

For a slimmer waistline?

THCV plants being grown for medical use in California; Cannabinoid may counter metabolic-syndrome symptoms

By O'S News Service

Cannabis varieties containing unusually high amounts of THCV —tetrahydrocannabivarin—will become available to medical users in 2016, thanks to kind fate and propagators who chose not to hoard their unusual bounty.

The difference between THCV and THC is slight at the molecular level (*two fewer carbon atoms in the "tail"* —see illustration on page 21), but substantial in terms of how they work and their impact on the body.

GW Pharmaceuticals began investigating THCV more than a decade ago in hopes that it could be useful in treating metabolic syndrome. The disorder is actually a set of symptoms —high blood pressure, increased abdominal fat, elevated blood sugar, and unhealthy cholesterol levels— that are associated with obesity, type II diabetes and heart disease.

Roger Pertwee and colleagues at the University of Aberdeen reported in 2005 that THCV blocked anandamide (the molecule made by our bodies that activates the CB1 receptor) while allowing THC to act almost unimpeded at CB1. John McPartland commented on Pertwee's finding: "It's as if cannabis was designed as a combination remedy that simultaneously gave our endogenous mechanism a rest (shutting down anandamide), and supplemented with an exogenous remedy (THC)."

Also in 2005 the pharmaceutical giant Sanofi-Aventis had begun marketing a drug called Rimonabant —which works by fully blocking the CB1 receptor— as a treatment for metabolic syndrome. The first-ever mention of the endocannabinoid system in the *Journal of the American Medical Association* was a paper entitled "Effect of Rimonabant, a Cannabinoid-1 Receptor Blocker, on Weight and Cardio-metabolic Risk Factors in Overweight or Obese Patients: RIO-North America: A Randomized Controlled Trial," published in February 2006 —about 14 years after the components of the system had been identified.

Unlike THCV, which has a partial blocking effect, Rimonabant is a full antagonist at the CB1 receptor. It proved to have serious adverse effects, including "suicidal ideation" in people. (Studies indicating that it caused tumors and seizures in rodents were suppressed by Sanofi and reported only in the publication you're reading.)

The U.S. Food and Drug Administration rejected Rimonabant, and in 2008 it was pulled from the European market.

Also in 2008 a team backed by GW Pharmaceuticals reported on "The Metabolic Effects of THCV and CBD." Michael Cawthorne and colleagues at the Clore Laboratory, University of Buckingham, conducted a five-week trial treating genetically obese mice with purified THCV, purified CBD, and a 1:1 mix of the two. The mix was most promising. The THCV exerted a thermogenic effect (increased energy expenditure) while the CBD raised plasma HDL-cholesterol concentration and reduced liver triglyceride levels.

"This is the first demonstration of potential beneficial effects of CBD in hypercholesterolaemia and non-alcoholic fatty liver disease," the authors concluded. "In combination with THCV, it potentially addresses a number of components of the metabolic syndrome."

The takeaway message for US doctors, patients and cultivators: a combination of THCV and CBD might be most effective in treating metabolic syndrome.

In 2010 GW filed patent application (EP 2151262A1), stating: "This invention relates to THCV and THCV containing extract derived from plant material. A botanical drug substance preferably comprises at least 70% THCV."

"A botanical drug substance (BDS) as claimed in claim 1, wherein the secondary extraction comprises 'winterisation'... wherein a substantial proportion of waxes, wax esters and glycerides, unsaturated fatty acid residues, terpenes, carotenes, and flavenoids and other ballast have been removed... by the following steps:

- "i) Harvesting and decarboxylating cannabis plant material;
- "ii) Extraction with liquid carbon dioxide (CO₂), and removal of CO₂ to recover a crude extract;
- "iii) Dissolution of the crude extract in ethanol followed by chilling of the solution to precipitate unwanted waxes; and
- "iv) Removal of unwanted waxy material by cold filtration."

GW's high-THCV plant extract may protect the insulin-producing cells of the pancreatic islets.

