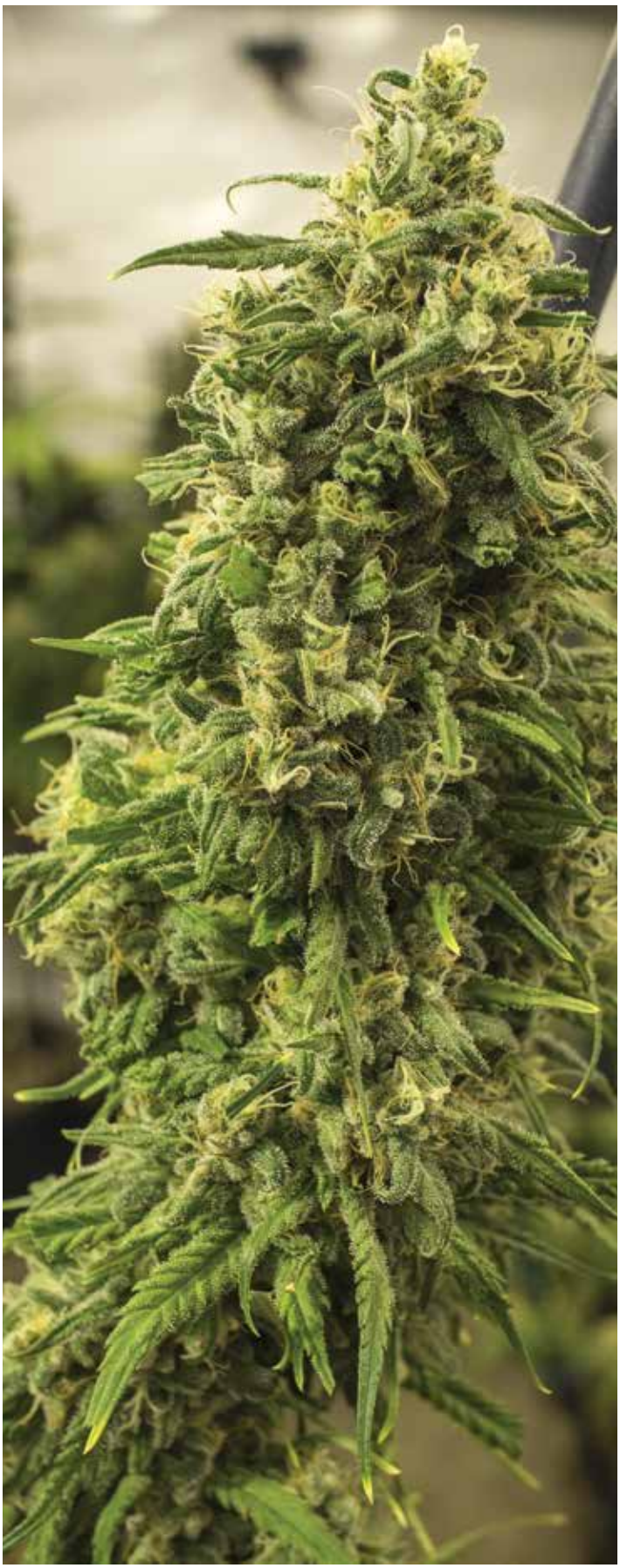


of both individual cannabinoid levels as well as overall cannabinoid potency. Whereas CBD was removed during the extraction at a 92% efficiency in the Low Pressure Condition, it was marginally higher (97%) in the High Pressure Condition. Similarly, THC extraction efficiency was relatively poor in the Low Pressure Condition (62%) and notably higher (92%) in the High Pressure Condition. Similar results were observed across reported cannabinoids with an overall extraction efficiency of 88% for the High Pressure Condition and 56% efficient for the Low Pressure Condition.

Comparing the final cannabinoid distillate forms of Early and Late fractions across the two pressure conditions, the results were similar when looked at holistically. Specifically, the High Pressure Condition yielded cannabinoid percentages of 28.3% THC and 37.5% CBD compared to the Low Pressure Condition with 25.3% THC and 39.2% CBD. However, looking more reductionisticly at Early and Late fractions, there are two key findings. First, although there were no notable differences between the two pressure conditions for THC in the Early phase, the High Pressure Condition was able to achieve an overall five percentage point increase in THC yield over the Low Pressure Condition. Conversely, whereas the Late phase of CBD extraction resulted in similar percentage outputs, the Early phase revealed that CBD levels were twice has high in the Early phase as compared to the Late phase with Low Pressure performing marginally better for CBD extraction.

Finally, as noted in Figure 2, extraction yield curves follow an asymptotic negative exponential function, translating to a majority of output being achieved in the earliest stages and marginally decreasing output over time. Although the total extract volume increased over time at a decreasing rate, the behavior of individual cannabinoids did not. While CBD tends to follow the same functional form of the extraction yield curve, THC is far more linear. Although overall biomass extract yield decreases exponentially, the percentage of volume of THC increases. Overall yields ranged between 15.8 - 17.2% in raw crude and approximately 10.8% in the final distillate yield.

Conclusion

Higher pressure yielded better results for THC and lower pressure yielded marginally better results for CBD. Because the acid forms of the compounds are far less soluble in supercritical CO_2, extraction yields of THCa and CBDa were inferior to the yields of the neutral compounds, THC and CBD. Post-extraction differences between the top and bottom of the extraction vessels were mildly different (within 0.5%) and not economically significant considering additional time or processing. Overall, based on these results, we confirmed that increased pressure

Figure 1. Phase Diagram (generic)

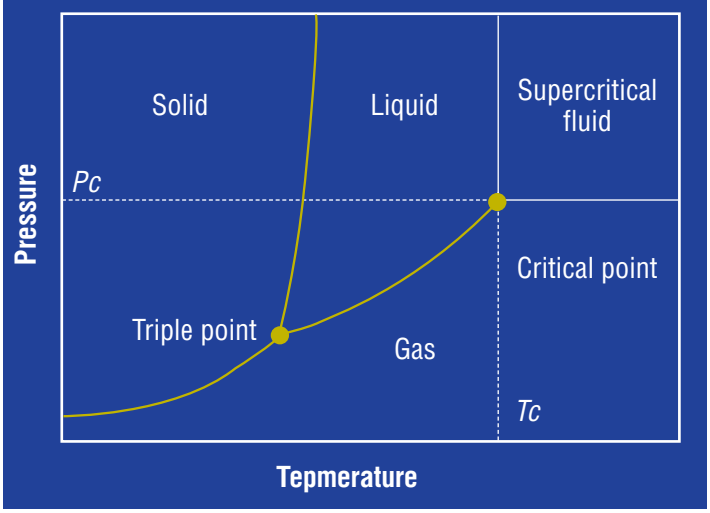
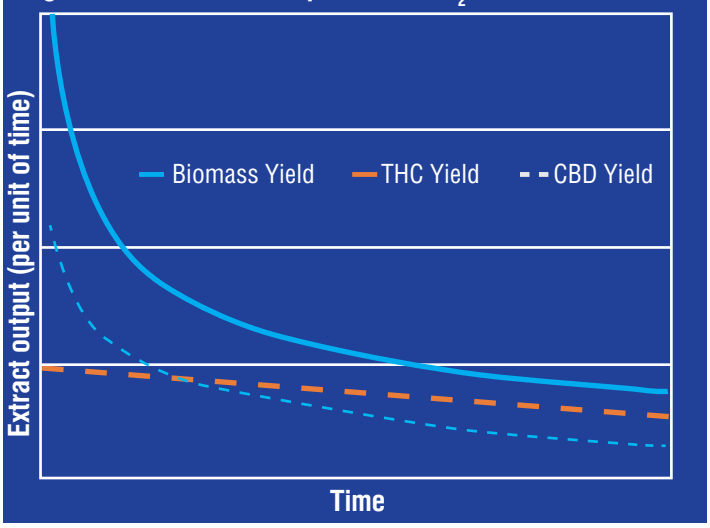


Figure 2. Yield Curve - Supercritical CO_2 Extraction



levels during supercritical CO_2 extraction can be significant with respect to overall cannabinoid yields. CBD tends to come out faster and earlier during extraction runs as compared to THC, which tends to be more monotonic and linear during a supercritical CO_2 extraction run. [12]

ABOUT THE AUTHOR:

Jim Parco, Ph.D, is a professor of economics and business. He hasadvanced degrees from the University of Arizona, College of William and Mary, and the U.S. Air Force Academy. Along with his wife, he co-founded Mesa Organics in Pueblo, Colorado, one of the first two counties to legalize cannabis in the United States in 2014. Mesa Organics is a supercritical CO2 extraction operation running high-production systems capable of processing 30 million grams of biomass annually. He is also the founder of the University of CannabisTechnology (UCANNTECH) teaching advanced extraction theory and methods using supercritical fluid technologies.

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- [10] Not to be confused with the "triple point" where the compound may exist as a gas, liquid or solid. Equivalently, the parameters can be stated a Pc=74.47 bar and Tc=31.12-degrees Celsius.
- [11] Laboratory instruments inherently have error but the likely introduction of error is sample preparation and the actual analytical method where variability is determined by acceptance criteria during validation, i.e. 25% typically.

- [12] We wish to extend our appreciation to the referees and editor for their thoughtful peer-reviews and suggestions.

The Processing Equipment Sales Process

Leading manufacturers are doing these three things in the sales process

By Conor Corrigan

I've learned a lot in 2017 and 2018, and I continue to learn every day. At my core, I am a salesman. I always look to identify, offer, sell, and share what I believe to be the best cannabis processing/extraction equipment solutions available. I enjoy "preaching the gospel" of quality products – it so happens that this is also how I've made a career for myself. Part of a successful career is understanding what the keys to success are, understanding what you're good at, and leveraging opportunities.

Who is doing the "selling" in your organization? Much of the time, it's not who you think. In order to be a good salesperson, you need to be intimately aware of how your potential customers perceive the sales process. Whether your manufacturing business employs engineers, marketing gurus, technicians, or scientists, **they all need to be salespeople.** The reason is simple: much of the time, it's not someone in the sales department who is called upon to answer questions. Now that we've demonstrated why all team members need to be salespeople. What does it take to be a good salesperson?

Good salespeople *listen* more than they speak

Rather than *telling customers what they want,* all team members (including engineers, service technicians, CFOs, etc.) need to be a source for information and support. One of the keys to success in selling processing equipment is making the sales process as easy as possible, no matter what you're selling. This applies to trimmers, laboratory benches, extractors, distillation systems, analytical tools, and everything else a processor might use in their lab.

Another part of "making the sales process easy" is by giving answers to questions asked of you. Sounds like a "no brainer," right? Surprisingly, this is not "common knowledge" across the industry.

Not unique to processing equipment sales, questions (and therefore answers) are sometimes extremely complex. At least this is the excuse that many manufacturers give (for not answering questions). As a buyer, I can quickly determine how the (unsatisfying) sales process will go when I get the following response: "It depends."

What's the throughput of [this] machine? "It depends." How much material can you process in a given day, week, month, or year? "It depends."

Sound familiar? Isn't this frustrating? You are not alone!

Do the answers *depend (on several factors)*? Of course they do! No *reasonable* consumer evaluates equipment without making assumptions. So, why then are manufacturers reluctant to be reasonable?

Here's an example that helps demonstrate the point: When we go to a car dealership, not only are the prices on the windows of cars, the performance expectations are also on the windows. Just imagine if the fact sheets on the windows said:

- MPG (miles per gallon): depends.
- From zero to 60 (in seconds): depends.
- Safety rating: depends.

Wouldn't that be annoying? Why, then, is it commonplace in the processing equipment sales market for salespeople to give the same response? It's not like manufacturers are posting an equivalent "fact sheet."

Apeks Supercritical, makers of super/subcritical CO_2 extraction machines, comes readily to mind when looking to identify a major manufacturer of extraction equipment that provides performance-based expectations. On the Apeks website, you

will find the data needed to identify performance expectations for the machines they manufacture, along with prices, options, and an invitation to connect.

There is a direct correlation between *transparency in the sales process,* and *customer satisfaction* and *sales.* It was months ago when **Apeks announced their 500th system in the field (in cannabis).** No other notable extraction manufacturer can hold a candle to the market share that Apeks enjoys. It's not a mystery why Apeks commands the "lion's share" of the market. How do you think Apeks "performs" when compared with the other two sales process indicators of success? Here's a hint: they go 3-for-3.

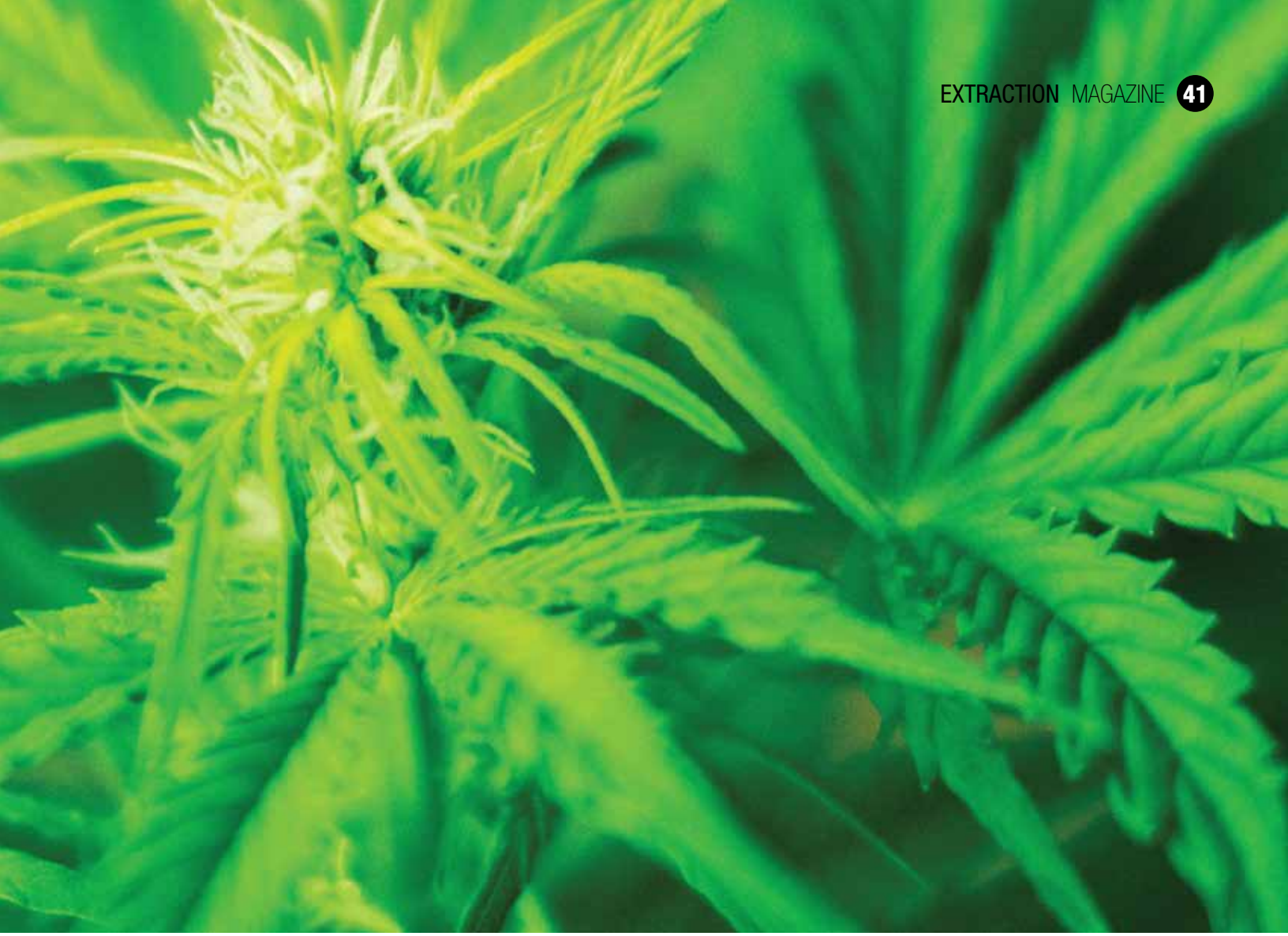
Do you know who else is annoyed with manufacturers' lack-of-transparency (other than me)? Many collective customers. Clients (in general) don't like getting the run-around when they ask simple questions. I'm not suggesting that manufacturers advertise *all* metrics, Key Performance Indicators, and prices – I'm just suggesting that manufacturers answer questions when asked.

The first step to improving a problem area is identifying that there is indeed a problem. Listen to our customers: they are dissatisfied with the sales process (in general)? Problem identified. Great news, though! We already have the recipe for success below.

Inferior equipment is sold every day because the sales process is informative and easy.

Sales are won and lost due to the efficiency (or lack thereof) of the sales process, and below you'll find three things that make a sales process efficient. Much of the time, satisfaction with the sales process is literally everything, even more significant than the soundness of the investment. This is evidenced by the fact that inferior equipment is sold every day because the sales process is informative and easy. In summary, make the sales process easier, and you will sell more equipment.

Not providing potential customers with direct answers to questions like "what is the price of this machine" is just one example of behavior that damages our collective ability to make the sales process as easy as possible.



The three things that successful manufacturers do to make the sales process easy.

