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 2 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 Cardiovascular 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 Clere 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, esters and glyc erides, unsaturated fatty acid residues, terpenes, carotenes, and flavonoids and other ballast have been removed... by the following steps:"

1) Harvesting and decarboxylating cannabis plant material;
2) Extraction with liquid carbon dioxide (C02), and removal of CO2 to recover a crude extract;
3) Distillation of the crude extract in ethanol followed by chilling of the solution to precipitate unwanted waxes; and
4) Removal of unwanted waxy material by cold filtration.

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

GW’s plant extract that is more than 70% THCV has been dubbed GWP24004. In 2012 the company published results of an “exploratory study” involving 62 Type-2 diabetes patients, concluding: “GWP24004 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 adiponecin, reduced systolic blood pressure, and reduced serum IL-6 levels. Several of these findings are consistent with pre-clinical data suggesting that GWP24004 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 —GWP24004— to treat Type 2 diabetes. Some 200 patients taking the placebo drug metformin added GWP24004 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 rediscovered in California cannabis, their research into THCV can now provide guidance to doctors, cultivators and patients who might form 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 produce 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 hustled 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 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 the name 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.

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 that’s when 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 to the clubs, but we just have had very little interest in it.

O’S: As a 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 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 a series of breeding. I’m setting up one of my own growing grounds to do just that. We have teamed up with the Winemuccia Indian Group. They want strictly a line of medicines—CBD and THC, 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 year ago. My wife and I were both poisoned in industrial accidents. Anyway, long story, 11 major surgeries. Canabiss had given me 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 clone business. 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?

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.

O’S: 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 has about half the amount of THCV. 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 don’t think we need to figure out how we can cut 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: I faked 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’s coming. To me, I think it’s going to muddy 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 tools 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 just like to have my name in this article that I can turn to this particular related to this medicine. That’s my business. I’m very adamant about staying involved in the medicinal side.

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 through law enforcement.

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 DNA testing.”

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

George B: I’d like to be the recipient of it—which is very easy to work with. It’s very easy to work with. It’s very easy to work with. It’s very easy to work with.
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 Schnell 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 Lauter. 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 flabby and stringy. They don’t make real good buds.

O’S: Do you grow indoors or outdoors?

Doug: Outdoors. I start my cuttings indoors but I put them outside. And I found that if you do normal lighting on them — 12 hours of dark to start growing — 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 THC and about 12.5 percent THCV.

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 flabby and stringy. They don’t make real good buds.

O’S: And where is Dougie’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 been a very potent mix — 15, 20 milligrams of alcohol per milliliter. But I didn’t feel anything from it.

O’S: Some people who worked at the lab tried it and said that the kief was unusually high clear. But they could have been pla-cebo-ing each other. GW Pharmaceuticals says it’s not psychoactive.

Doug: From what I’ve read, it is actually more psychoactive than THC, but it acts differently. It’s supposed to be an “up,” en-ergetic 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 simi-tus 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 avail-ability? 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 fol-lowed—

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.

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 trim-ming 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 grow-ing, have you had them tested in the veg-etative stage?

Doug: No 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 that 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 THC are one-two punch in treating diabetes.

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

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 com-ponents 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 34 percent of U.S. adults, it was found that marijuana users had only 18 percent of the overall condition, with current marijuana users having the lowest incidence at 14 percent. Among past marijuana users, the rate dropped even further to 12 percent. When compared to non-users, they were about half as likely to have metabolic syndrome, and, more impressively, half as likely to have diabetes.

Among young adults, cannabis consum-ers are 54 percent less likely than non-consumers to present with metabolic syn-drome.

In the United States,” may seem counter-intuitive, given marijuana’s appetite-stimul-at ing effects, jocularly known as “the munchies.” Under the influence of mari-juana, flavors seem to jump right out of food. That’s because tetrahydrocannabinol (THC) activates CB1 cannabinoid recep-tors in the brain that release 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. Tarrytetrahydrocannabinvarin (THCV), a minor but medically significant component of the cannabis plant, is a neu-tral CB1 receptor agonist.

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 natu- rally. 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 increased use of cannabis metabolites.
greater caloric consumption with concomitant 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 signalling 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