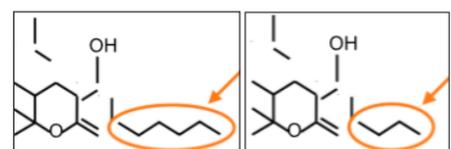
GW's plant extract that is more than 70% THCV has been dubbed GWP42004. In 2012 the company published results of an "exploratory study" involving 62 Type-2 diabetes patients, concluding:

"GWP42004 produced a variety of desirable anti-diabetic effects including reduced fasting plasma glucose levels, an increase in fasting insulin, improved pancreatic beta-cell function, increased serum adiponectin, reduced systolic blood pressure, and reduced serum IL-6 levels. Several of these findings are consistent with pre-clinical data suggesting that GWP42004 protects the insulin-producing cells of the pancreatic islets, a highly desirable feature of a new anti-diabetic medicine, increases insulin sensitivity, and reduces fasting plasma glucose levels."

In 2014 GW undertook a 12-week randomized, double blind, placebo controlled study of a THCV-dominant plant extract —GWP42004— to treat Type 2 diabetes. Some 200 patients taking the diabetes drug metformin added GWP42004 at three dose levels —or placebo— to their regimen to see if it improved their glucose levels. The study was ongoing as we went to press. (GW also expects it to establish the safety of THCV to the satisfaction of British regulatory authorities.)

Follow the leader

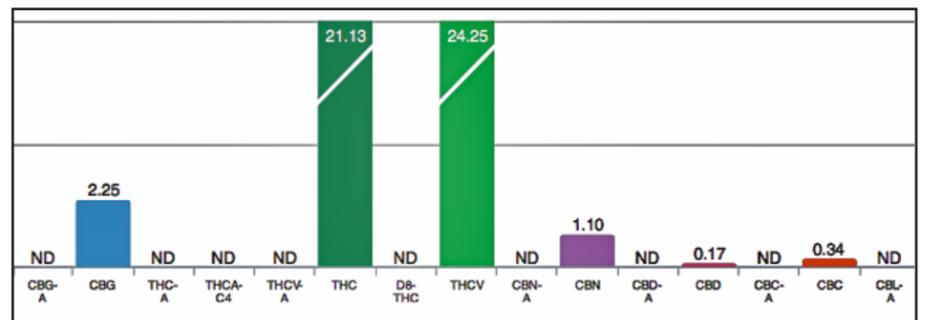
Just as GW Pharmaceuticals' studies established the safety and efficacy of CBD in the decade before the compound was re-discovered in California cannabis, their re-



WHAT A DIFFERENCE A TAIL MAKES: Δ⁹-tetrahydrocannabinol (THC, at left) has a five-carbon molecular tail called a pentyl group. Δ⁹-tetrahydrocannabivarin has a three-carbon tail known as a propyl group.

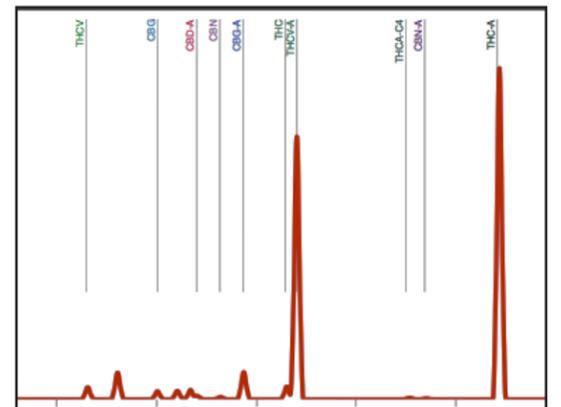


'BLACK BEAUTY' PLANTS HIGH IN THCV were grown in western Marin County, California, in the summer of 2015. Elevated pots enable "wicking" of water (with fertilizer).



THCV (TALL BAR AT RIGHT, 24.25%) AND THC (21.13%) are the dominant cannabinoids in kief sample after decarboxylation. Heating causes cannabinoids to lose a carboxyl group (an oxygen atom bound to a hydrogen atom) and the compound goes from acid (electronegative) to neutral. Lab director Kymron DeCesare notified the grower that he had a unique plant, and dubbed the strain "Doug's Varin."