Take a look at the most successful equipment manufacturers on the market. The top brands in the processing equipment market share these important characteristics:

1. Transparency – after a conversation with the manufacturer, the customer knows exactly what the associated costs are, the best available option is for their needs, and a high-level perspective of what the buying process is (with the given manufacturer or distributor). The customer also understands *what manufacturers don't know*, too (more on this later in the article).

2. Clearly Stated Features & Benefits – customers are informed of exactly how the features of the equipment will potentially impact their business after an initial conversation. An extra amplifier of this important deliverable is that these benefits are quantified (production increases, cost savings, etc.).

3. Clearly Stated Cost(s) – how much does this system cost? The top manufacturers will be willing to quickly give you an idea of what costs (or ranges) are associated with a given solution. Here's an idea for a frustrating activity: randomly call five equipment manufacturers and attempt to get a straight answer regarding cost. I promise, you will NOT be satisfied.

It's that simple. These three deliverables will help you sell more equipment. When we make the decision-making process as straightforward, transparent, and informative as possible, we earn the respect of buyers. Part of being straightforward, transparent and informative is telling customers the following (when justified):

I don't know.

We can't make every potential customer happy, but we can make a concentrated effort to improve the manner in which we field questions. Dishonest manufacturers risk damaging the powerful manufacturer-client relationship generated when trust is apparent. We shouldn't be afraid to answer questions with "I don't know," *especially when we don't know.* Voicing this honest answer has never once deterred a potential buyer from

purchasing equipment I personally sought to sell.
Don't have data regarding throughput? Don't know exactly what the flow rate is? Haven't sold a particular model yet and feel embarrassed to say so? These are a few reasons (taken from a list of dozens) why some manufacturers don't want to provide straight answers. While these are "good" reasons to feel concerned, they are also excuses. The good news is that these excuses are easily overcome.

You guessed it (or should have): you can overcome these concerns by plain, old honesty. When we are honest with customers about these things, it not only helps build rapport, but it also improves the sales process by aligning your goals with theirs. When salespeople demonstrate that we are helping customers by *learning along* with them, our goals are aligned. Customers appreciate this *infinitely.* Each and every time I've said, "I don't know, but I'm going to find out," I have been met with understanding and appreciation. Honesty and the alignment of goals can help win the trust of any buyer, acquaintance, vendor, or partner.

So, for my fellow equipment manufacturers: can we agree that the customer experience is of the utmost importance? Great! We're on the right path to selling more equipment!
I invite you to investigate on your own, though. You will quickly identify the manufacturers you want to work with, and importantly, what manufacturers you want to spend a lot of money with. My prediction is that you will respond favorably to the manufacturers who embody the three characteristics from above: Transparency, Clearly Stated Features & Benefits, and Clearly Stated Costs.

Let me know your thoughts – find me on LinkedIn or by reaching out to *Extraction Magazine.*

Terpenes and Teas: Exploring the Relationship Between Cannabinoids and Catechins

By Carlton Bone, Chief Information Officer, Upward Cannabis Kitchen

Cannabis and hemp extract beverages are taking markets by storm to consumer and patient delight. Many of these beverages utilize cutting edge technology to create versions of various cannabinoids that behave as if they are water-soluble, such as the numerous "CBD Waters" available at various retail, online, and other outlets. However, outside of the "Ready-to-Drink" assortment of THC and CBD beverages are steeped beverages, which include various types of ground and whole bean coffee as well as whole and loose leaf teas. As a manufacturer of THC infused tea products with the Upward Cannabis Kitchen in Portland, Oregon, I have become intimately familiar with the synergistic relationship between these two plants, and have become a strong proponent of cannabinoid tisanes (i.e., herbal teas).

Teas are aromatic beverages made by pouring hot water over different types of plants. They have a long cultural history as herbal remedies in various Eastern cultures. As a beverage, tea incorporates a variety of sensory elements, including the heat of the water used to extract the delicate chemicals from the plants; the mouthfeel and texture of the liquor after the tea is steeped; as well as the aroma of the plant and drink—thereby creating a drinking experience that is holistically pleasant. Cultivation and preparatory techniques are crucial to creating proper beverages, and the potential blends (e.g., combinations of aromatics, tea cultivars, and other flavors) of teas are nearly endless. While the potential parallels between tea cultivars and cannabis cultivars are certainly worth discussing, the biochemistry of the two plants continues to be explored. From a cultural standpoint, both plants share the role of a health aid with tremendous social value. Delving deeper, these similarities persist as both plants contain a hearty array of similar compounds, the most important of which, for this discussion, are the *catechins* and *cannabinoids,* two defining classes of molecules that dominate these plants respectively. Catechins are a type of anti-oxidant that has been well studied as a disease preventative and scavenger of free radicals. A 2009 study illustrated how catechins operate through direct and indirect cell modulation and work in harmony with other flavonoids to magnify impact, similar to the way the endocannabinoid system relies on allosteric modulation. [1]

The most significant connection between the two is arguably their unique dynamic when combined. Cannabis exerts its effects by acting on the body's endocannabinoid system (ECS). We have begun to learn more about how this system functions in the body. A popular metaphor to explain the interaction between the plant and body is the "Lock-And-Key," where THC and CBD, acting as exogenous neurotransmitters, are the specifically shaped "keys" to the "locks" that are the body's endocannabinoid receptors. While we can follow the metaphor further to say that, from this connection, a variety of potential medicinal benefits are "unlocked," the nuances of ECS metabolism are certainly far more complex and in need of study.

As such, the research is still not completely positive. A 2010 study considering tea catechin's affinity for cannabis receptors documented a modulating effect on the CB1 receptor. [2] Another study from that same year, however, failed to validate these

findings. [3] The article, which focused on addressing other plants thought to contain cannabinoids, did discuss how the polyphenol content of tea may have modulating effects on the ECS, yet singular findings can't be conclusive. Even though the science is still being sorted, the benefits of a warm cup of tea should not be dismissed, especially if only as an extension of a cannabis consumption ritual.

For many, the aroma of a cup of tea invokes a cascade of pleasant images and memories creating a sense of comfort. For those without these experiences, though, the *aromatherapy* aspect of tea is still an added benefit of the beverage. When crafting our Upward Indica blend, we add a touch of relaxing lavender (the plant most associated with the terpene linalool, which has been documented as a mild sedative in research contexts) to provide an aromatic nose and start the consumer's experience from the moment they open the package.

The blend we use from our partners at the Jasmine Pearl Tea Company includes delicate white teas (high in catechins) and chamomile, another sedating herb. While less tangible benefits accompany drinking tea, such as the meditative effects of slowing down to brew a beverage, the sociability of tea, the warmth it brings internally and externally, as well as the benefits of hydration and satiation that come with it all combine to make it a healthy drink.

As cold weather season descends on us, consider stopping by your local tea shop to pick up a quality tisane. I recommend using the same questions and mindset you would take when looking for a cannabis or hemp product in terms of flavor and effect; you may be surprised at how far this will get you in finding a good "match-a." Further incorporating tea into your cannabis ritual can mean brewing a cup if a capsule hasn't taken effect or a topical isn't providing the complete sense of relief, rather than potentially over-consuming. Furthermore, when dealing with cannabinoid distillate and isolate, the robust entourage of tea can compensate for the lack of other plant terpenes.

Finally, when access to cannabinoids may be difficult, consider how scientists have come to recognize *beta*-caryophyllene, a major terpene in cannabis plants, as a modulator of the endocannabinoid system. *Beta*-caryophyllene meanwhile can also be found in spices like black pepper and cloves, making beverages like hemp milk chai lattes "Near Spectrum" cannabinoid products!

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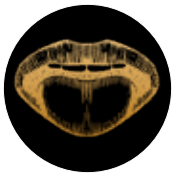
Christmas (or New Year's) Pudding

By Luis Narciso, Pastelaria 6 Sentidos



Notes: I suggest giving priority to organic ingredients for best results. A gluten-free version can be prepared with gluten-free oats and gluten-free flour mix. This pudding recipe, as most of my suggestions, should be interpreted just like a personal experience (be it recreational or therapeutic) in order to be adapted to one's needs and tolerance. It also may vary according to cannabis or cannabis product availability. Ground cannabis, or resin/hashish, could be used in the dough or the coconut oil, mostly depending on circumstances and possibilities. Readers are encouraged to infuse when and where they see fit.

In this case, I played with the terpene pinene due to the season and diluted it in the pudding garnish.

6 servings

INGREDIENTS:

- 100g Oatmeal
- 50g Spelt flour
- 200g Prunes, apricots, figs, dates mix (weight without seeds)
- 50g Chopped currants and cranberries
- 1 Orange zest
- 1 Apple
- 100g Ground pecan nuts or walnuts
- 50g Almonds with skin + 200ml water
- 50g Coconut oil or other vegetable oil
- 200mL Brandy, sherry or rum
- 2 Tablespoons lemon juice
- 1 Teaspoon ground ginger
- 1/2 Teaspoon ground vanilla
- 1/2 Teaspoon cinnamon
- 1 Teaspoon mixed spice
- 1/2 Teaspoon baking soda
- Pinch of salt

CONFECTION:

Soak the prunes, apricots, figs, dates with the grated apple (with skin), ginger, cinnamon, and mixed spice in the liquor for 24 hours. Reserve in the fridge in a covered recipient.

Take the fruits out and drop the chopped currants and cranberries in the same liquid. Let soak for a few minutes.

Melt the coconut oil in a bowl on hot water or vapor from a pot. Remove from the heat and add the coconut syrup, almond milk and pulp resulting from the almond and water processing. Add the vanilla and salt at this point.

Incorporate the ground pecans, the previously ground oatmeal, flour, bicarbonate, the ground fruit mix and then the drained chopped currants and cranberries. Save the soaking liquor. Adjust texture if needed.

Display this dough in individual non-sticky cupcake or bowl molds to cook in the oven in a tray half-filled with water. Cover the molds with baking paper and then cover and seal the tray with tin foil all around it.

Let cook at 120°C (top and down heat) for about 2 hours. Remove from the oven and let cool in the molds.

Reduce the remaining liquor from soaking the fruits in a pot on slow fire. Add a little more of the coconut syrup if needed. Mix your seasonally special pinene-rich extract (or other according to your needs) when reduced and garnish the top of your unmolded puddings. Decorate according to season and your taste. I use malt instead of sugar to simulate snow by pouring it through a strainer and use some Holly tree as well.

Wishing you a happy season and a prosperous 2019 for all of us.

Christmas Pudding

Efficient Decarboxylation is Paramount to Creating Dispensary-Grade Extracts at Home

By Shanel Lindsay, Ardent Cannabis

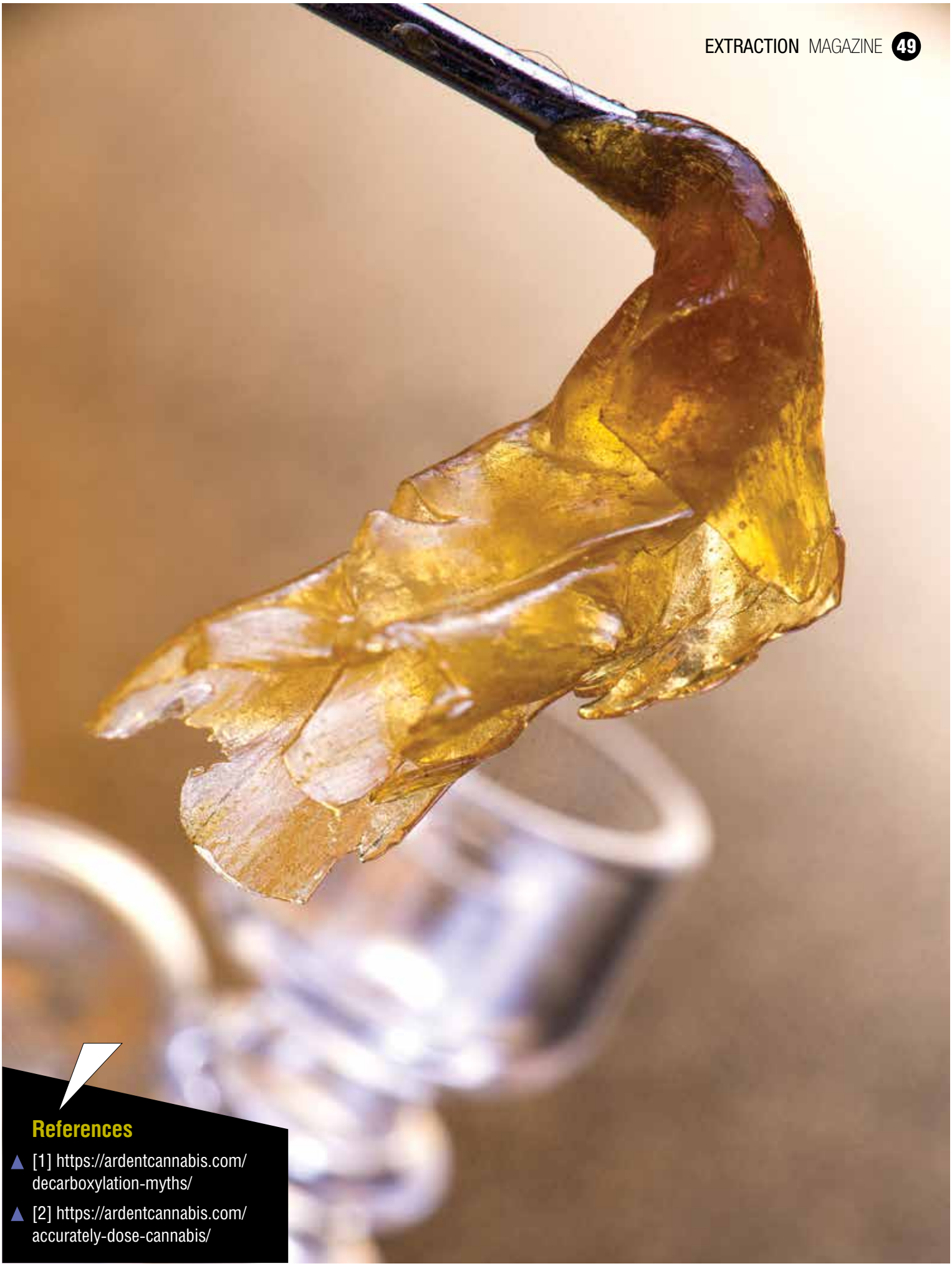
As cannabis legalization spreads across the country, consumers are discovering a variety of new options to manage their health and wellness. This coincides with an increasing distrust of prescription painkillers and pharmaceuticals among the American public. Though studies show that attitudes about cannabis are shifting, many of those who grew up under prohibition find themselves unprepared to engage with the product. The science behind creating cannabis products from raw plant material at home is nuanced with supporting data that can be used to achieve reliable results lacking in most instances. This issue is exacerbated as the demographic of many uninitiated consumers does not align with the "cannabis lifestyle" skew of many of the space's publications and educational resources. Ironically, many of the first medical cannabis laws were passed to benefit precisely these uninitiated potential patients.

As the legal cannabis market expands, connecting with these potential consumers will be essential. Engaging with this segment of the cannabis market requires a willingness to focus on the basics. Those new to the space require extensive product education and do not respond to the same marketing used to promote recreational consumption. Medical patients as a whole also have very different pricing needs than recreational consumers. While it makes sense to price recreational products as luxurious indulgences, this rubric leads medical cannabis consumers back to prescription drugs, if only because that's what insurance will cover. Worse still, those who live in states without medical cannabis are forced to choose between potentially dangerous legal drugs or trusting their health to merchants of the illicit market.

Effective *decarboxylation* (more commonly thought of as THC "activation") is the initial solution to many of the aforementioned issues faced by medical cannabis patients, as it allows them to produce dispensary-quality products within the comfort of their homes at a dramatically lower price. Unfortunately, at-home decarboxylation has always been an imperfect science, at best. While many cannabis users will swear by their own personal kitchen decarboxylation methods (a boiled mason jar in a crock pot, a long roast in the oven, a double boiler full of butter), it's an unfortunate fact that few consumers actually go the extra step, where possible, and test the products they've created. Were they to do so, they'd find their decarboxylation rates max out at around 70% efficiency, due to the sensitivity of the process and lack of precise, even heating.

This efficiency problem may not be a significant concern for the recreational consumer who occasionally makes a batch of brownies for their friends. Medical patients using cannabis for daily wellness management, however, are in a much more complex situation. Managing tolerance, intoxication, and budget requires predictable dosing and reliable rates of infusion. Quality control is a significant factor in a patient's decision making, particularly for those managing some sort of chronic pain.

Preserving the maximum amount of bioavailable cannabinoids through a precision decarb is the first step toward the efficient use of the plant, and many common myths about approaching this process have been outlined through a comparison with the standard oven, toaster oven and crockpot. [1] In addition to a proper decarb process, it's also important to understand



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the nuances of what starting materials require decarboxylation. There's a common misconception that extracts are decarboxylated, when in reality the large majority do require activation for use in edibles, topicals, or suppositories. A close look at testing results shows that products like kief and hash, as well as products like rosin and butane hash oil, are primarily composed of THCA, not THC. Ethanol extractions and home-processed, full-extract cannabis oils as well as CO_2 extractions are decarboxylated in some instances but not others, depending on whether the equipment used to process the concentrate introduced sustained heat during the extraction.

Determining whether starting material needs to be decarbed and then completing that process properly is key.
After the decarb step, the product is fully active and can be used directly in food, and many users enjoy the addition of a small amount of vegetative material. Doses of less than 0.1 g can deliver an excess of 20 mg THC with flower exceeding 23% starting THCA, resulting in incredible cost savings for the average user. [2] However, a large segment of users is interested in further processing the active flower or concentrate into an oil or butter. This can improve the ability to consistently blend the active product with a lotion or salve, and lead to an end-product with a smoother texture, as the plant vegetation is removed during the butter/oil infusion process.

Major issues of efficiency are raised during infusion -- how does one ensure that all of the active material makes its way from the plant material into the oil or butter? The process is easiest and most efficient with concentrates, as the decarboxylated concentrate can be mixed directly with the warmed butter and oil and doesn't need a straining step. For flower material, the key is ensuring enough time for the THC molecules to migrate from the plant into the butter or oil. An oil bath between 180°F - 200°F for two hours will yield 85-95% infusion rates depending on the type of oil used. The infusion process is less sensitive than the decarb process. It is important to decarb prior to the infusion step as butter and fatty oils will act as insulators during the infusion process, which will prevent significant decarb during the process. This insulating function is also what prevents THC from being damaged during the infusion step.

Grasping cannabis science fundamentals and putting those concepts into action through simple tools and processes allows the movement to proliferate even where the industry or regulations fall short. The impact of the plant will be amplified if more people gain the knowledge to harness its power.

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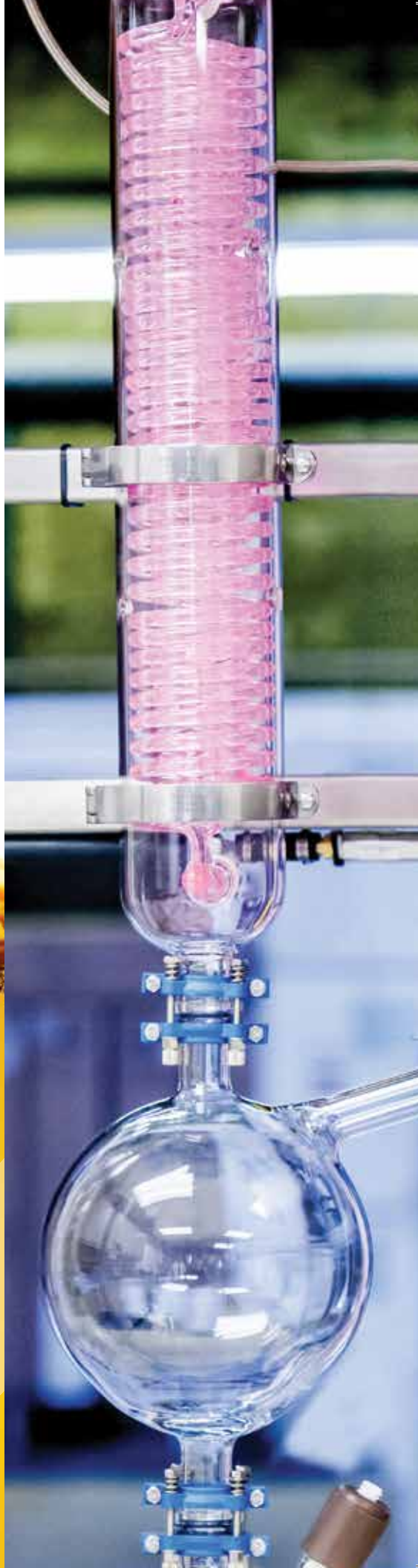

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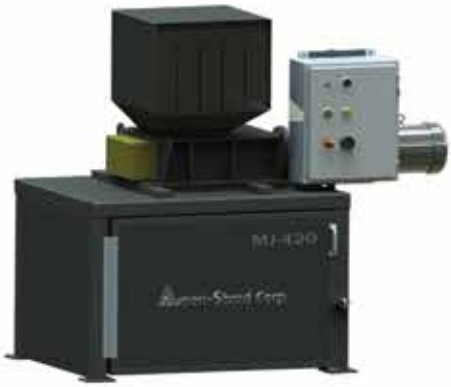

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Letter from the Editor

December 17th, 2018

As we head into the year 2019, we wanted to do things a little differently. Actually, this year will reveal several issues of T&T that veer off from what we've done before. As the cannabis plant and industry evolve, so do we.

This issue revolves around how cannabis influences our senses, whether by getting a whiff of an elegant terpene bouquet, using our vision to look over and appreciate the buds and crystals, or even through a blurring of multiple senses in a phenomenon called synesthesia. When we consider all of the ways that we can experience the nuances of cannabis, it's easy to see why there is such a mystique surrounding this strange and inspiring plant.

We will delve deeper into the medical realm than we've gone before, from a discussion of cranial nerves and of course our endocannabinoid systems, to the origin of how we sense things in the first place. It's easy to take these daily physiological processes for granted. Our senses are often blunted by the near-constant bombardment of sensory information our bodies are exposed to. But when cannabis augments those senses, it can feel like experiencing the real world for the very first time.

I've often heard people say that cannabis helps them achieve a balance, to feel more *human*. And while they often say this from a perspective of almost disbelief, that's exactly what cannabis does. Given what we now know about our endocannabinoid system, and the functions it serves, it's becoming easier to understand exactly how cannabis consumption helps us achieve a more harmonious and universal state of being.

I'll leave you with a favorite quote of mine, from one of my favorite Earthlings: *"The illegality of cannabis is outrageous, an impediment to full utilization of a drug which helps produce the serenity and insight, sensitivity and fellowship so desperately needed in this increasingly mad and dangerous world."* Carl Sagan said this as he clearly recognized the exquisite marriage of cannabis and our senses. And while he said this sometime near 1969, I can't think of a more relevant time when serenity and insight, sensitivity and fellowship are more urgently needed than at this very moment.

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The Endocannabinoid System

By John Metcalf, M.D., Ph.D., ABIM, CFMP, Releaf Specialists

The other day I was discussing cannabis and chronic pain with an anesthesiologist pain specialist colleague of mine. His comment to me was that cannabis is not a medicine, there is no empirical research to support cannabis use, and that he doesn't want his patients "stoned"! I was flabbergasted by his statements. I said to him, "do you know anything about the endocannabinoid system (ECS)" to which he replied that he didn't. Then, I said to him that he was unqualified to make any comment on cannabis as a medicine.

Currently, approximately 5% of physicians in the United States are aware of the ECS and roughly 13% of medical schools in the U.S.A. teach an abridged version of cannabis and the ECS. In fact, only one medical school, Brown University, teaches a course on the ECS. PubMed, which is a medical search engine, lists 9,100 published research articles on endocannabinoids. So, what is the ECS?

In 1964, Dr. Raphael Mechoulam at the Hebrew University in Israel discovered the phytocannabinoid (plant-based cannabinoid) of THC (the main psychoactive compound in cannabis). In fact, Dr. Mechoulam called the ECS the "Global Protection System." In 1988, Dr. Allyn Howlett at St. Louis University discovered the cannabinoid receptor and how THC affects this receptor in the brain. The receptor works like a "lock" on the cell membrane and THC acts as a "key" that binds to this receptor creating a chemical reaction within the cell. In 1992, the first endogenous cannabinoid, called anandamide, was discovered by Dr. Lumir Hanus and Dr. William Devane. In 1995, a second endocannabinoid (endo meaning made in our bodies) was discovered called 2-AG. These were named the endocannabinoids. Therefore, the ECS is made up of 1A) endogenous cannabinoids (anandamide and 2-AG), or 1B) phytocannabinoids such as THC, CBD, CBG, CBC, CBN, etc., (approximately over 100 phytocannabinoids are produced within the *Cannabis* plant) that mimic the body's own endocannabinoids, and 2) the endocannabinoid receptors.

The CB1 receptors are located in the central nervous system, the enteric nervous system (GI system), liver, lungs, kidney, and reproductive system. In general, the highest density of these receptors are located in the hippocampus, cerebellum, and basal ganglia regions of the brain. There are no receptors in the brainstem, so there is no risk of cessation of breathing or heart rate upon overconsumption of chemicals binding the CB1 receptor.

The CB2 receptors are located in the immune system, peripheral nervous system, circulatory system, gastrointestinal system, hemopoietic system, and the musculoskeletal system. There are also areas within the body that express both CB1 and CB2 receptors such as the autonomic nervous system, heart, liver, gastrointestinal system, and the skin. Recent research has probably located a third (CB3) endocannabinoid called the G protein receptor 55 (GPR55) which is linked to energy homeostasis and energy dysregulation associated with diabetes and obesity. It is now known that cannabinoid interactions extend beyond the CB receptors and interact with other CB-type related receptors located on the cell membrane and ion channels. Other receptors, like TRPV1, are associated with pain transmission; GPR119 functions as a "fat sensor" to reduce food intake and weight gain; and the PPARS, which regulates gene expression of metabolic functions that involve fatty acid storage, glucose metabolism, and malignancy progression. Finally, the enzymes that compose and degrade the endocannabinoids were isolated. (For example, FAAH and MAGL are degrading enzymes for anandamide and 2AG, respectively.)

How does the ECS work? It is a bidirectional, cell-signaling system utilizing neurotransmitters between cells within our bodies trying to maintain balance or homeostasis. It samples the extracellular environment around the cell membrane and modulates changes

intracellularly to balance the body's systems. The endocannabinoids are made on demand in response to a trigger that unbalances the body. These triggers are varied and include injury, pain, illness, and inflammation. These imbalances create medical illnesses that cause the ECS to initiate physiological changes to try and restore the body's balance. Some of these bodily physiologic pathways include gastrointestinal, cardiovascular, pain perception, neuroprotection and neuroplasticity, immunity, hormonal regulation, inflammatory reactions, inhibition of tumor progression, etc.

Two neurons consisting of the presynaptic neuron send a neurotransmitter signal to the postsynaptic neuron that receives the signal. When the presynaptic cell sends an overabundance of neurotransmitter signal to the postsynaptic neuron, this creates an imbalance. This imbalance, in turn, creates an influx of calcium by removing the magnesium plug on the NMDA postsynaptic-cell receptor, which signals the endocannabinoid to make a "key." This "key" is sent back to bind to the cannabinoid receptor "lock" on the presynaptic cell. When the receptor is activated by the endocannabinoid, the presynaptic cell downregulates the neurotransmitter, thus, restoring homeostasis or balance.

THC, a phytocannabinoid, can substitute for the endocannabinoid (such as anandamide) and act as a "key" to restore neurotransmitter balance. Underactivity or over-activity of the ECS has been linked to medical illnesses. It is essential to understand how the dysregulation of the ECS can create disease or can result from a disease or trigger. In 2003, Dr. Ethan Russo, a neurologist and cannabis researcher, hypothesized that an endocannabinoid deficiency could create medical illnesses. He proposed that an endocannabinoid deficiency would limit the body's ability to maintain homeostasis and would lead to disorders such as migraine headaches, irritable bowel syndrome, fibromyalgia, and other "treatment resistant" diseases. His research found many patients with these illnesses who used cannabis and made clinical improvements. This endocannabinoid deficiency can be caused by trauma, epigenetics, genetics, chronic stress, and poor lifestyle choices. In 2016, Dr. Russo updated his list of conditions to include autoimmune disorders, epilepsy, cardiovascular disease, anxiety, depression, failure to thrive, schizophrenia, multiple sclerosis, Parkinson's, etc. In 2008, Dr. Vincenzo Di Marzo reported that over-activity of the ECS was associated with obesity and Type 2 diabetes. He hypothesized that elevated endocannabinoid levels may be related to lack of degrading enzymes of these endocannabinoids which would result in longer-acting cannabinoids around the receptors.

This would create increased hunger and weight, which would continue to recycle this endocannabinoid over-activity. In fact, when obese men with elevated endocannabinoids were enrolled in a one-year lifestyle change study that included healthy foods and physical exercise, their endocannabinoid levels decreased. In fact, their overall weights were reduced, and their healthy cholesterol and triglycerides improved. Dr. Di Marzo hypothesized that maintaining healthy weight, dietary choices, and exercise helps to maintain normal ECS and homeostasis. In conclusion, if the ECS is dysregulated, then your body is not in balance or homeostasis. If the ECS is the cause of your illness, then treatment with medications does not address the situation. Subsequently, a patient's disease symptoms are not improved. Chronic poor lifestyle choices can lead to chronic stress which negatively impacts the ECS. It is essential to maintain healthy diet, stress reduction such as meditation, supplements such as Omega-3 and probiotics, socializing, intermittent fasting, restorative sleep, regular exercise, and medicinal cannabis to maintain healthy ECS and health. As my dad, Donald J. Metcalf, told me many years ago, "Live life fully, choose a healthy lifestyle, and be well."

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Suggested Online Educational Sources:

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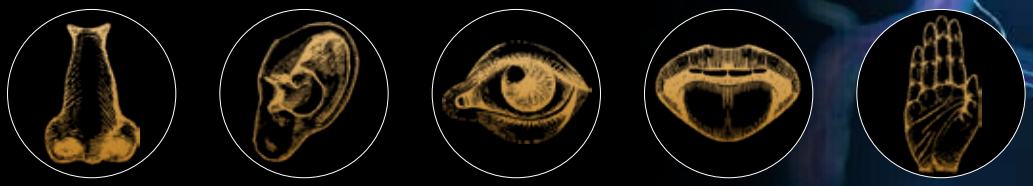
Multifaceted Augmentation: How Perception is Influenced Even by the Way We're Built

By Tamir Bresler



This issue of T&T is all about the senses and how cannabis use affects them. I think before doing that, it would be worthwhile to spend a minute trying to understand what our senses are *really* all about. Where do they come from? How do they work? We don't realize it, but even our basic anatomy ends up having an effect on how we perceive the outside world.

Just imagine you're in a twin-engine airplane. Or perhaps a live performance. Even a loud car. What do these things have in common? A high-decibel environment, of course. We perceive sounds such as music or engine noise through our ears. Soundwaves agitate the tympanic membrane ("ear drum"), which in turn drives the three bones of the middle ear *(incus, malleus, stapedius)* to translate the soundwave signal into liquid waves, and the nerve of the inner ear, which translates, for a second time, the liquid wave signal into an electric impulse that is carried into the auditory nucleus of our brain.

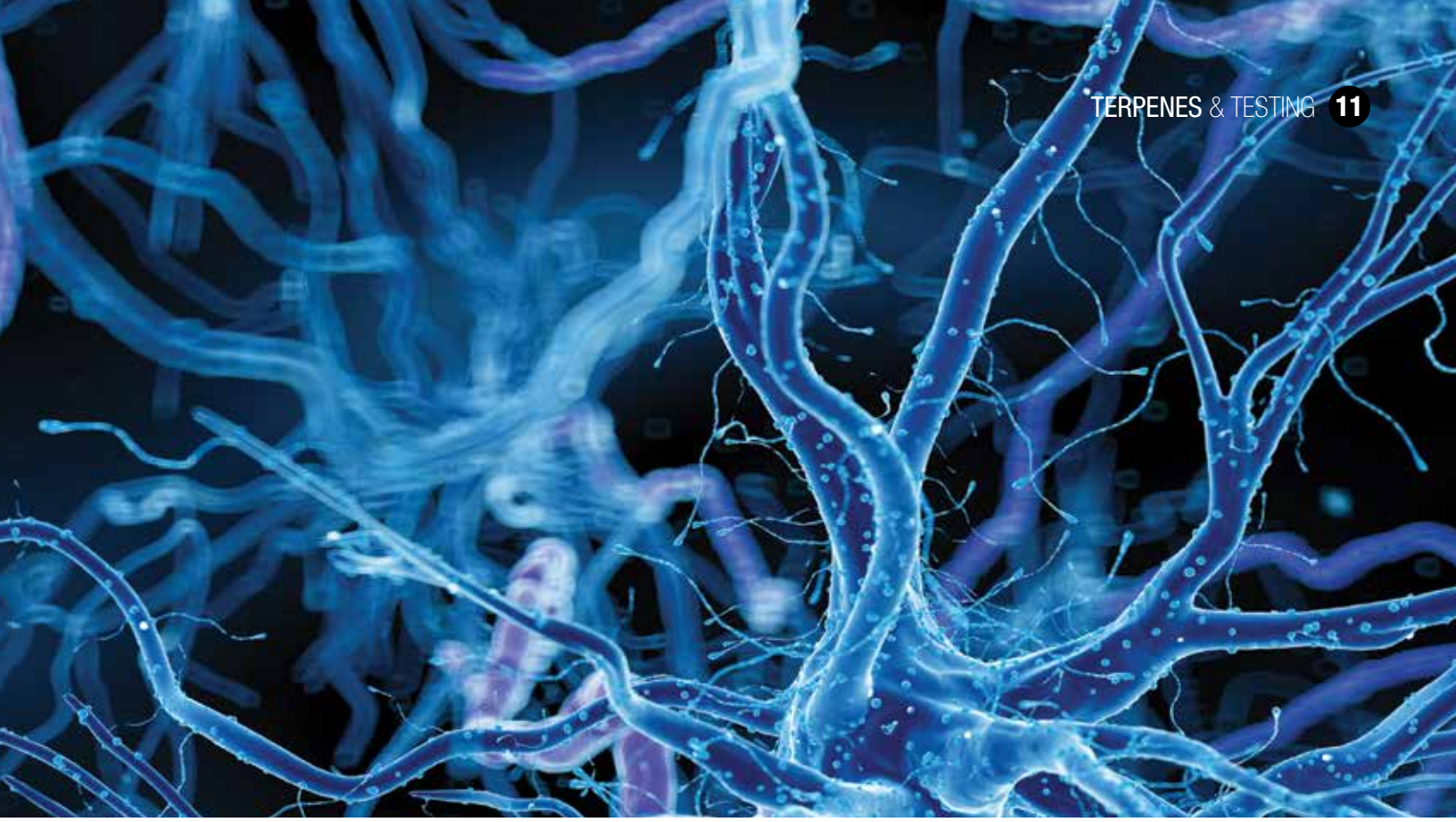
Even though all of the environments mentioned before are loud, not all of the noises are as perceptible as others. When the sound around us is repetitive and unchanging, we call this "white noise," because after a while we forget that it's there. Our ears normalize to the environment and you snooze through your transcontinental redeye in no-time. So, it seems that as long as the sound is "white," its loudness won't really affect our perception or the lives around us. All it poses is a minor inconvenience, does it not?