CHROMATOGRAM AT RIGHT SHOWS THCV (TALL BAR AT RIGHT, 24.25%) AND THC (21.13%) are the dominant cannabinoids in kief sample after decarboxylation. Heating causes cannabinoids to lose a carboxyl group (an oxygen atom bound to a hydrogen atom) and the compound goes from acid (electronegative) to neutral. Lab director Kymron DeCesare notified the grower that he had a unique plant, and dubbed the strain "Doug's Varin."



DeCesare did not know why decarbed THCV exceeded THC (above) when before heating, THCA exceeded THCV (at right).

search into THCV can now provide guidance to doctors, cultivators and patients who have a couple of homegrown plants to work with.

Although nowhere near the potency of the THCV plants referenced in GW's patent application —70% and higher—

two strains rich enough in THCV to start a breeding program are being grown in Northern California, and breeders can producing three generations of crosses a year.

On the following pages are interviews with the growers of "Black Beauty" and "Doug's Varin."

The story of Black Beauty, as told by its savior

GEORGE BIANCHINI: About three or so years ago, when Richard Lee from Oaksterdam was busted by the feds, I had just rented one of Richard's spots [for cultivation] on 15th Street, and I got a phone call that this address was on the search warrant—a heads-up that the cops were coming. So we were packing everything up into black garbage bags and tossing them out the back of the building, getting ready for the bust—which, by the way, never happened.

The next day we realized that some mother plants, one of them being what we now call Black Beauty, went into the garbage. We had pulled it out by the roots because putting the dirt in the garbage bag would have taken too much space.

So we retrieved it, as well as several others. We were able to revive some, including this Black Beauty. It regenerated and we were able to get some clones. I gave a few away to friends and we continued to grow it.

O'SHAUGHNESSY'S: Where did you get it in the first place?

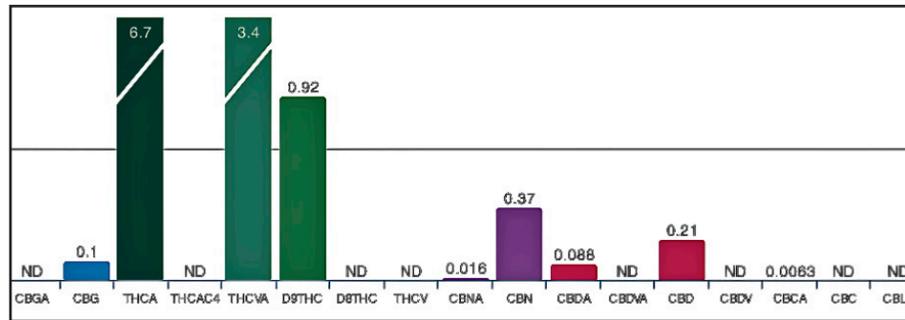
GEORGE B: This plant came out of Oaksterdam. It was among the clones they sold at their dispensary. It was known as their CBD plant, although it was only like two or three percent CBD and about 11 percent THC. Nothing really much to write home about, as far as what the clubs liked to grow.

O'S: If it was Oaksterdam's CBD plant, Project CBD may have given it to them. It might have been Soma A+, grown by Parker in San Francisco—the first one we IDed.

GEORGE B: Oaksterdam was selling it under Purple Pineapple, Pineapple Purps. But somehow the plant went through a complete change. I don't know what caused it. I don't know the scientific reasons.

So, three months later, I got a call from a friend of mine. I had given him some clones. He said, "George, this thing is flowering in my vegetation room under 18 hours of light."

And I said "Wow, that's weird." And so I tried it myself. My veg room is 24 hours [of light], so I never noticed it flowering.



BLACK BEAUTY TEST RESULTS FROM STEEP HILL LAB were reported in August 2014. Sample had been recently harvested. The raw flower contained 3.4% THCVA, 6.7% THCA and 0.92% THC—approximately 2:1 THC to THCVA.