Well, if you think so, you'd be wrong, and your mistake would come from lack of knowledge of anatomy. You see, there are twelve so-called cranial nerves, each defined by their exiting from the cranium (the brain-containing, inner chamber of the skull). Cranial nerves are fascinating, and are the pathways by which we feel four out of our five human senses, the missing one being the sense of touch, which comes from all sorts of nerves throughout the skin and body.

The vestibulocochlear nerve, or CNVIII (cranial nerve #8), is the cranial nerve responsible for audition. It passes through a region of the skull known as the internal auditory meatus. Accompanying it in the meatus is CNVII (cranial nerve #7), also known as the facial nerve. Cranial nerve seven is the main motor nerve of the face, responsible for all our fine-motor, emotion-showing, "mimetic" facial gestures. Smiling? That's the facial nerve. Frowning? Facial nerve again.

However, on its way to the facial muscles, the facial nerve gives off a small branch, called the *chorda tympani*, which ends up receiving all taste sensation from the front two thirds of our tongue (*psst*—that's where most of our taste sensation happens). On its way to the tongue, the chorda tympani passes over—you guessed it—the eardrum!

Normally this would just be an obscure anatomical factoid. But when in an environment of loud noise, it becomes of significant interest because it turns out that the continued reverberations of the eardrums mess with the ability of the chorda tympani to pass along taste signals from the tongue, in effect, *modulating our perception.*



A study by Yan and Dando at Cornell University seeking to explain why airline food has such a bad reputation placed subjects in environments of increasing auditory stimulation and had them taste liquid solutions representative of each of the five flavors: salty, sour, bitter, sweet, and umami (savory). [1] No differences in response were found for salty, sour, or bitter tastes. However, sweetness intensity was rated "progressively lower" as the volume was turned up. Simultaneously, perception of the umami flavor seemed to enhance, with greater effects being seen at greater concentrations of the flavor. Maybe that's why tomato juice is almost as sought after as beer even on the lager-loving German airline Lufthansa! [2]

As we can see, just the way our bodies are built can have an effect on the ways in which we perceive the world, in a very complex fashion. How much more of an effect, then, can our perception experience when consuming psychoactive and physiologically-modulating compounds like cannabinoids and terpenes?

Cannabis use, specifically THC consumption, has long been known to have a modulating effect on the way users perceive time, [3] inducing temporal "overestimation and underproduction" in a non-dose dependent manner. Our sense of time has been shown to affect everything in our daily lives, from cognition and behavior even to motor function. [4] It would therefore not be a large leap of faith to say that cannabis use, by affecting our sense of time, indirectly affects many other processes in our bodies, in ways which have hitherto been unexplored. This is where a major part of neurobiology research needs to take us in years to come, exploring this complex relationship between the modulation of one sense affecting the perception of another.

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Molecular Cannabinomics

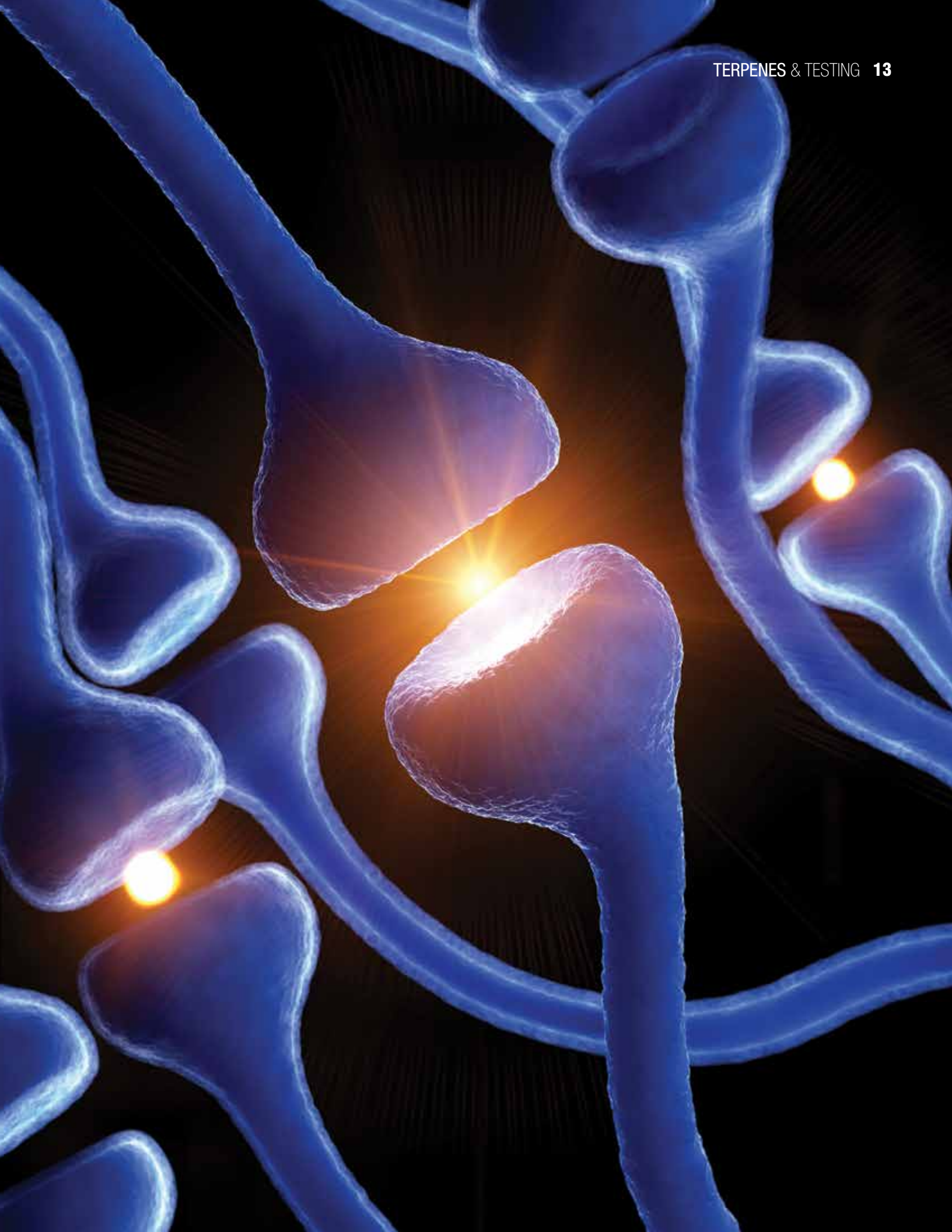
By Steven Bennett, Prescott Logic Technologies, LLC.

Whether you believe cannabis can cure cancer or you are convinced it is debauchery only used by the lowest forms of the human race, everyone can agree that cannabis use causes changes within the body. We all know it can make some people hungry, sometimes talkative, and at other times tired. Some are convinced the plant makes them lazy while others can attest that it provides them with focus and clarity. Regardless of your own experiences or beliefs, it is evident that this plant changes the way a person feels or behaves, and often in significant ways. We can say the same for alcohol, caffeine, and even pain relievers like aspirin and morphine; they *all* change the way we feel. And whereas one substance might cause analgesia and another intoxication, every molecule that we take into our bodies alters our existing physiology in some fashion.

Human beings are a complex integration of tissues that perform in diverse yet *orchestrated* ways to *coordinate* our daily activities. As such, each tissue is comprised of varied cell types and functionalities that *communicate* with each other and with cells of other tissues to regulate processes like gene activation, metabolism, and immunity. In the nervous tissues, this communication is primarily electrochemical in nature; the *concerted distribution* of positive and negative ions on opposite sides of a cell surface creates a difference in charge. This potential energy or voltage *induces* "depolarization" along a nerve fiber and thus the rapid *transmission* of electrical activity to your muscles allowing virtually instantaneous response to your physical environment. When considering metabolism and endocrine *function*, high levels of blood glucose following a meal *trigger* the pancreas to *release* insulin into the bloodstream. Insulin is then responsible for *communicating* to cells throughout the body to *stop* whatever they are doing and *take in* the needed shipment of energy that is going around. Even through this mouthful of physiological jargon, the use of italics above denotes complex daily operations that occur within the body that sound more like a construction site than medical science.

Central to all activity within the construction of a building, or the execution of any successful project, is communication. As important as communication is between humans to thrive as a community, the cells of the body need to have constant communication with the cells directly next to them *and* those in remote regions of the body for the organism to thrive. One of the most common means for this to occur is through a class of biomolecules called "receptors." Receptors are types of antennae that cells manufacture and place on their exterior surface with an active portion still inside the cell. Specific molecules (ligands) will interact chemically with the receptor and positively or negatively influence specific molecular communication networks inside the cell. These networks, termed "signal transduction pathways," might decrease the expression of a particular gene or facilitate the uptake of glucose as mentioned above. Receptors are a ubiquitous part of biology and different types are found on different cells that allow it, effectively, to interact with its environment. They are a key concept to understanding cancer biology or neurotransmitter release, and represent a principal mechanism behind antibodies and immune function. Moreover, receptors are pivotal in understanding pain, primarily through the opiate class of receptors, and serve as a topic central to all cannabis-mediated responses.

The Endocannabinoid System (ECS) describes the vast network of cannabinoid receptors and ligands that the body produces "endogenously" or on its own. That's right folks, our bodies have receptors that bind cannabis. Our bodies even manufacture (endo)cannabinoids to communicate through these receptors irrespective of your use, let alone opinion, of the cannabis plant. We have 2 well-characterized receptors: CB1r and CB2r. CB1r has been historically associated with the central nervous system and psychoactivity, whereas CB2r has been associated with peripheral tissues and circulating white blood cells. More recent scientific discovery is demonstrating that while generally accurate, this description is highly oversimplified, and some may argue it is even inaccurate. There are other receptors that have been less characterized like GPR55 and GPR89 [1], which demonstrate varied responsiveness to THC and CBD. Some researchers claim that these and other "orphan" receptors might actually be the CB receptors, namely CB3r. [2] That is, these receptors might be manufactured by the body *specifically* for ECS activity.



If at this point you're thinking that these structures seem far-fetched, please recall the opioid class of medications. Opiates are morphine derivatives extracted from the poppy plant that have been used by humans for centuries to relieve pain. Decades of research on these compounds has allowed the pharmaceutical industry to make seemingly endless iterations of drugs in this class. Over the last 60 years, research has deduced that these drugs work through interaction with specific receptors distributed throughout the body, which we now call mu, kappa, and delta opiate receptors. They also work with a few orphan receptors under investigation. Not only do the receptors bind these poppy-derived molecules but also their endogenous equivalents like endorphins and encalphalins, which our bodies naturally produce to reduce pain following exercise and even traumatic injury.

As interesting as it is that we have these endogenous systems at work, it is just as fascinating that molecules existing in nature can mimic those that we produce internally, eliciting similar effects within our bodies. We can alter mood and appetite through subtle manipulations of our biochemistry or what I like to refer as "better living through modern pharmacology."

Insects rely on dopamine and serotonin for neurotransmission just as humans do. Bananas share 65% of the same genes with us. [3] Our planet relies on many of the same, or at least biosimilar, molecules that are responsible for our intricate design and allow us to "adjust" ourselves, and to theoretically and actually heal/treat ourselves. Am I saying that all of the treatments for human disease can be found in dense forests and ocean depths? Probably, since that is where we have been getting them so far! Minimally, one cannot refute the scientific logic of plant-based or plant-sourced medicines.

There is, of course, much more to this story. First, we have to consider the mode of cannabis delivery to the patient. The product can be combusted, ingested, applied topically, or inhaled without heat. There is no shortage of creativity when producers want their products to corner market share. There is also no shortage of bioactive molecules found within the plant. We frequently hear of THC and CBD, but they are only 2 of the 113 cannabinoids [4] currently identified. They are a big part of the story, just based on their prevalence, but they are simply the main players on the steering committee. Terpenes and terpenoids, known primarily for the smells and tastes they impart on the varieties we enjoy, are formed through the same biosynthetic pathways as cannabinoids within the cannabis plant. We can envision a terpenoid as a "part" of the

larger class of cannabinoids that can logically interact with the receptors, but with less predictability and consistency in effect. The pharmacokinetic profile of drugs, including cannabis-derived bioactives, describes the duration of onset and blood concentrations over time as well as their specific binding interactions at the receptor level. This last point is not an easy one to articulate; hundreds of molecules in the cannabis plant exist, and they all behave very differently.

THC, for example, is a direct agonist of the CB1 and CB2 receptors. That is, when THC binds to the receptor it activates that receptor. [5] CBD, however, has almost an opposite effect and is considered a reverse agonist or even antagonist to these same receptors. [6] When CBD binds, the receptor is inactivated, which likely explains the reported reduction in psychoactivity from users as CBD is increased. All other active compounds in the plant can fall in this range of pharmacological activity as full agonists, partial agonists, or antagonists that can either activate or inactivate these receptors to various extents. This process describes the pharmacology behind the entourage effect of cannabis. The overall effect elicited is determined by a seemingly nuanced "tuning" of the receptor by the sum of these individual signals.

To add another level of complexity is the concept of pleiotropic pharmacology. That is, CBD has been reported to have binding activity at numerous other receptors. It may have antagonistic activity in CBrs, but shows agonism (activation) at D2A [7], a subset of dopamine receptors. Even more remarkable is that opiate receptors and cannabinoid receptors are in the same class of G-Protein Coupled Receptors. Extensive research demonstrates that these receptor classes interact with each other at the cell surface under certain conditions. They share signal transduction pathways in the cell and even heterodimerize in some instances; that is, subunits from the cannabinoid receptor and subunits from the opiate receptor can come together to form a new receptor altogether with obvious mechanistic implications in treating various forms of pain.

To conclude, the complexity of cannabis is not so difficult to understand; rather, the simplicity of products about which we have been effectively brainwashed by Big Pharma is. There is, for example, no such thing as a silver bullet "cure" to handle pain without unwanted side effects like lethargy or constipation. All drugs elicit effects directly or often indirectly in other parts of the body, once metabolized and broken into pieces generally recognizable by the body (metabolites). Yet somehow we have all been taught to believe that the "medicines" we take are designed specifically to target

whatever ailment afflicts us. Without even being aware of it, we are barraged with advertisements of drugs that show us that a great life is one pill away. The pharmacology of cannabis is complicated, to say the least, but the false expectation that each of us has been sold at our local pharmacy is the true culprit of misunderstanding.

Only the pharmaceutical companies have the financial capability to organize thousands of patients in randomized, placebo-controlled, double-blinded clinical trials to generate results to allow them to make "claims" to their effectiveness. As such, the business of developing treatments for human suffering is more elitist than it is altruistic, and we are sold drugs that generate billions of dollars rather than enhance billions of lives.

The generic pharmaceuticals and over-the-counter (OTC) medications are often produced by subsidiaries of the pharmaceutical companies, while other plant extracts of less pronounced effects are listed as natural health products (NHPs) and sold in stores like GNC. In theory, all of these industries are regulated from a production standpoint, yet different standards exist to ensure that the same product is produced each time with narrow thresholds of tolerance. The main difference with a bonafide "pharmaceutical" is that the company has done the proper research to say "this relieves pain" and can back it up with scientific data, both through preclinical mechanisms and clinical efficacy.

OTC medications have been FDA approved as safe and effective with minimal risk from misuse or abuse and some restriction on what advertisers can say a product actually does. In the NHP markets, claims are virtually absent yet people swear by some of them and the products are allowed to be sold for the consumer to decide what is best for them. Cannabis is a veritable chameleon as it is a therapeutic, a nutraceutical, a cosmeceutical, an OTC, a pharmaceutical, an NHP, and something that is enjoyed "recreationally." Strangely, we believe that the plant deserves its own laws, its own stores, and its own user when the reality is that it's not really any different. To quote Emerson: "A weed is a plant whose virtues have not yet been discovered." Much of the cannabis story still remains untold, and it is the opportunity of our lifetime to tell it.

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The Best Laid Plans of Fish and Men: Animal Research, Human Driving Studies, and Night Fishing

By Jahan Marcu, Ph.D. Director of Experimental Pharmacology and Behavioral Research, International Research Center on Cannabis and Mental Health; Chief Scientific Officer, Whole Plants, LLC

The study of cannabis and endocannabinoids (eCBS) has exploded into almost all parts of the human body. The attention devoted to the effect of cannabis on vision and the eye has been limited compared to other parts of our anatomy. For example, a quick search on Pubmed for "cannabinoid + brain" easily yields over 2000 articles from the last few years. In contrast, a search of "cannabinoid + retina" and "cannabinoid + glaucoma" retrieves a few dozen studies from the last few years.

There are two main pathways to understanding the effects of cannabis on vision. One pathway is to look at the effects of drugs like THC and CBD on the mechanisms of the eye, such as increasing or decreasing eye pressure. And the second pathway involves how our brains process that information. To paraphrase a researcher, *"The effect [of THC on vision] is subtle and modest as might be expected since smoking [cannabis] does not render the smoker blind".* [1]

The Eye-Brain Connection

You see with your brain, not your eyes. The brain is responsible for everything we will ever think, know or experience. Our brains are completely shut off from the world we require it to navigate. All of our brain experiences, such as vision, are electro-chemical signals rocketing along neurons at 268 miles per hour. If you put your hand on the back of your head, you are very close to the parts of the brain that are extremely important for processing visual information. Our brain relies on the retinas of our eyeballs to break down incoming visual information to specific signals related to color and depth that our brains process to make sense out of the environment.

Visual perception is a complex mechanism that embraces the cognitive processes for the retrieval of information from environmental light in order to construct a meaningful representation of the environment. Briefly, visual processing begins in the retina with the absorption of light by photoreceptors, thus initiating the conversion of light into brain activity.

Cannabis and many other substances can affect visual processing. The brain is full of receptors and proteins that respond to compounds in cannabis, which may influence the decisions that the brain is making about what it is beholding. It seems simple, but modern research shows that this seamless processing of reality is complex. Depending on how you measure it, the brain uses 1/3 to 1/2 of its real estate to help you perceive and make sense of light signals from the retina.

The most obvious application of this research field is to understand the effect on driving ability, which combines potential effects on the retina or eyeball itself, and how we process the flow of signals from our retina to our visual processing centers. Our brains, for example, can tell us if we are moving next to an object, or if we are moving and the object is standing still, or if both the object and we are standing still while the environment is moving. Sometimes the brain struggles to figure out what is moving. Imagine trying to park a car while the car in the adjacent spot pulls out.

Driving is no doubt a direct concern for anything that could affect vision. Since the 1960s at least 20 studies have been published regarding the effect of THC on driving ability. Three main consistent points have emerged from these studies: [2]

Cannabis produces a consistent, mild to moderate impairment on tracking ability, such as keeping in the center of a lane, and some variability in speed of driving. The effects observed are significantly far less than that seen with a blood alcohol concentration of 0.08%. [3] Cannabis produces an extra delay in decision time, a "moment of reconsideration" before undertaking an inherently dangerous maneuver. [4] Cannabis induces more cautious driving habits.

A review of this research by GW Pharmaceuticals' researchers concluded "*…driving ability does not appear to be substantially impaired by cannabis. Any impairment is well with the range of (or lower than) what is currently produced by pharmaceutical agents which are commonly used for similar conditions.*"

The researchers from the U.S. Department of Transportation, National Highway Traffic Safety Administration study published in 1993 concluded, "*Drivers under the influence of [cannabis] retain insight in their performance and will compensate…by slowing down or increasing effort. As a consequence, THC's adverse effects on driving performance appear relatively small. Of the many psychotropic drugs, licit and illicit, that are available and used by people who subsequently drive, [cannabis] may well be among the least harmful.*" The significance is that the decrements in driving performance induced by exposure to cannabis with high THC content most significantly result from a non-selective decrease in attentional or processing resources. [5]

In the National Longitudinal Survey of Youths (NLSY79), a nationally representative sample of 12,686 young men and women surveyed in 1979 to 2010 was used. The quality of eyesight of 1304 heavy cannabis users was compared with

1304 respondents with light or no cannabis use. There was no statistically significant difference in the self-reported quality of eyesight among heavy cannabis smokers compared with youths who never used cannabis or are light cannabis users. [6] Among heavy cannabis smokers, males and high school graduates have decreased odds of reporting a poor quality of eyesight.

If science has shown us anything, it's that studying cannabis is far from straightforward. Cannabis can both improve and impair vision under different situations and the effects may be sex-dependent. However, the precise brain mechanisms underlying impairments due to cannabis use, in particular those in cognitive functions critical for car driving, are still being debated.

Animal Research, Human Driving Studies, and Night Fishing

There is an evolutionary perspective which adds depth to our discussion and reasons for the prevalence of fish in research studies on cannabis and vision. The receptors that THC stimulate, the cannabinoid receptors (i.e., CB1 receptor), are part of the family of rhodopsin receptors. Rhodopsin receptors were most likely the first G-protein coupled receptors to evolve when our ocean-dwelling ancestors wiggled and waddled onto land. This rhodopsin receptor evolved in the eye, or what passed for eyes several hundred million years ago. The purpose of CB1's great, great, great, great…great grand-daddy was to notify the brain of incoming light. The structure of the receptor was so useful, our ancestors began using other versions of this G-protein to carry out other functions that help us to eat, sleep, relax, forget, and process visual information.

Fish, such as goldfish, are the preferred animal model for basic eye research, and much data in the literature is generated by studying eCBs and THC in these eyeballs. The second most popular animal model are mice, which may

represent a better model for studying the effect of cannabinoids on visual processing. Goldfish are used for two main reasons, despite mice perhaps being the superior research model to base human research upon. One is that goldfish are less expensive, and the second is that the use of goldfish provides reproducible mechanisms about how eyes work in response to cannabis compounds and eCBs, mechanisms of eyeball function preserved across species from evolution.

It has been known for nearly 50 years that cannabis and the psychoactive constituent THC reduce intraocular pressure (IOP). IOP means the pressure in your eyes. Left untreated, high eye pressure can cause glaucoma and permanent vision loss in some individuals. However, some people can have ocular hypertension without developing any damage to their eyes or vision. [7] According to studies in ocular hypertension treatment, 4.5 to 9.4% of Americans age 40 or older have ocular hypertension, which increases their risk of developing sight-threatening conditions. Elevated IOP remains the chief hallmark and therapeutic target for glaucoma, a major cause of blindness.

THC's effect on decreasing IOP may be sex-dependent. For example, a recent study measured the effect and found it more pronounced in male mice lasting upwards of eight hours versus four hours in female mice. A sex-dependent effect has not been confirmed in the goldfish.

While THC exerts beneficial effects on the eye (i.e., IOP and the retina), it can affect the visual processing of information, such has been shown in some driving studies. However, it is a convoluted area of research as it is unclear if THC's effect is significant on visual processing as opposed to its effect on attention.

Isolated reports exist that describe cases involving seeing spots and blurred vision as

a result of using or quitting the use of cannabis. [6] Those reports appear rare, far from predictable or reproducible in controlled settings, and limited by potential product contamination (studies involving "street cannabis"), drug-drug interactions or pre-existing conditions.

The best example of the effect of chronic cannabis use on vision comes from studies on humans fishing at night. If cannabis impaired vision and visual processing to a significant degree, then coral fishing at night after smoking hash or cannabis flowers would often result in the subjects sinking boats and going hungry. The study of fisherman has been evaluated at least three times. The base study involved subjects smoking kief, taking tinctures, and even up to 20 mg of pure THC before navigating coral reefs and hunting for fish at night. Jamaican fishermen who smoked or ingested a crude tincture of cannabis were apparently able to see and navigate their boats through dangerous coral reefs in the darkness of night and able to see fish jumping out of the water in order to know where to throw their nets. [8] The improvement of night vision after consuming cannabis has demonstrated a degree of reproducibility observed in both Moroccan and Jamaican fisherman.

Two takeaways from this section are that fish continue to be important for research studies on cannabis and vision. And the second is that the benefits of cannabis improving night vision may be limited to THC, because CBD blocks the effects of THC on the CB1 receptor in the eye and the brain.

Is CBD Good for Your Eyes?

Like THC, there have been no significant reports of detriment to the eye from CBD use, except for some reports that it can block CB1 receptors. Thus CBD can block the beneficial effects of THC in eyeballs. Research surrounding cannabis on eye health, vision, and visual processing has been contradictory at times. Three of four studies that have tested CBD for effects on IOP have reported no effect, but the fourth has reported an increase in IOP. Unlike previous work, this fourth study used topically-applied cannabinoids in the eyes of mice.

At least one physician has been outspoken about the concerns regarding the potential trade-off of vision for the health benefits of CBD [9], as there appears to be no risk or toxicity studies looking directly at IOP related to long-term CBD use in humans. Additionally, the semi-

well-known study published in 2010 on CBD protecting the eye in diabetes was retracted. [10] The statement from the journal of *Molecular Vision* reads "*The authors made substantive errors in figure images of this article such that the hypotheses were not tested and the conclusions were not supported.*" This study is a ghost – no one can read it anymore. Yet, this article continues to be cited and used as a basis for theories and research as if it still existed in the scientific literature.

CBD is a major constituent of cannabis that has been found to be without effect on IOP in most studies. CBD, contrary to expectation, has two opposing effects on IOP and can interfere with the effects of THC in the eye. Of particular importance to consider is its ability to block THC's activity at CB1 receptors in the eye, effectively blocking THC's ability to reduce eye pressure.

Terpenes Influence How We Perceive Colors.

Terpenes such as pinene can increase eye blink frequency. Blinking cleans the surface of your eye of any debris and also nourishes your eye with oxygen and nutrients, keeping your eyes healthy and comfortable. Terpenes may play a significant role in perception or visual processing. For example, why did Van Gogh use so much yellow in his later paintings such as his portraits and self-portraits? [11] According to one historical account, "*Van Gogh also had some digestive problems, for which he may have taken santonin, a terpene, used at the time to treat and prevent intestinal parasites and known to cause yellow vision. He was presumed to have pica, which caused him to have abnormal cravings for other terpenes similar to santonin: thujone, turpentine, camphor and absinthe.*" These common terpenes have been reported in various cannabis preparations.

Terpenes also affect how we see our environment. "*Hydrocarbon particles released by vegetation (such as terpenes) react with ozone creating 'blue haze' that limits vision in the distance.*" [12]

Conclusions

Applications of cannabis' therapeutic potential include persevering vision, protecting us from age-related blindness, treating migraines by altering light sensitivity and brain activity, and macular degenerative diseases via

antioxidant and anti-apoptotic effects. The neuroprotectant and brain elasticity imparted from cannabinoids are important for potential benefits in eye-brain health.

It is valuable to understand the mechanisms by which THC and CBD regulate intraocular pressure, particularly at a time when their changing legal status and the perception of phytocannabinoids as safe contribute to a continued growth in their availability and popular embrace. CBD in particular has recently been approved by the FDA as an antiepileptic and is available in many grocery stores. The regulation of ocular pressure by THC and CBD is more complex than previously appreciated. THC acts via a combination of CB1 and other receptors in a sex-dependent manner, while CBD can both raise IOP and interfere with the effects of THC. The potential of CBD to elevate ocular pressure should be evaluated further as a potential side effect, particularly with long-term use.

And until more research clarifies CBD's effect on the eye or produces reproducible science in fish, mice, and humans hunting fish—please avoid putting pure CBD directly into your eye.

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Cannabis Induced Sensory Enhancement

By Tamar Wise

What are the senses that make us human?
Our senses help us perceive and gather data from the world so we can safely interact with it. A sense is defined as "a system that consists of a group of sensory cell types that responds to a specific physical phenomenon, and that corresponds to a particular group of regions within the brain where the signals are received and interpreted." [1] Most of us are familiar with the five main senses: sight (vision), hearing (audition), taste (gustation), smell (olfaction) and touch (somatosensation), but humans also have the ability to detect other stimuli beyond the ones perceived through the traditional senses. These sensory modalities include temperature (thermoception), kinesthetic sense (proprioception), pain (nociception), balance (equilibrioception), vibration (mechanoreception) and other internal senses like hunger and thirst. These internal senses are called interoceptive senses while exteroceptive senses perceive the body's own position, motion and state. [1]

Throughout history, cannabis use has been anecdotally associated with creativity and altered perception in addition to the physiological changes that occur through stimulation of the endocannabinoid system. But up until recently, these effects were not well understood. Currently, some of the effects that cannabis has on human senses have been elucidated and are fairly well-documented, like cannabis' positive effect on reducing nociception (pain). [2] Similarly, some of the side effects of cannabis include distortion of other senses like balance (equilibrioception) and thermoception (a consumer feeling too hot or cold). [3]

Some cannabis consumers also report a distortion of time perception. In 2012, a study showed that cannabis use can dilate time (e.g., ten minutes is felt as twenty). The cannabis user has a subjective experience that time is passing slowly externally because their internal, subjective time felt sped up. Time perception is linked to the cortico-basal ganglia-thalamo-cortical loop (CBGTC), a brain network that contains a large number of cannabinoid receptors, which could explain this effect. Over time, this time dilation dissipated with regular cannabis use and consumers no longer felt this effect. [4]

Taste and Smell
Humans are able to detect at least five basic tastes: sweet, sour, bitter, salty and savory (umami). Specialized cells in the mouth and on the tongue have receptors that can detect the five main tastes as well as possibly fat and calcium. [5] Olfactory sensory neurons in the nose can detect many types of smells and play an important role in the perception of food flavors as well. Flavor is created not only by responses from the taste buds but also feedback from the smell, texture and heat/coolness of the food being ingested.

In 2009, findings from the Monell Chemical Senses Center and Kyushu University showed that endocannabinoids act directly on taste receptors on the tongue to enhance the sweet taste (other tastes: sour, salty, bitter, and umami were not affected by administration of endocannabinoids). Additional studies revealed that the CB1 receptor and the T1R3 sweet taste receptor are both present in the same taste cells. This could partially explain a cannabis user getting the "munchies" and craving for sweeter food. The other factor of increased appetite is most likely due to increased ghrelin (the hormone that controls hunger) production after cannabis consumption. [6]

Another study conducted in 2008, showed that cannabis could make certain foods more appealing, particularly sweets or fatty food. The researchers activated the brain's parabrachial nucleus in mice, which caused them to eat sugary and fatty foods, but not bland items. The fat and sweet taste are the two flavor profiles that are enhanced when THC activates this region. [7]

Cannabis has been shown to enhance our sense of smell as well. A European study conducted in 2014 showed that cannabinoid receptors in the brain promoted food intake in fasted mice

by increasing odor detection and processing. Further, the researchers showed that THC fit into special receptors in the brain's olfactory bulb, which in turn would allow cannabis consumers to smell and taste food far more acutely. [8]

Sight

There have been anecdotal stories about cannabis consumers having better vision. This could be due to cannabis affecting blood pressure, which in turn increases blood flow to the eyes and dilates the pupil, which would equate to more brightness and perceived increased vision. A study done in 2011 used fMRI to show that cannabis does have some effect on auditory and visual processing in humans. THC and CBD were tested separately and found to have different effects on the auditory and visual systems. However, more research is needed to determine what these findings mean and the underlying mechanisms that are occurring. [9]

Touch

Cannabis' effects on pain relief have been well documented and it is now known that the skin has its own ECS system, which could explain cannabis' broad effect. [10] Cannabis has been shown anecdotally to enhance the somatosensory feeling a user can experience. However, outside of pain relief, not much study has been done on the effects of cannabis on touch.

Hearing

Some cannabis consumers report hearing more acutely after cannabis use or that the music they listen to sounds better and clearer. However, to date there is not a lot of clinical data supporting these potential auditory effects. A well-known study done in 1976 showed that there was no negative link to cannabis use and hearing (cannabis did not cause a decrease in auditory ability), but not many studies have been done since then specifically on the auditory effects of cannabis. [11] The 2011 study using fMRI did find that different parts of the visual complex in the brain lit up with either THC or CBD administration, but the meaning of those findings is still not understood. A potential explanation for cannabis users feeling like they have enhanced hearing could be instead due to enhanced levels of dopamine, which would not enhance their hearing abilities but would enhance their *reaction* to auditory stimuli.

Crossed Senses? Synesthesia and ASMR

Is it possible that cannabis affects the senses even further and in more complex ways than just directly through our traditional senses and sense mechanisms? While most of the senses are defined by distinct, specific stimuli and the neurological systems that perceive them, there can sometimes be "crossing" of the

senses, which is referred to as synesthesia. Synesthesia is a perceptual phenomenon in which stimulation of one sensory or cognitive pathway leads to automatic, involuntary experiences in a *second* sensory or cognitive pathway (usually unrelated to the first sense). Some examples include chromesthesia (seeing of color when sound is heard), grapheme-color synesthesia (the perception of numerals and letters is associated with the experience of colors) or mirror-touch synesthesia (experience of a similar sensation in the same part of the body (touch) that another person feels) as well as many other examples of this blurring of senses.