But I put it down to 18 hours of light and the thing started flowering! I let it flower. I took it down for testing, and the results came back and it had dropped down to about 7 percent THC and no CBD. And I thought, okay, whatever happened to this plant, it's doing some weird stuff here and it's not going to be viable because most of the clubs want higher THC. But then I got a call from Steep Hill Labs, from Addison [DeMoura, the co-founder].

He said "George, you know what you have here?" And I said "No." And he explained it. So we researched a bit and realized that we had a very interesting, unusual cannabinoid. From that time we've been working with the plant and we even released it out to the clubs, but we just have had very little interest in it.

O'S: You released it as a Medi-Cone pre-roll or as clones for people to grow?

GEORGE B: As product in our pre-rolls because we're really not in the clone business. We give clones to friends and other growers. I don't sell—I give.

So anyway, we had this plant that had this THCV and we started working with it. One of the other characteristics that the plant had was that it was hermaphroditic at about six weeks, although it ripens in about six and a half weeks—an extremely fast flowering plant. And, where it had purple hues before, now it would start going black.

It went through some sort of metamorphosis that had nothing to do with me, or anything I did with the plant or any kind of breeding. I just happened to be the recipient of it—which I'm very thankful for.

I was able to force the plant to produce seeds and, even though it hermaphroditic before, it wouldn't make seeds. It just had 'banana hairs' and some of the characteristics of a hermaphrodite plant.

With the seeds we were able to derive three distinct genotypes. Now, grown under the right conditions, all three genotypes produce about the same level of THCV. One of them is black in color. One of them produces its own hermaphrodite flower heads, little banana hairs. The third one does not. They all finish fast. They have a similar look but they have different terpenoids.

A couple of our associate farmers that we gave the plant to grow outdoors, up north in the hills of Mendocino, had more

intense THCV. When I grow it indoors, it has about half the amount of THCV, unless I introduce ultraviolet light in the 300-nanometer range. I've been working with Ed Rosenthal on that, and we have been able to introduce radiation to bring out this THCV.

I was hoping to meet up with other growers, because while we don't have seed for this plant, we can produce the seeds. One of the genotypes will produce those yellow banana hairs, which do have a limited amount of pollen. So we may be able to artificially inseminate, so to speak, other strains.

O'S: Will the seeds all be female seeds from that process?

GEORGE B: Yes, they will. But if we can use the pollen, as I just described, into somebody else's plants, we very well may be able to get male and female seeds out of it. It's just going to have to go through a series of breeding. I'm setting up one of my own growing grounds to do just that.

We have teamed up with the Winnemucca Indian group. They want strictly a line of medicines—CBD and THCV. I'd like to just start breeding and figuring out how to get more medicine out of this plant.

I am a real patient for this. I was supposed to be dead a while ago. My wife and I were both poisoned in industrial accidents. Anyway, long story, 11 major surgeries. Cannabis was my savior. I'm 60 years old and I had just been a casual smoker all my life, other than growing a couple of plants here and there. I was never really in the industry. And then I got involved in the industry. And I'm putting everything that I have into it. I'm more excited about the medicinal side.

O'S: How big does Black Beauty get?

The big thing is, it finishes in six and a half weeks. It's not temperamental at all.

GEORGE B: As big as you have ceilings. It will continue to veg if you leave it under 24 hours of light. The largest I have grown so far is a five-pound plant. I normally don't concentrate on growing monster plants. This plant would grow large and produce a lot of weight.

The big thing is, it finishes in six-and-a-half weeks. It's not temperamental at all. It's very easy to work with. It's very easy to clone. It being hermaphrodite raises some concerns that there's degradation in its genetics or something. I don't have the science behind me to understand that. I put mom and dad together and breed them, test them, smoke them, try them.

O'S: Where is your main garden? Where have you been growing these plants?

GEORGE B: In West Marin. I've lived there since '86. I have an acre and a half there. I've been on the front page of the *IJ [The Marin Independent-Journal]* several times. We get regular visits by the Sheriff's department, who treat us very nicely because they can tell that we're really doing it for the medicine. We have all of our water saving devices out there, too—our



BLACK BEAUTY BUD has yellow "banana hairs" that occasionally produce pollen, Bianchini says.

wicking system.