There have been upwards of 80 types of synesthesia reported and it can occur between nearly any two senses or perceptual modes, and while rare, it is possible to experience synesthesia that is linked to all five senses. In general, synesthesia is a rare condition, affecting less than 5% of the population, but there has been some discussion on being able to induce or at least enhance synesthesia with the use of chemical agents like cannabis. A study done in 2013 showed that serotonin agonists (like cannabis) can elicit transient experiences of synesthesia and implicated the serotonergic system in synesthesia. The researchers also found that synesthesia was enhanced in people who already experience the phenomenon. [12] Synesthesia and cannabis consumption could be linked through cannabis' effect on serotonin. Not only are cannabinoid receptors found on serotonin neurons, they're also apparent in the corresponding inhibitory receptors. In 2016, a study was performed wherein mice were administered a chemical that mimics CBD. This led to the antidepressant effects from CBD's effect on serotonin receptors. When the researchers blocked the serotonin receptors, the effects were no longer noticeable. This further suggests that cannabinoids and the serotonergic system are in fact linked. [13]

Another form of synesthesia is called auditory-tactile synesthesia, in which certain sounds can induce sensations in part of the body. A new potential sub-type of this form of synesthesia is called autonomous sensory meridian response (ASMR) and it has been increasingly utilized for insomnia and anxiety relief. While most information on ASMR is still anecdotal, there has been more clinical focus on it in the last few years.

ASMR is a physical response characterized by a peak (hence the word meridian) of static-like or tingling sensations on the skin that typically begins on the crown of the scalp and can move down the back of the neck and upper spine. It could be a form or subset of auditory-tactile synesthesia and may overlap with frisson (i.e., French for "shivers"; aesthetic chills one receives usually in response to moving music or visual stimuli; feeling of skin tingling sometimes with piloerection (goosebumps) and pupil dilation). Similar to cannabis' effect on hearing through dopamine interactions, cannabis could positively affect the frisson effect, especially in those that already experience it.

ASMR-triggering stimuli are often social and intimate in nature (e.g., close whispering, brushing of hair or scalp massage), but can also be related to certain sounds like nail tapping or scratching or visual stimuli like slow hand movements. The physical tingling sensation is intermittent and usually comes in short bursts. The ASMR response is also associated with a calm and relaxed emotional state. Some of ASMR's positive effects could be due to mimicry of haptic communication, a branch of nonverbal communication that refers to the ways in which people and animals communicate and interact via the sense of touch. Haptic communication is extremely important for overall communication and it is vital for survival (e.g., babies who suffer from failure to thrive seem to do better when volunteers offer skin contact regularly). Another potential mechanism could be through stimulation of our mirror neurons (a neuron that fires both when a person acts and when that person observes the same action performed by another) and our ability for empathy.

Cannabis use has been shown to increase empathy as well as neural connections and cognitive functions in regular users (especially those with anxiety). Cannabis use could be a possible explanation for an increase in ASMR reactions or synesthesia in general. A lot of the anxiolytic effects of cannabis seem to be mirrored in ASMR experiencers (e.g., reduced heart rate, deeper breathing, more relaxed state). To date, there is no study on how cannabis affects ASMR experiencers, but perhaps similar calming mechanisms could be elucidated with more research.

A 2018 study examined the brain activation of subjects who were prescreened for ASMR-receptivity as they watched ASMR videos. It was found that subjects who experienced ASMR showed significant activation in regions associated with both reward and emotional arousal. Brain activation during ASMR showed similarities to patterns previously observed in musical frisson as well as affiliative behaviors. [14]

Another study showed the default mode network (DMN), a large-scale brain network of interacting brain regions known to have activity highly correlated with each other and distinct from other networks in the brain, of individuals with ASMR showed significantly less functional connectivity than that of controls. An overactive DMN has been associated with the development of depression so less connectivity in that region could be beneficial. The DMN of individuals with ASMR also

demonstrated increased connectivity between regions in the occipital, frontal, and temporal cortices, suggesting that ASMR was associated with a blending of multiple resting-state networks. [15] This atypical functional connectivity likely influences the unique sensory-emotional experiences associated with ASMR. Dedicated regions of the brain are specialized for given functions. Increased crosstalk between regions specialized for different functions may account for the many types of synesthesia including ASMR. Further, cannabis use has been shown to increase neural connectivity in general, which could explain its positive association with ASMR.

The most clinically relevant recent paper, published by Barratt and Davis, is a study of 475 people who experience ASMR which showed that ASMR helps users relax, deal with stress, and get to sleep with greater ease. The authors also show that ASMR elicits a positive effect on mood/depression and causes a significant reduction in symptoms of chronic pain for several hours following an ASMR session. There was also a higher prevalence of synesthesia within the sample group suggesting even more a possible link. [16] Further, sometimes ASMR is used for focus and calming of the mind to be able to do other things. This study showed that some reports of ASMR experiences also appear to share some features with the state of "flow," which is the state of intense focus and diminished awareness of the passage of time that is often associated with optimal performance in several activities, including sports. [17] Anecdotal reports of ASMR describe states of focus, of greater "presence" and of relaxation, which are consistent with the non-active aspects of flow. This concept of flow has also been linked anecdotally to cannabis use and historically many great thinkers and creators used cannabis to enhance this ability.

Conclusion

Cannabis' effect on the senses could hold interesting applications in commerce and tech. For example, similar to the miracle berry (a berry that when eaten causes sour foods to taste sweet), cannabis could be used in specific formulations to help chefs and food scientists create more palatable food. Or specialized formulations could be researched and administered to people who have had a loss of a sensation (like taste or smell) to help them gain some of it back. Further, eyedrops could be developed to assist in improving vision. There are over 400 bioactive molecules in cannabis and countless combinations of formulations to experiment with to find the right effects.

In the future, cannabis could be used in conjunction with virtual-reality type applications of ASMR and haptic communication. For example, someone using cannabis who has overconsumed could watch an ASMR video to assist in mitigating side effects and to keep calm. Another application could be used for children removed from abusive situations who could be given low-dose THC formulations of cannabis along with ASMR therapy and more traditional cognitive therapy. Yet another application could go further and increase our empathic and emotional intelligence by forced empathic experiences (for example, using a VR and integrative setup to not only see through the eyes of an endangered animal or domesticated animal bred for slaughter, but to actually feel their emotional and physical pain as if it were your own). Evolving our emotional and empathic abilities is the only way we can continue to survive and thrive as a species; perhaps the combination of cannabis and enhancement of our senses could be a feasible method to further that goal.

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Cannabis Cliffs: The Physiological Effects of Inhaling Terpenes From Cannabis Essential Oil

By Jason S. Lupoi, Ph.D.

This issue is themed around how cannabis interacts with our senses. Indigenous knowledge and good, old-fashioned trial and error have helped weed out the landscape a little, allowing us a glimpse into the mechanisms by which cannabis operates within us. Seemingly each day someone learns something new. This ever-increasing body of scientific knowledge about cannabis likely co-evolves with our less spastic and archaic ways of thinking when it comes to this inspiring natural source of so many phytochemicals, many of which likely possess medical attributes. We grow, and it grows.

The beauty of this synergistic relationship is evidenced by the volume of scientific literature being published on cannabis, whether regarding lab testing standardization, such as the work of the D37 subgroup of the American Society for Testing and Materials (ASTM International); through the sizeable research efforts of cannabis companies and labs and burgeoning interest in cannabis at the university-level; or through the relatively nascent inclusion of cannabis at more traditional conferences like those sponsored by the American Chemical Society.

While many studies are focused on cannabinoids, there's a burning desire to know more about the *terpenes*, which for us at T&T, is downright perfect. And while there are already medical studies on lots of different terpenes from a wide assortment of plants [1], a recent study evaluated the medical efficacy of cannabis essential oil. [2]

Scientifically speaking, an essential oil is a "highly volatile substance isolated by a physical process from an odoriferous plant of a single botanical species." [3] But there is a far cooler, historical explanation, as provided by the National Association for Holistic Aromatherapy. [4]

You see, "essential" oil is a shortened form of *quintessential oil,* which can be traced back to Aristotle, who believed that matter was composed of four basic elements: fire, water, air, and earth. But there was a fifth element (*quintus* meaning "five" in Latin), the life force or spirit, which could be extracted through distillation or evaporation of the plant. Distilled spirits should ring bells, right? So, an essential oil is a collection of fragrant molecules that give a plant its trademark aroma and flavor. This is why essential oils are the very foundation of aromatherapy and are also commonly used as flavoring agents.

The cannabis essential oil evaluated in the study was predominantly composed of myrcene (23%), *beta*-caryophyllene (19%), terpinolene (12%), *alpha*-pinene (8%), *alpha*-humulene (6%), limonene (4%), caryophyllene oxide (4%), *beta*-ocimene (4%), and *beta*-pinene (4%).
The goal of the study was to document how this cannabis oil affected brainwave activity and autonomic nervous system (ANS) responses like heart rate, blood pressure, respiration rate, or skin temperature, as well as overall mood. Unfortunately, the study evaluated the responses of just five people, three males and two females, who were between 30 and 57 years old. The authors acknowledged this limitation, but pointed to this work as "preliminary," noting that much more research needs to be conducted.

Rather deliciously, the experimenters used sweet almond oil as a placebo, the chemical breakdown of which was not provided.

Rather than ingest the oil, however, the subjects inhaled the oil from gauze. This experiment sought to reiterate the work of previous studies in showing that the pleasantness of an aroma would alter autonomic activity. [5,6] The researchers found a statistically relevant (read: slight) increase in skin temperature. Three of the five subjects had an increase in heart rate. In four of five subjects, blood pressure decreased, however, these changes were not statistical changes, meaning an analysis of the average responses did not prove the mean values to be different when the error in the measurement was factored in. The authors went on to hypothesize that the "stimulation" of the ANS could be explained by the presence of both limonene and *alpha*-pinene.

Limonene has been previously shown to affect what's called the *sympathetic nervous system*, which, among other things, serves to accelerate one's heart rate and raise one's blood pressure, as well as activate the "flight or fight" response. [7] Thus, it was postulated that limonene could also account for the increase in skin temperature. *Alpha*-pinene has been shown to inhibit acetylcholinesterase [8], an enzyme that stops the signals between nerve and muscle cells. [9] The neurotransmitter acetylcholine carries signal from our nerve cells to our muscle cells along synapses. Once it performs its mission, however, it needs to be destroyed to prevent confusion with other spent neurotransmitters, which is where acetylcholinesterase comes in, as the enzyme breaks down acetylcholine into acetic acid and choline. When this enzyme is inhibited, though, muscular paralysis can ensue. Doctors are now purposely inhibiting this enzyme in an attempt to reverse the symptoms common to Alzheimer's disease.

Thus, *alpha*-pinene has been one exciting phytochemical evaluated for neuroprotective potential for enhanced management of memory disorders like dementia. [10] Interestingly, though, when acetylcholinesterase is inhibited, it activates the *parasympathetic nervous system*, which functions to permit our bodies to rest, digest, feed, and breed. And since *alpha*-pinene inhibits this enzyme, the researchers hypothesized that the reduction in diastolic blood pressure could have resulted from pinene's presence.

After inhaling the cannabis oil, subjects found that their moods had been uplifted. They reported feeling calmer, more relaxed, and energetic. One person previously had a headache that they reported had gone away after smelling the oil. The authors hypothesized that these mood attributes could be explained by the presence of myrcene, limonene, and *beta*-caryophyllene in the essential oil. *Beta*-caryophyllene has been shown to have anti-anxiety and

anti-depressant properties. [11, 12] Interestingly, despite the author's previous discussion of limonene being the potential cause of the increased heart rate and skin temperature, they also attribute the terpene's presence as a possible cause of the stress-reduction reported by the test subjects, citing the anti-stress properties lemon oil exhibited on mice. [7] And of course, myrcene has well-known sedative properties. [1, and references therein]

The effects the cannabis oil had on delta, theta, alpha, beta 1, and beta 2 brainwaves was also evaluated. The power and amplitude of alpha waves increased following inhalation of the cannabis essential oil. Conversely, delta waves decreased in the back of the brain, as did the relative power of beta 2 waves. Alpha and theta waves *increased* in the back of the brain. Studies that have evaluated the brain activity of people who were meditating showed increases in alpha and theta brainwave activity [12, 13], indicating that the relaxed states-of-mind the subjects found themselves experiencing were likely due to the increased alpha and theta activity. Thus, the effects measured from the responses of the nervous system, coupled with the mood profiles reported by the subjects, and their corresponding brainwaves, all pointed to a heightened state of relaxation free from any anxieties just by inhaling the terpenes common to cannabis.

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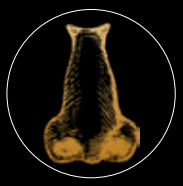
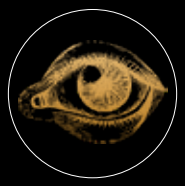
Can Growing Techniques Influence Terpene Content?

By Kevin Jodrey





Today, everyone is abuzz about terpenes – and for good reason. As cultivators have long known, terpene content will greatly influence the plant's or product's profile. The specific proportion of terpenes in a plant will create the "entourage effect," which significantly impacts how it makes a person feel upon consumption.

Terpenes are aromatic compounds produced in the plant's trichomes that give cannabis its various scents. Terpenes have been shown to interact with cannabinoids (including THC and CBD), and will influence and enhance the plant's physiological effects. While not specifically classed as cannabinoids themselves, terpenes play a significant role in the body's uptake of cannabinoids.

Take a variety that's high in limonene, for example. It's energizing not just because it has high levels of THC. It's the terpenes that help shape the user's experience.

Terpenoids are similar to terpenes, except that they contain additional elements, often oxygen. The terms terpene and terpenoid are often used interchangeably even though they are technically different. For simplicity, I will use the term "terpene" to mean both compounds.

According to some studies, terpenes are strongly inherited, and little influenced by environmental factors. [1] In fact, terpene content has been used as a biochemical marker to characterize and catalog certain plant species.

So, if terpene content is mostly inherited, can growers do anything to influence it? The answer is yes. Cannabis is especially susceptible to terpene alteration through a variety of techniques. Terpene content is influenced by the plant's genetic potential, by the environment (air, dirt, nutrient mix, water), and by the cultivator's processes in growing, drying, and processing. Depending on whether the plant is destined for processing or is being sold as flower, the approach to terpene content can vary. For instance, if the plant is being processed and extracted, most processors want very high terpene content for efficiencies. However, for flowers, the highest levels of terpenes may not produce the best experience. Sometimes a lower level of terpenes or a blend of terpenes may give the consumer the best end result.

Here are some techniques growers can use to alter terpene content. For outdoor grows, plants can pick up subtle characteristics from the environment, which will influence its terpene profile. The many factors at play in an outdoor grow can make it difficult for an amateur grower to try and reproduce the exact conditions that create a specific terpene profile. And while many cultivators look at the major terpenes, the smaller ones often greatly influence the plant's effects. If those smaller terpene profiles are overlooked, it will become impossible to reproduce the harvest.

For indoor or chemically-enhanced growing, it can be easier to reproduce the exact conditions that create a terpene profile if attention is paid to every contributing factor. Neither technique is necessarily better, but they are different paths to creating a predictable, repeatable outcome.

Terpenes are also best measured dry at the end of the cycle. But if we dry the cannabis at too hot of a temperature, or too quickly, some of the terpenes, particularly monoterpenes like linalool limonene, or myrcene, can evaporate and take away the scent or nose of the plant.

Sesquiterpenes, like *beta*-caryophyllene or *alpha*-humulene, which are sensed more in the mouth or through taste, are less affected by drying. These terpenes can handle greater temperature variations due to differences in their chemical structures. Accordingly, sesquiterpene-dominant cannabis can have a very low signature, but can produce a phenomenal smoke – especially in a joint.

In the old days, cannabis sales were based on monoterpenes, because when you opened the jar or the bag, the odor filled the room. But without the right mix of sesquiterpenes, the consumer would wonder what happened to the flavor.

The challenge then for cultivators is to find the plants that hold the potential for optimal combinations of terpenes, and then grow them in the correct environment. For instance, if the same plant is grown in a cooler environment,

it will automatically have a higher monoterpene signature. If it is grown in a warmer environment, it will have less.

One technique used in outdoor cultivation is adding humic acids as a soil conditioner, which will improve nutrient uptake and influence terpene levels. Another technique that can be used by growers to influence the terpene profile is "companion planting." For example, thistle can have a large impact on a plant's terpene content. It is surmised that the cannabis plant produces greater levels of certain terpenes as a defense mechanism when grown near thistle.

The bottom line is that "more" is not always better when it comes to terpenes. The goal is to generate the best synergistic blends. This is accomplished through careful attention to the type of plant and its individual genetics; the location or environment where the plant is being grown; the inputs including air, water and nutrients – whether biological or chemical driven; curing and drying; and enhancers.

Of course, books could be written about any one of these factors. Drying and curing is both a science and an art, and each grower has his or her own techniques that they have enhanced through the years. As any good grower knows, the cannabinoid process continues after the harvest, and good drying and curing techniques are critical to forming the final product.

Some growers say that most of the moisture should evaporate from the bud during the first three days of drying, and then the process should be slowed by lowering the temperature. To achieve this, the temperature and relative humidity must be tightly controlled, which is not always possible – especially in traditional or outdoor farming. However, cannabis dried and cured in a farmhouse will pick up different elements from the environment, whereas cannabis dried in a sealed, indoor environment will not. These elements can often enhance the flower's profile.

Often, if the drying process is done too quickly, more chlorophyll will remain, and the smoke will be bitter and have a green aftertaste. If the process takes too long, THC will degrade into CBN and other cannabinoids.