That was something that I started working on four years ago. Water wasn't an issue at the time but it was a matter of, you know, we're growing next to redwood trees and oak trees, and what may be good for the cannabis is poison for the big trees. Fertilizer gets in the ground water and it's a problem.

So we developed a closed system so there wouldn't be anything leaching into the ground. The wicking system can save 40 percent of your costs of fertilizing, because you're not washing it away. And you also can save 50-60 percent of your water.

We just leased a 350-acre farm up in Lodi, where we hope to do tests on this product.

The Native Americans that we're teaming up with—the Winnemuccans—are very adamant about staying involved in the medicinal side. They are especially interested in THCV medicine, because they have a big—not only do the Reservations have an alcohol and drug problem, they have a large diabetic problem.

O'S: We know from GW Pharmaceuticals' research that this is where THCV is most promising.

GEORGE B: Phytologie [a dispensary in Oakland] did a little study with my product with some of their customers and the feedback they got was that some of them were getting withdrawal symptoms. I told them I found you can't replace THC with THCV. I think we need to figure out how we can put it into a pill form, a spray form, and then take it like an hour before mealtime. We need to figure out a way to turn off that pleasure center before you go consume 4,000 calories.

O'S: Jere Visalli and I just got a tour of a company that makes gel caps.

I deal with law enforcement in West Marin. I think they see me as a true medical pioneer on this.

GEORGE B: I'm familiar with that stuff. I've been in this industry now for a while. I go to all the shows. I just came back from the Vegas show. Many people have gotten into it to make their millions of dollars. I know it's going to be a for-profit industry. I know that that's coming. To me, I think it's going to muddy up the water a bit.

I want to do this. I know that if I do this right and with my heart into it, it will pay off. And besides, I was successful before. I have all the toys that I need. I don't even use them. I don't chase money. I buy my clothes at Costco. I don't need fancy stuff. I'd just really like to have my name at some point be related to this medicine. That's my goal in life right now.

O'S: So we can use your name in this article?

GEORGE B: Absolutely. My life is an open book. I deal with law enforcement in West Marin. I think they see me as a true medical pioneer on this. So I have no problems there.

We already gave some of the clones to friends up north. My business attorney says, "George, you can't be giving that away. We have to do that DNA test and get

continued on next page



HEDGE OF BLACK BEAUTY PLANTS grown by George Bianchini. "We grow it like landscaping with yellow coreopsis underneath it," he says. "The coreopsis draws the bugs. Bees go to the yellow and that solves the bug problem." They certainly make an attractive hedge.

THCV from page 50

The Fortuitous Discovery of ‘Doug’s Varin’

This phone interview with the proprietor of “Doug’s Farm,” conducted in July, 2015, provides the back story. In November we met in person at Care By Design headquarters in Santa Rosa and I got an update. Thanks to Susan Schindler for the introduction. —FG

Doug: ... I purchased what was supposed to be Harlequin seeds from a website online—the only place I could find that had, that listed Harlequin seeds.

O’S: I think it’s been grown from clones all along, starting with Wade Laughter.

Doug: I ordered them and they turned out to have essentially no CBD. They were not Harlequin. Out of 15 seeds, I had a couple of males and four females that survived. The four females were not very big. They looked like sativas, kind of an open grower, narrow leaves. And the buds are kind of open and fluffy and stringy. They don’t make real good buds.

O’S: Do you grow them indoors or outdoors?

Doug: Outdoors. I start my cuttings indoors, but then I put them outside. And I found that if you do normal lighting on them —12 hours of dark to start flowering— that does not work with these. I had to give them 15 hours of dark to get them to flower. I did that again this year.

The first year, when I grew them from seedlings, they grew fine outside. I didn’t get much off of each one. I had a lot of spider mite problems that year.

This was a few years back. So I had the four plants that didn’t have much on them. So I put all four together to make the kief. I was still thinking it was supposed to be Harlequin, but I had it tested at Halent Labs. This was when they were

in West Sacramento, before they merged with Steep Hill. The sample came back that it was about 24 percent THCA and about 12.5 percent THCVA.