By simply changing the drying time by a few days, a grower can create a world of difference. Sometimes, these changes are subtle and are not always evident to the novice, but they will make a big difference to the cannabis connoisseur.

Similarly, the curing process will change the overall terpene profile. Like a fine wine, a well-cured crop will exhibit a much different profile than a plant that has been rushed through the process. Finely cured cannabis holds a more complex and refined flavor, and gains depth and variation in the bouquet.

In summary, virtually every aspect of a cannabis plant's growth cycle can alter the terpene profile. Of course, genetics matter, but so do all the other details, such as using high-quality soils; controlling the quantity of light – whether by spacing of plants so that each receives a healthy dose of the sun's rays, or using full-spectrum bulbs; additives and soil amendments; water quality; when to start and stop nutrients; drying and curing…it all adds up to a complex, interconnected system of influencers that will affect the terpene profile.

So, pay attention to everything…it all matters. Then start experimenting to get the profile you desire. And if you've paid incredibly close attention to all the details, then you can have a shot at replicating the process over and over again.

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Cannabis Microdosing Latest Fad or Effective Treatment Strategy?

Unraveling the effects of cannabis dosing on pain

By Loren DeVito, Ph.D.

Cannabis "microdosing" has grown in popularity, perhaps stemming from the widespread use of taking low doses of psychedelic substances like LSD. And while this method has recently become quite trendy, microdosing actually echoes back to the use of very low doses of cannabis in ancient China. [1] Prior to the evolution of cannabis breeding, traditional plants had much lower concentrations of cannabinoids and yet were still effective as therapeutics. With a wider availability of cannabis products and a greater wealth of scientific data, let's take a closer look at the concept of microdosing and how it could benefit the modern cannabis patient.

The Neuroscience of Subthreshold Effects

The goal of microdosing is to achieve subthreshold effects – that is, the smallest amount of a substance that can produce physiological effects without causing major perceptual changes. This concept of "subthreshold effects" is taken from the basic principles of neurophysiology. The language of the brain is electricity, and electrical signals must reach a certain threshold to trigger an effect within neurons, which are "tuned" to respond to specific levels of stimulation. Once that level is achieved, signals will propagate from one neuron to the next, creating a chain reaction that dictates how information is passed through neural circuits. [2] But even if that trigger level is not achieved, the stimulus, such as a drug, can still influence cellular activity – thus, prompting a subthreshold effect. [3]

Subthreshold effects explain changes that are just "under the surface." Thus, taking a very low dose of a substance like cannabis would produce subtler effects compared to the whole-body effects experienced from taking a normal dose. While those who use cannabis recreationally may find this concept to be a bit strange, medical-cannabis patients may find microdosing very appealing.

The "Entourage Effect" for Medical Cannabis

The most straightforward way to avoid the intoxicating effects of cannabis is to use products that are high in cannabidiol (CBD) and low in tetrahydrocannabinol (THC). And while CBD has widespread health benefits, cannabis is most effective when the whole plant is consumed. [4]

CBD and THC work best when they are together – a phenomenon known as the "entourage effect." Due to their differing effects on cannabinoid receptors, CBD and THC, in addition to the effects of terpenoids and flavanoids, create synergistic effects that boost their benefits on the brain and body. [5] And while research is underway to provide recommendations on precise formulations for specific conditions, it is important to consider the benefits of all phytochemicals for medicinal use.

Patients using medical cannabis may therefore benefit from microdosing to maximize the benefits of subthreshold effects without experiencing psychoactive effects that may disrupt their daily activity.

The Neurophenomenology of Pain

Cannabis produces widespread effects, from psychological to physical and sensory changes. And one of its key medical benefits is analgesia.

Pain is a tricky and prickly concept. Although there exists a basic and solid understanding of how the sensations of pressure, heat, and other factors cause the physical sensation of pain, its perception is quite complex and is confounded by psychological and environmental influences. [6]

Patients who experience chronic pain (that persists from more than one month) are often prescribed opiate medications,

which are very effective for pain control. [7] However, opioids come with a high risk of overuse and abuse and those taking them often become addicted. In the midst of the current opioid epidemic in the U.S., alternative therapies are desperately required to treat patients without introducing the potential for addiction. [8]

Medical Cannabis and Pain

Several studies and clinical trials have demonstrated that cannabis is quite effective in treating neuropathic and chronic pain associated with the human immunodeficiency virus, or HIV. [9,10] In fact, states where cannabis is legalized have significantly lower rates of opioid overdose mortality rates. [11]

Some studies have looked at the effect of dose escalations of cannabis on analgesia and pain relief. One small study evaluated the effects of three doses of smoked cannabis (2, 4, or 8% THC) on induced pain in 15 healthy participants. [12] Forty-five minutes after consumption, those who smoked the middle dose experienced a reduction in induced pain from the injection of capsaicin under their skin, compared to those who smoked a placebo; however, those who consumed the high dose experienced a statistical increase in pain, again relative to the placebo (there was no observed effect at the low dose). These results hypothesized a therapeutic "window" for maximum pain relief, although the researchers also caution against over-generalizing their work given the small sample size (there is said to be greater than 2.1 million medical cannabis patients in the U.S. alone) and bias towards only healthy subjects; of course, it is important to note that this was a high-THC formulation and 1:1 or high-CBD formulations will likely produce different effects. A similar study found that a middle and high dose (10 and 15 mg, respectively) of a cannabis extract *was effective* for post-operative pain management. [13] So, although these studies provide interesting results, they also are conflicting, since in one case, the highest dose considered was not as effective as the middle dose, and in the other study, the highest dose was effective. And it stands to reason that different types of pain, and ways of recording that pain, add variables that must be accounted for.

But, what about microdosing for pain control? There is some evidence suggesting that cannabis can be effectively microdosed to provide pain relief at subthreshold levels. One study found that a low dose of vaporized cannabis (1.3% THC) was effective for neuropathic pain control; in addition, the cannabis-associated psychoactive effects were minimal and well tolerated. [14] So, does that mean you should take this dose for subthreshold pain effects? Well, it's not that simple.

Determining Personalized Microdoses

Cannabis dosing is complex. The rate at which cannabis is metabolized, absorbed, and processed by the body is highly variable and depends on the type of cannabis consumed (formulation), method of consumption, and other very individualized factors, such as weight and height. [15] So, while microdosing cannabis may be very helpful for pain relief, it takes some time to first determine an effective *personal* dose. Once that level is established, you can titrate down to find a minimally effective dose that works for you.

Additional research on cannabis dosing may provide more precise recommendations on how to achieve subthreshold effects. For now, trial and error is the best way to land on an effective dose with maximum benefit.

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I've Got My Eye on You: How Visual Cues Provided by the Plant Can Help the Cannabis Farmer

By Harry Resin, URB Delivery

Our senses are the most important way we perceive the world around us. The same holds true about the way we perceive our cannabis. Affective memory or emotional recall is a technique used by many actors to refer to the recall of physical sensations surrounding emotional events. They use their senses to access emotions. The sensory experience of cannabis can be very similar. When inspecting a bud for the first time our eyes are usually the first sense to explore the look of the cannabis while the scent is the second. These experiences of seeing and smelling the bud are our first foray into the sensory experience that is cannabis. This is the connection to the sense-memory experience the actors refer to. Great smelling and looking cannabis can invoke feelings and take you back to certain moments in time. The differences in sight and smell of different flowers are what make the cannabis genetic pool so diverse. There are few flower species out there with such diverse subspecies and the well-over 400 chemical compounds found in cannabis have a lot to do with it. It's also through our senses that we experience the memory of the experiences we have with the cannabis plant.
When we perceive cannabis, the main senses used are taste and smell, both of which are closely connected. The very first sense we use is actually sight. Usually we first perceive the cannabis through our eyes, determining if we like the color, the amount of trichomes and what the structure of the bud looks like. All of these factors are pre-determined by the plant's genetics. However, in some cases, structure and trichome density as well as finished bud color can also be affected by the environment in which the plants are grown. For example, turning down a room's temperature at the end of the cycle can increase the purple tendencies in certain varieties.

In addition to color, other visual characteristics of the cannabis plant also help us define what it is. Often you could discern the difference between indica and a sativa plant using visual cues. Typically, "sativa" plants have thinner leaf morphologies and grow taller and longer compared to "indica" plants. However, this visual classification does not tell us much about the chemistry of the plant, and thus how it will make us feel. This is why we must also rely on our other senses like taste, smell, and our perception of the style of high to help us understand what terpenes are present and the strength of the other cannabinoids.

Genetics play a very important role in how biological organisms express themselves. The same holds true with cannabis via its DNA. Alleles are tiny points along the genetic arc of the plant and it's these devices that trigger various aspects of how the plant looks. As these genetic switches change so too does the color of certain cultivars. This is what makes some plants golden and others more purple, like the differences between an Acapulco Gold or Golden Goat and a Granddaddy Purple or a Sunset Sherbet.

As more research is published regarding cannabis and genetics, we are starting to be able to identify various markers which define the way in which cannabis plants look. Using these advanced breeding techniques, the modern cannabis breeder can now use a marker-assisted genetics program to better select for traits. In the past breeders were forced to use morphological cues as the science just wasn't there yet. This led to the diverse color and look of the various cultivars. We know that in the past the visual aspect of the plant was used to discern between the classic notions of what is an indica and what is a sativa. The morphological cues of the short and stocky indica versus the taller and lankier sativa are what first led to *Cannabis sativa L.* being subdivided into more subspecies. Now these cues have led us to develop cultivars with deep color differences as well as deep structural changes. Cookie cultivars, as an

example, all tend to have the same visual structure: a tight, hard, compact nugget, whereas certain sativas are more open and have a longer structure to their buds.

These visual cues are an important way that we enjoy, consume and are informed by cannabis. These looks are what define the plant and the various cultivars that we know and enjoy. Color in the cannabis plant can inform us as to what flavonoids are present. Flavonoids are mostly plant pigments and also have potential healing properties.

For example, the molecules responsible for the purple color in the world of fruit and flowers tend to be strong in antioxidant activity, and can be extremely healthy for us, which is why fruit like Açaí has been so popular as of late. This color is an indication that the phyto-chemical known as anthocyanin is present. The color ranges from a reddish to a bluish purple and the shade is dependent on the plant's pH. This phyto-chemical is known to help plants deal with cold temperatures and has arisen as a defense mechanism against frost. This is normally seen in tomatoes. The anthocyanin's presence in a plant's leaves reacts with oxygen and keeps the plant's internal temperatures warmer. There has been a study done on this effect and tomatoes, but further research needs to be done on the cannabis plant. The purple color can also sometimes mask the plant from certain predators who often rely on a plant's green color to see them.

Flavonoids also have other medical properties including anti-inflammatory abilities and cardiovascular support. They can also have anti-bacterial properties. [1] Hesperiden is a flavanone, a compound in the same family as flavonoids, found primarily in citrus fruit. A group of Japanese scientists are currently studying the chemo-preventive properties of this compound. [2] This flavonoid is, like anthocyanin, a chemical that has defensive capabilities.

Flavones are another important group of flavonoids as they include luteolin. In a thesis from the 70s submitted to the University of British Columbia, a study was done in collaboration with a grad student who looked at the cannabis cultivars available at the time including various hemp varietals. [3] It was found that luteolin was present in plants that were considered sativas due to their taller and thinner leaves compared to their indica or hemp sisters. The student found luteolin to be a determining factor when looking at the differences between sativas and indicas. The color of these flavones is also a more of a red-purple color.

It seems that when looking at the visual cues present in the cannabis plant, a farmer or consumer can determine a lot. As we learn more about the cannabis plant, we are starting to better understand the more than 400 chemical compounds present. This includes not just terpenes and cannabinoids, but also secondary compounds like flavonoids. These chemicals largely make up the visual cues that we see when examining the plant and, in some cases, have additional medical or beneficial properties when we consume them.

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The Evolving Sensory Relationships of Cannabis

Varied and multi-dimensional sensory experiences with cannabis serve as a guide for our changing relationship with the plant

By Laurel Friesen, Heylo Cannabis

Human interaction with plants is inherently sensory. Memories and experiences are associated with and influenced by visual images and aromas. Stopping to smell flowers in full bloom, walking through a dense pine forest, or peeling an orange can all trigger changes in mood and well-being. *Cannabis sativa* (cannabis) is far from an exception. Rather, the species exemplifies the multi-faceted, human-plant sensory relationship. The visual and aromatic stories of cannabis flower are not just for show - these interactions are guiding indicators to our experience.

The familiar phrases "your nose knows" and "sticky buds" are common examples of the ritual of smelling and touching cannabis prior to consuming it. Given the plethora of vastly different experiences cannabis can enable for an individual, forecasting potential effects is imperative for effective consumption.

We now know that understanding the aroma and flavor of cannabis flowers can narrow down the effects of each variety. The complex chemical profiles of cannabis pave the way toward more controlled cannabis experiences for both medical and recreational users.

Aromatherapy is defined as inhalation or bodily application of fragrant essential oils for therapeutic purposes. [1] Egyptians were some of the first groups to have used essential oils in a variety of healing practices. Since then, botanical extraction has significantly evolved and essential oils have gained traction in antibacterial and physiological applications. While research on cannabis has been stunted for much of the modern era, the aromatics of cannabis can be understood through other plants that share significant overlapping chemical compounds. A wealth of scientific therapeutic research on fragrant herbs and flowers is now revealing potential mechanisms for the therapeutic use of cannabis. [2]

The most abundant aromatic compounds in cannabis are terpenes and terpenoids, which make up the aromatic profile of each cannabis chemotype. Some of the most studied and recognized of these compounds are limonene, myrcene, *alpha*-pinene, linalool, *beta*-caryophyllene, caryophyllene oxide, nerolidol and phytol. [3] Each of these compounds works alongside phyto-cannabinoids and endo-cannabinoids to create the therapeutic effects of cannabis use. [2,3] Plants, including cannabis, have been developing their chemical profiles for hundreds of years, and cannabis has successfully enthralled a large population of the human race through its many practical and medicinal applications.

While cannabis use increases, the demand for a variety of products and experiences also augments. The many techniques for extracting essential oils and compounds from cannabis have opened up the door for a new world of products (oil for vaporization, edibles, topicals and more). Although most companies are aligning products with the familiar "Sativa, Indica, Hybrid" terminology, some companies are utilizing the established cannabis research and understanding of aromatherapy to determine which terpenes and compounds produce different effects. Consumers continuously motivate company marketing and production to meet the wide range of products from holistic full-spectrum, terpene-rich products to artificially-flavored, high-THC "clear" distillate.

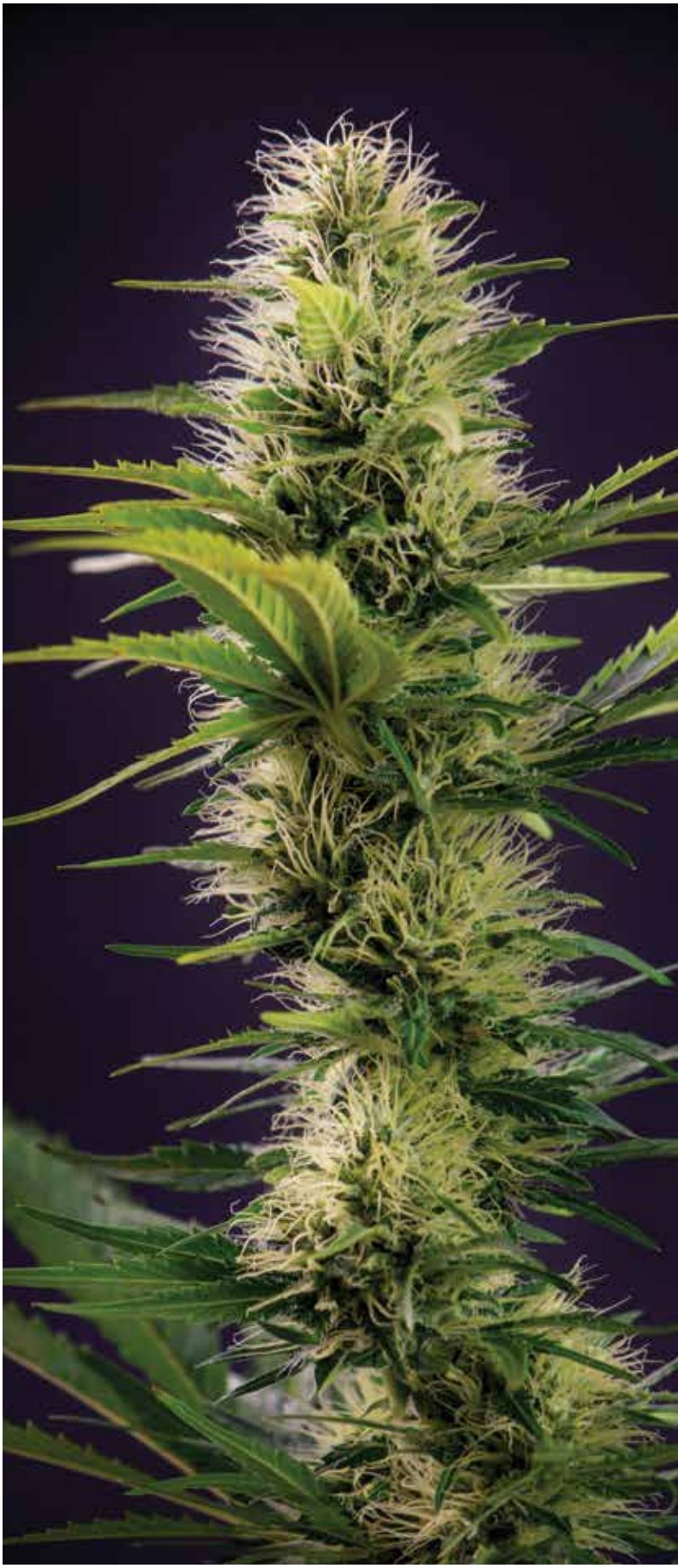
There is a significant difference between the consumer experiences from a full-spectrum product versus a distillate product due to the chemistry of each product's makeup. Consumers aiming to switch from smoking to vaping have

often stated that vaping oil does not provide the same experience as smoking flower. This is why companies like Heylo, based in Seattle, aim to provide extracts that are "as close to the plant as possible" by maintaining the chemical profile of the flower throughout their extraction and processing steps. The closer the products align with the chemistry of the plant, the closer the experience for consumers will be to smoking flower. Keeping the hundreds to thousands of active compounds like cannabinoids, terpenes and flavonoids together, in their native ratios, is crucial to developing products that provide consumers with the effects that have captivated them for so long.