They were really excited about that. They had never seen anything more than just about three percent of THCVA.

So I thought, “I want to keep this.” I took the best male and I crossed it with all four.

And I got some seed from each one of them. And I grew from this.

And the next year I grew from seed and the best one out of that I had tested, and that is the one that came out to be “Doug’s...”

O’S: And it was Kymron at Halent who named it that?

Doug: He suggested it. And I said “That sounds good. Let’s go with it.”

O’S: Do you want your name used or kept out of my story?

Doug: Just say it was produced by Doug’s Farm.

O’S: And where is Doug’s Farm located?

Doug: It’s in Sacramento County.

O’S: Have you tried this strain yourself?

Doug: I’m not a smoker. I did try some; I made an alcohol-based tincture from kief. I tried the tincture. I didn’t feel anything at all.

O’S: An honest man!

Doug: Yes, I didn’t feel anything at all. I figured that, from the amount of kief and the amount of liquor that I used, it should have had between 10 and 15 milligrams of each per milliliter. But I didn’t feel anything from it.

O’S: Some people who worked at the lab tried it and said it gave them an unusually clear high. But they could have been placebo-ing each other. GW Pharmaceuticals says it’s not psychoactive.

Doug: From what I’ve read, it is actually



DOUG’S VARIN PLANT had not yet finished flowering when this photo was taken in late November 2015. Grown in a five-gallon pot, it can be taken into the garage to trigger flowering —and to avoid the cold.

more psychoactive than THC, but it acts differently. It’s supposed to be an “up,” energetic high, but not with a buzzy feeling.

O’S: We’re about to find out in the period ahead.

Doug: It does have a strong effect. A lady who has back problem and also has tinnitus tried it. First time she tried it she had just come back from vacation was really feeling kind of lethargic, like she had jet lag. She smoked some of that, and her back pain went away and she felt like doing housework. It was invigorating, she says. And the ringing in her ears went away.

O’S: What if a reader wanted to try it? What’s the state of it now in terms of availability? How much has been grown out?

Doug: That I am not sure. Elemental Well-

ness in San Jose is one of the places where Kymron originally sent three plants to be grown out. There’s another grower in Santa Cruz. And there’s a lady up in the Redding area. And she got the bulk of the plants — eight or nine plants last year.

O’S: And did she succeed? Have you followed —

Doug: As far as I know. I haven’t heard anything back from her. I need to get in contact with her again. She’s not always easy to talk to because she’s traveling around a lot.

O’S: I assume you kept some yourself.

O’S: Yes. I’m growing them. I have three plants, and they’re flowering well now.

O’S: And what are you going to do with those flowers?

Doug: I’m going to trim some. They’re a pain to trim. Because you do a lot of trimming and not get an awful lot. They have kind of an open, stringy flower structure. They just don’t produce the type of bud that people typically see in cannabis stores.

O’S: These three plants that you’re growing, have you had them tested in the vegetative stage?

Doug: Not this year.

O’S: Do you have any other plants of interest that are unusual?

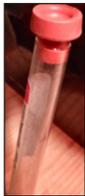
Doug: Well, there’s one that I did last year. I had crossed USO-31, an industrial hemp strain with Doug’s Varin. From the initial testing on the leaves, it was basically a 4:3:1 ratio, four parts CBD, three parts THC, one part THCV.

O’S: That’s very promising. GW did one study showing that CBD and THCV are a one-two punch in treating diabetes.

Doug: Maybe they’ll find out more when they test the kief made from them.

Black Beauty from previous page

the rights and own the rights on this.” I said, “Personally I don’t believe anybody should own the rights to this kind of medicine.” But that’s just my personal feeling on this. I think it needs to be out there to the public first.



The Las Vegas show two weeks ago — the investor show— what a difference from 10 years ago where it was a smoke-filled room and you’d get contact highs. Now it was all suits and guys that were talking millions of dollars.

O’S: I was given one of your pre-rolled joints last year. I still have the little glass tube with the beautiful rubber stopper that looks like a terra cotta flower pot. Whoever did the industrial design for you did a great job.

What is known about the effect of smoking Black Beauty? You mentioned appetite. Anything else?

GEORGE B: Okay, here’s what I find. The THCV seems to give you an instant spike on whatever THC was there. We believe

My goal is to produce a plant that has about five percent THC, about five percent CBD, and maybe two to 2.5 percent THCV.

it’s the THCV not necessarily the terpene profile doing it. It brings the high up faster and then it comes down quicker than the normal reaction to THC in the body.

As far as how it works on appetite, we have not gone through a test because when I do the test, I want it in a pure oil form.

O’S: Are you trying to breed up the THCV?

GEORGE B: My goal is to produce a plant that has about five percent THC, about five percent CBD, and maybe two to 2.5 percent THCV. I think that would be the perfect medical plant for the guy that has a grow tent in his garage or bedroom, who’s really growing it for medicine.

I really think that THCV is going to have to be in a pill or a tincture form, and then taken at a certain point before meals to get the appetite-suppressant effect of it. But that’s going to take a full-on clinical study. If we can get enough people interested...

The market is such that 95 percent of what we do is THC-driven. So it’s hard for me to turn that into economical sense. That’s why I’m hoping that teaming with the Native Americans is going to allow me to do more laboratory work.

I told the Chief, William Bills, “I don’t want to be CEO, if you’re going to give me a title, I just want to be ‘Chief Medicine Man.’”

The Winnemuccans are based in all the western states. It’s a cooperative, so to say, of many smaller groups that came together to exercise their sovereign rights.

They really want to concentrate on the pure medicinal side.

8,500 people in study:

Marijuana use reduces risk of developing metabolic syndrome

By Martin A. Lee

THCV may prove to be an especially helpful component, but marijuana users can feel encouraged by a recent study in the *American Journal of Medicine* showing that they are much less likely than non-users to develop metabolic syndrome —a significant risk factor for obesity, type II diabetes, and heart disease.

Scientists at the University of Miami in Florida examined the relationship between cannabis consumption and individual components of metabolic syndrome such as high blood pressure, increased abdominal fat, elevated blood sugar, and unhealthy cholesterol levels. Nearly 8,500 people from age 20 to 59 provided information for the study.

Participants were separated into three categories —current marijuana users, past users, and those who had never smoked the herb. Whereas metabolic syndrome afflicts 22 percent of the U.S. adult population, less than 14 percent of current cannabis-using adults in this study had the defining symptoms.

Among young adults, cannabis consumers are 54 percent less likely than non-consumers to present with metabolic syndrome. Past marijuana use is associated with lower odds of metabolic syndrome among middle-aged adults. And seniors who medicate with cannabis tend to be slimmer and less insulin-resistant than seniors who just say no.

The munchies receptor

The results of the study, entitled “Metabolic Syndrome among Marijuana Users

Among young adults, cannabis consumers are 54 percent less likely than non-consumers to present with metabolic syndrome.

in the United States,” may seem counter-intuitive, given marijuana’s appetite-stimulating effects, jocularly known as “the munchies.” Under the influence of marijuana, flavors seem to jump right out of food. That’s because tetrahydrocannabinol (THC) activates CB1 cannabinoid receptors in the brain that rouse one’s appetite and heighten one’s sense of smell.

The munchies are a scientifically proven phenomenon. THC is a CB1 agonist that turns on the appetite receptor and causes it to signal. An antagonist is a compound that binds to the receptor and prevents it from signaling. Tetrahydrocannabivarin (THCV), a minor but medically significant component of the cannabis plant, is a neutral CB1 receptor antagonist.

Scientists have also synthesized “inverse agonists” that can activate a cannabinoid receptor and cause it to signal in the opposite manner from how it functions naturally. A CB1 inverse agonist will curb appetite and reduce food intake, whereas THC stimulates appetite and food intake by binding to CB1.

One could reasonably assume, given what we know about the munchies, that increased use of marijuana will result in

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SOFTPOT BASE with wicks showing is lowered into reservoir, which can be drained, sparing nearby trees exposure to fertilizer.