The commercialization of cannabis has encouraged and facilitated isolation and formulation of cannabinoids in order to increase scale and consistency. Isolating cannabinoids like tetrahydrocannabinol (THC) and cannabidiol (CBD) aligns with standard pharmaceutical practices, however using the singular compounds has not historically served patients well. THC, especially in high doses, has significant negative side effects which can often be mitigated by the presence of other cannabinoids like CBD. In addition, using the singular compounds often results in reduced efficacy.

Cannabis companies have begun to introduce other components, like artificial terpenes or non-cannabis, plant-derived terpenes, to enhance the effects of products that had been previously stripped of these compounds. Although introducing plant-based and artificial terpenes to highly concentrated vape products may help improve the experience and flavor of these products, consumers are still exposed to high concentrations of THC. There is a large population of consumers who desire this type of intense and flavored experience. However, users seeking lower doses of cannabinoids, wellness, holistic experiences, an introduction to cannabis, or full-spectrum medicine, will not be served by these high concentrations of THC. Dr. Ethan Russo explores dosing with cannabis and consistently states that THC functions extremely well in low doses and discusses the importance of dosing with high concentrations of CBD. [4] "Use of high doses of THC-predominant cannabis above 5g per day are probably unjustified, except in the case of primary cancer treatment (vide infra) and suggest possible tolerance or misuse." [4] Without the moderation and balance, THC will continue to induce and amplify the negative side effects of cannabis.

Topical products also benefit immensely from introduction of essential oils and cannabinoids. Terpenes like linalool, *beta*-caryophyllene, and *alpha*-bisabolol are all found in the cosmetics industry for their dermatological benefits. These terpenes,



and more, are also found in cannabis. Using terpenes and cannabinoids in creams and salves has amplified the benefits of these compounds as they work even better together to treat ailments like eczema, poison ivy, and inflammation. [3] The majority of topical products do not penetrate the hypodermis and do not enter the bloodstream; the effects are limited to the area of application. Because of this, a wider population is open to introducing topical products to their healthcare regimen as they will not experience intoxication from the product. Skin, the largest organ of the body, stands to be one of the parts of the human body most positively impacted by cannabis.

Cannabis has a unique and engaging relationship with every sense humans experience. As the applications and reputation of the plant blossom across the world, more information will be uncovered about how the earth can benefit from cannabis. Perhaps the idea that cannabis was ever referred to as "weed" will be laughable as it adorns aromatic flower gardens and serves patients and the general population alike. By following our senses, we have new worlds to unlock and discover.

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Dissecting, Understanding, and Reconstructing a Plant's Aromatic Profile

By David Heldreth, True Terpenes

With the passage of the 2018 Farm Bill, it appears federal hemp legalization has finally come to pass. This opens new frontiers for cannabis farming and product development with varieties that contain below 0.3% tetrahydrocannabinol (THC). Furthermore, the November elections raised the number of recreational states to 10 and medical cannabis legal states (allowing THC products) to 34, including Washington, D.C.

It appears the march towards full legalization of the cannabis plant is on the horizon. However, with that comes the rules, regulations and risks of traditional business. At the intersection of these is product integrity. Do you know your supply chain? Do you know your manufacturers' methods? The romaine lettuce recall for *E. Coli* in November and December did more than ruin a few Thanksgiving meals and spawn jokes about the Devil's lettuce. It could possibly open the farms, distributors and stores involved in the recall to lawsuits or even worse it could endanger the health of the public they were trying to serve.

While these topics are just now bubbling to the surface in the mainstream consciousness, True Terpenes and the scientific community have been reporting on them for years. Former president of the International Cannabinoid Research Society and popularizer of the term "the entourage effect," Dr. Ethan Russo, has written and spoken on the danger of contaminants in cannabis products including: heavy metals, solvents, pesticides and microbial contamination. During one study he found 84.6% of cannabis samples from Washington tested positive for pesticides. [1] There are already ongoing lawsuits in California and Canada regarding pesticide-laden products. [2]

Every state is addressing these problems in their own way through legislation. California has some of the nation's strictest standards regulating inhalable products including flower and vaporized extracts. The state mandates testing for more than a dozen different solvents, dozens of pesticides, a variety of microbial pathogens and even the heavy metals: arsenic, cadmium, lead and mercury. [3] While California may be heavy on regulation, the list of items to test for to be compliant varies by state.

Does your terpene or flavor source test to the California inhalation standards? Will your product fail a test, not because of tainted cannabis, but because of an additive? Manufacturers are quickly learning that these are the types of questions they absolutely must address and ask of their suppliers.

The Regulatory Solution

As the legality of cannabis changes and markets expand, there will be an increase in government oversight. We currently test our terpene profiles and isolates for solvents, pesticides and purity, and we do this such that we are in compliance with each state's respective regulations.

In service of these higher standards, we recently secured registration as a Food and Drug Administration food facility. Registration is required for food manufacturers, packagers, formulators and related industries. [4] While often the source of ire in the cannabis industry, the FDA plays an important role. They are tasked with protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices, and by ensuring the safety of our nation's food supply and cosmetics.

In order to be registered, we had to identify all products from raw materials to finished goods in the realm of sourcing, storing, labeling, and process flow through the facility. Requirements include SOPs, LOT Code assignment (which allow brands to track supply chains), Good Manufacturing Practices (GMPs), and labeling specifications.


Lemon Cake
TERP
FLAVOR
120mL / 4oz

Furthermore, the FDA food facility registration opens a company to audits from the Food and Drug Administration and its partners, which include the health and agriculture departments in a number of states. This also ensures a company is adhering to compliance within the FDA mandates subject to food safety rules and regulations.

Many recalls are due to labeling mistakes, not the typical tainted foods you hear that make the news. Process flow can be a huge issue with a wrong label being applied to a bottle. The ingredient statement has to be representative of contents in the bottle. This is normally the main cause of recall throughout the food industry.

In order to solve problems like this, newer labeling machines come with barcode automation that will detect an incorrect barcode on a label if it doesn't match the recipe that is programmed into the labeling machine. As our industry scales in size in both volume and revenue, this will allow manufacturers to showcase an essential certification to further consumer trust in commercial products. Consumer confidence with respect to food safety is instrumental in delivering a trusted brand of product. Adhering to the strict guidelines set forth by the FDA justifies a manufacturer's commitment to customer satisfaction.

Difficulties with Flavor Standardization

Terpenes are basically the building blocks of essential oils from lavender (linalool) to clove (*beta*-caryophyllene), and are responsible for the aroma, taste and effect of a variety of plants we know and love. They're also the reason we smell skunky hops (*alpha*-humulene) or pine trees (*alpha*-pinene) in our cannabis. Terpenes, like the linalool in lavender or pinene in rosemary, are also known to be responsible for the soothing or uplifting effects users experience. [5]

However, terpenes are not the only compounds involved in the aroma and taste of fruits, flowers or herbs including cannabis.

In fact, what many refer to as the terpene fraction in cannabis extraction is comprised of hydrosols, alcohol esters, ketones and many other compounds. [6] Furthermore, cannabis extracts and flowers, like the plants they come from are unique and individual. That diversity is part of the allure of the experience. However, small changes in a plant's environment, the way it's extracted, or any other factor can also alter the terpene profile and thus taste or physiological effect.

Although cannabis contains terpenes, they're often destroyed during extraction or processing. For example, decarboxylation of THCA (tetrahydrocannabinolic acid) to create THC (tetrahydrocannabinol) for edibles is a process that uses heat (around 220°F) and thus cooks off terpenes which are volatile at much lower temperatures. However, decarboxylation is necessary as THC and THCA have differing physiological effects. These terpene-degrading temperatures are often reached in other extraction and processing methods as well.

Formulating customized terpene profiles of different cannabis cultivars is something that we've recently been beta testing, such that the natural chemistry of the plant can be retained in the final product. We will be offering three levels of customization options. The first tier is a secret menu of terpene profiles, while the second allows for customers to add unique accentuating enhancers to any profile. These enhancers include a variety of individual terpenes and other aromatics. The highest tier involves creating a terpene profile completely from scratch.

The first step to creating a profile is having a blueprint of where you want to go. In order to get that, formulations should always start with a gas chromatography–mass spectrometry (GCMS) report which provides the quantification of the plant's terpene profile. There are a lot of variables in this process, starting with the analytics used to create the formula. Many analytical labs test for 10-15 terpenes. We've needed to partner with labs that test for over 100 unique terpenes, such that we have a better picture of what's there and thus how to recreate it.

Cultivars of cannabis, hops or other herbs and foods can produce flowers with varying terpene profiles both on the same and separate plants based upon environmental conditions. This means that testing done on the top of a plant may show significantly different data from testing done on flower from another area on the plant. We've all smelled or tasted these differences when consuming cannabis. It is best to have a few samples tested and terpene profiles blended for each if there is significant variation between these tests.

The testing and initial formulation from the results is the easiest part. The hardest part is predicting the outcome.

Some varieties can more easily be recreated because their profiles are simpler. They rely more on common mono- and sesquiterpenes to produce their flavor and aroma. Other varieties depend on unidentified lesser-known terpenes and other compounds to create their unique profiles.

There is a concept in aroma sciences known as "low volume, high impact," meaning that there are compounds which produce a disproportionate scent-to-volume ratio, emanating far more aroma than would be expected. So while myrcene and *beta*-caryophyllene might volumetrically be the most dominate terpenes, the aroma produced by minor terpenes is often much more potent, contributing to differentiation between cultivars which share similar dominant primary terpenes.

A study entitled Characterizing the Smell of Marijuana by Odor Impact of Volatile Compounds: An Application of Simultaneous Chemical and Sensory Analysis backs these ideas up. [7] It showed that nerol, for example, was ranked a 6 (on a scale of 0 to 60 with lower numbers equating to lower levels) for quantity in the cannabis oil, but ranked 51 for the level of perceived aroma in a human olfactory trial.

Creating a faithful representation of the aroma and flavor of a plant is nearly impossible using analytics alone. Whether a client is looking to replicate their plant as close as possible or they wish to add a flavorful accent such as strawberry or lavender to their profile, flavor professionals turn to their noses and a litany of aromatic compounds to bridge the gap.

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Utilizing GC Testing for Your Cannabis? Here's Why You Should Be

By Cree Crawford, Ionization Labs

While opinions are highly split on the matter, it's clear to many that cannabis and its growth needs to be regulated in a similar way to other medications and supplements. Although the industry is still waiting for the U.S. Food and Drug Administration to greenlight the use of cannabis in various applications and for specific medical treatments, the interim has left cultivators and retailers with a heavy load of rules and regulations that must be carried out to the letter. Not adhering to these standards can jeopardize the future of these operations and ultimately may cost business owners immense amounts of money.

For growers who are just getting their feet wet in the cannabis world, the concept of quality control and product consistency testing may seem overwhelming on both a mental and financial level. However, this important element will not only guide your continued efforts and ensure that your product is legal to sell, but it can also help to better inform you of cultivation and production nuances that can make your product and business the best it can be. When it comes to specific in-house testing of cannabinoids and terpenes, what methods do you use?

For cannabis and hemp, potency testing is one of the top operational datapoints needed to project value and revenues. Whether you are pushing high THC numbers or trying to keep below the required 0.3% THC content for CBD and hemp production, it's top-of-mind data. High-performance-liquid chromatography (HPLC) is a solid go-to. However, what many often don't realize is that this only addresses one piece of the puzzle. When one is seeking to evaluate cannabinoid potency, it must be understood that cannabinoids have a heavier mass than lighter, volatile terpenes and solvents, thus it requires more heat to turn them into vapor. Additionally, the temperatures commonly used in gas chromatography (GC) can transform, or decarboxylate acidic cannabinoids, like THCa, into the neutral species like THC, making the assessment of acidic cannabinoids less straightforward. While cannabinoids can be measured with GC, they are much better suited for HPLC analysis. Terpene and solvent testing can be effectively done with GC.

GC in a Nutshell

If you've been growing cannabis for some time, you may be familiar with the basics of GC, or perhaps you've let an outside lab deal with all of the chemical analysis to date. Both new and experienced cultivators can benefit from the increase in aggregated data that in-house GC testing can provide, so let's get a very general understanding of how this process works.

Chromatography enables the separation of a given cannabis sample into its individual constituents. HPLC directly measures an often diluted extraction liquid to determine the chemical components of a product. GC works a bit differently. A specific column is used to separate out the individual constituents and, as the sample is heated, volatile gases are released, which subsequently migrate into the top of the vessel in which the sample is contained. These gases can be collected with a special gas collection syringe that only samples the top, or the "headspace," of the sample, enabling the user to selectively analyze volatile species. This type of testing can quantify terpenes native to the cannabis flowers, or both terpenes and any residual solvents in extracts or concentrates.

Why Would It Matter?

Some readers may be under the impression that potency testing via HPLC will provide all of the data needed for characterizing a specific cannabis variety. The potency profile alone does not differentiate between cannabis cultivars. Rather, having the combined cannabinoid and terpene profile

enables us to chemically distinguish between cannabis plants. The true benefit of measuring starting materials and products using both HPLC and GC lies in one's ability to gather layers of various chemical information to come up with the "chemotype" of a specific cultivar. When this information about potency and terpenes comes together, you have the specific fingerprint for your plant or product.

To an outsider, it may seem like cannabis is cannabis and these details wouldn't make a difference. Depending on the state you live in, however, and your goals for growth, the ways this information plays into current legislation could have a huge impact on your cultivation, product manufacturing, and business operational decisions. Currently you cannot ship cannabis products across state lines. Many of the larger successful cannabis operations are multi-state. How can one ensure product and brand consistency? The answer is to have close access to frequently acquired chemical data to give the farmer the ability to reproduce a crop, which should subsequently translate into the reproducibility of the formulation of a cannabis extract, concentrate or other product.

As of mid-2018, growing hemp for commercial use is federally illegal in all 50 states. While the 2014 Farm Bill had allowed for cultivation under the statue of research purposes only, the ability to grow hemp for fiber and specifically for CBD is still prohibited. Although the 2018 Farm Bill specifically recommended that hemp be recognized as an agricultural commodity, the failure of Congress to pass the proposed legislation still leaves growers in a difficult space.

To date, there are only 17 states that have actually permitted the legal growth of commercial hemp despite it still being illegal on a federal level. If you live in one of these states, how can you ensure your crops are being cultivated adequately without having in-depth knowledge about their chemotypes?

A Well-Rounded Process

The use of HPLC to determine a plant's cannabinoid makeup is certainly invaluable, and in no way should grow operations skimp on this important testing procedure. While sending samples out to certification labs is inevitable, there's no reason that in-house testing solutions can't be used in addition with the intent of making educated decisions in real time. Yet when you look at the overall picture of just how detailed you can get, it's clear that the addition of GC testing can make a huge impact.

Since the GC process can determine the terpene profiles of your plants, and the levels of any residual solvents left in extracts and concentrates, users of the instrument could potentially save untold amounts of resources through more educated decisions and product refinements from the analysis of the acquired chemical data. These measurements could include the terpene profile and level at different growing stages, or evaluating whether solvents are contaminating a sample *prior* to it being submitted for analysis by a state-certified testing lab. If the implementation of these hyper-accelerated chemical analysis tools sounds too expensive, you're not alone.

Much of today's testing market is dominated by equipment that is either cost prohibitive for small to mid-sized operations, requires an advanced science degree to use and interpret the data, or both. However, there are new options available for those looking to scale their business in a way that allows for simple, accurate, and cost-effective testing solutions.

About the Author:

Cree Crawford is the President & Co-Founder of Ionization Labs, a Green Ocean Sciences, Inc. company. Ionization labs is committed to simplifying the testing process by developing testing and data analytics solutions that meet the needs of professional operators in the cannabis industry. Ionization Labs has created high-frequency/low-cost in-house testing solutions that are easy to use, affordable, and utilize the same technologies as state certification labs. They combined this platform with proprietary industry-specific software and a turn-key testing package subscription that delivers exceptional results. Crawford's passion is cannabis education and he sees Ionization Labs' data analytics testing solution as an industry platform that can perpetually help the industry with aggregation of chemical data acquisition.

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