MJ vs Metabolic Syndrome *jump*

greater caloric consumption with consequent adverse metabolic outcomes, including obesity. However, the results of this study and other reports indicate that such is not the case. Indeed, the opposite appears to be true.

In addition to underscoring potential health benefits of herbal cannabis, these findings highlight the discrepancy between human research that links marijuana use to lower rates of obesity compared to preclinical studies with synthetic isolates in which CB1 antagonism (blocking the munchies receptor) and CB1 inverse agonism (flipping the anti-munchies switch) are shown to prevent obesity.

How is it possible that activating cannabinoid receptors via marijuana consumption is associated with preventing obesity in humans, while blocking or reversing the CB1 receptor with a synthetic, single-molecule compound results in weight-loss in animal studies? What can explain this apparent contradiction?

It may have something to do with the complementary, yet opposing functions of two different sets of cannabinoid receptors.

CB2 receptor activation

Australian scientists recently examined the role of the cannabinoid CB2 receptor “in modulating energy homeostasis and obesity-associated metabolic pathologies.” The CB2 receptor is concentrated in the peripheral nervous system, immune cells, and in metabolically active tissue. The Australian researchers found that CB2 receptor activation by JWH-015, a “selective CB2 receptor agonist,” reduces food intake in mice and prevents the build-up of body fat.

The fact that THC and other cannabis components (including the aforementioned THCv) also activate CB2 receptor signaling may explain why marijuana users are less likely to develop metabolic syndrome than marijuana abstainers. Metabolic syndrome is a generalized, low-grade inflammatory condition, and the THC-sensitive CB2 receptor regulates immune function and inflammation.

CB2 receptor activation —through healthy diet and cannabis-enabled stress reduction— may prove to be a better strategy for preventing and treating metabolic syndrome than the misguided attempt by French pharmaceutical giant Sanofi-Aventis to market Rimonabant, a synthetic CB1 inverse agonist as an appetite suppressant. Promoted as a blockbuster diet drug in 2006, Rimonabant was soon recalled in Europe because of severe adverse side effects, including neurological deficits, depression, and suicide. The anti-munchies pill was never approved for sale in the United States.

Sorry Big Pharma, but when it comes to preventing or mitigating metabolic dysfunction, synthetic isolates are much less effective than whole plant cannabis with its synergistic treasure trove of natural medicinal components that enhance and balance each other's effects.

Sources

Englund A, et al. “The effect of five day dosing with THCv on THC-induced cognitive, psychological and physiological effects in healthy male human volunteers: A placebo-controlled, double-blind, crossover pilot trial.” *Journal of Psychopharmacology*. 2015 Nov 17.

The Context of Prohibition

The collage features several prominent headlines:

- 'Dr. Drew' Was Paid by Glaxo**: A photo of Drew Pinsky with a sub-headline 'Dr. Pinsky: Influential and on the side.'
- OxyContin Trial Planned for Kids**: A large headline in the top right.
- Blacks Are Singled Out For Marijuana Arrests, Federal Data Suggests**: A headline in the top right.
- Alzheimer's Drug From Lilly Misses, but Offers Promise**: A headline in the top middle.
- Police Hoping Drug Scanner Is Narcotics Game Changer**: A headline in the middle left.
- DuPont Says A Death Claims Over In Innovation Herbicide For Key Drugs**: A headline in the middle right.
- FDA Advisers Had Ties To Bayer**: A headline in the middle right.
- Monsanto Corn Plant Losing Bug Resistance**: A headline in the middle right.
- Glaxo Sets Guilty Plea, \$3 Billion Settlement**: A headline in the bottom left.
- Drug Merger Discussion Leaves Out A Key Risk**: A headline in the bottom left.
- New Surge In Shootings By Officers**: A headline in the bottom right.
- Disclosure of Ill Effects In a Drug From Questcor**: A headline in the bottom right.
- Questioning of Soldiers' Care Draws Reprisals**: A headline in the bottom right.
- Venture philanthropy risks benefiting companies, not patients.**: A headline in the bottom left.

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