# The Endocannabinoid System and the Important Role it Plays in Human Health: A Special Interview with Carl Germano

**By Dr. Joseph Mercola**

**JM:** Dr. Joseph Mercola
**CG:** Carl Germano

**JM:** Alright. Welcome, everyone. This is Dr. Mercola, helping you take control of your health. Today we have something very exciting to talk about – a product that will absolutely contribute to your improved health that has been outlawed – yes – illegal in the United States for nearly a century, since 1938. That natural product is hemp. It has been vilified. Thankfully, Donald Trump signed into law the Farm Bill at the closing of 2018. Now, hemp is legal.

To discuss and elaborate on the exciting potential implications of this change in the law, we have an expert in phytocannabinoids, who is a board-certified clinical nutritionist from the state of New York. It's Carl Germano.

**CG:** Thank you, Dr. Mercola. It's a pleasure to be here.

**JM:** Well, I'm very excited to discuss this topic. Perhaps we can start – Maybe just start about how the law has changed. You've been following it very closely. Just explain what that means, and help differentiate the difference between hemp and cannabidiol (CBD) products. They're not the same. Even though CBD is in hemp, you can't sell a product with hemp legally, at least.

**CG:** Correct. In order to understand all of this is to kind of distinguish and differentiate between hemp and marijuana, because they seem to be interchangeable with people. But it is actually two different plants, so to speak. Both are considered Cannabis sativa by genus and species, but that's where the similarity ends.

Hemp has been cultivated for many reasons for the past few thousand years – food, clothing, fiber and fuel. In the plant itself, it contains these naturally occurring active compounds called phytocannabinoids, of which CBD is just one of them. Marijuana, on the other hand, has been cultivated for its primary phytocannabinoid, tetrahydrocannabinol (THC). While it has recreational value at small levels, it does have medicinal value.

Nevertheless, many decades ago, hemp has been dumped into the definition of marijuana. Hemp was dumped into the Controlled Substances Act (CSA), which kind of hampered its access, its ability to have U.S. farmers grow it, or to have even medical or academic institutions actually study it. We've been in the dark ages for decades. Thanks to Israel and Europe, who've championed all the research, we've unraveled something like no other out there. That is the discovery of the cannabinoid system in the body.

What that means – Getting back to your question, yes. Trump did sign a Farm Bill that finally deregulates hemp. It finally takes it out of the CSA, which should never have been there in the first

place. It gives the rights of farmers to grow it. It will open up the doors for academic and medical institutions to study it. It will give access to consumers this important plant that is probably the most important botanical we have on this planet. You'll get to see that as we go on.

**JM:** Great. The difference, as I understand – I just want to make sure that people understand it that it's still possible to sell hemp. It is now possible to sell hemp legally, but there are many companies who are selling CBD. Maybe it's just from hemp, but if they say CBD on the label, that is the problem. Essentially, it's making a claim, because CBD is classified as a, I believe, a Schedule 2 drug. GD or GW Pharmaceuticals earlier this year got the patent on it, so there are going to be major problems. You can sell whole hemp, which is better for a whole variety of reasons in single CBD, which we'll discuss about shortly. Why don't you expand on that important topic?

**CG:** Simply stated, the hemp plant has over 100 different phytocannabinoids, of which CBD is only one. Now, the CSA that held hemp hostage, which has now been released from the signing of the bill, takes the Drug Enforcement Administration (DEA) out of the picture, because DEA has jurisdiction over the CSA. It does absolutely nothing to FDA's position on labelling a supplement or an ingredient that comes into the dietary supplement industry.

With the passage of the Dietary Supplement Health and Education Act, DSHEA, you have several things against CBD. Number one, CBD was not in commerce prior to 1994, so it could not have been grandfathered as a dietary supplement, yet hemp oil has been in commerce prior to 1994, so we're okay there. Secondly, the other part of the DSHEA law states that if you want to submit a new dietary ingredient application, you can do so to prove to the FDA whether or not this ingredient can be deemed a dietary supplement.

Well, if you were to do that today, you would get rejected in three seconds, because the other part of DSHEA states if Big Pharma takes a natural ingredient and makes drugs that get approved, it's hands-off to the dietary supplement industry. GW Pharmaceuticals has two drugs using isolated purified CBD in it. Therefore, we've got several strikes against putting CBD on the front panel, calling it a dietary supplement, and I say, "Why bother?" Because, yes, the story is much bigger than CBD, both clinically, scientifically and legally.

Why bang heads with the Food and Drug Administration (FDA) right now? This is not too dissimilar than the red yeast rice story we have in our trade. Red yeast rice, a food. Hemp oil, a food. Red yeast rice has lovastatin in it. We cannot put that on the label, but we could put the class of compounds in monacolins, which companies are doing.

Well, the same thing here. Hemp oil is a food. It's got CBD in it. It's still in a grey area. But it has a larger class of compounds called phytocannabinoids, of which CBD is one. CBD is not alone and cannot truly support the body's cannabinoid system by itself. You need the rest of the family there anyway. Again, from a scientific, clinical and legal standpoint, it makes no sense to put CBD on the label and call it a dietary supplement.

**JM:** Thank you for explaining that and helping clear up a lot of the confusion on this. Because I, myself, was confused prior to the Farm Bill passing, because I thought that GW Pharmaceutical's patenting of this and classifying CBD as a drug was the end of CBD oil. But actually, it's kind of

good news. I want you to expand on this a little bit, with respect to the cost of GW Pharmaceuticals. Because I have no idea what the cost is. My guess is it's just really high. They have to recover their investments and sell it at profit, of course. But even if you got their CBD product for free, it is nowhere near as getting the complete whole plant product with the more than 100 phytocannabinoids that's in a plant like hemp. Why don't you expand on that? Because it's really exciting news.

**CG:** Right. Those of us in botanical medicine understand that the sum of all the parts of the plant is greater than any one single ingredient. That's a widely held view that natural products are much better than the single, isolated compounds pulled from them, and no different here.

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Let's face it. There's more than one ginsenocide in ginseng. There's more than one curcuminoid in curcumin. There's more than one isobutylamide in Echinacea. There's more than one ginkgolide in ginkgo. Well, there's more than just one phytocannabinoid in hemp other than CBD.

Back in 2013, Dr. Ethan Russo in the British Journal of Pharmacology wrote it best. He talked about the entourage effect of all the phytocannabinoids and terpenes needing to be present to give rise to full clinical, meaningful benefit. We're no different here in that the story is much more important and greater when we look at providing the whole family. While CBD may be the most dominant phytocannabinoid in hemp, the others are there in minor in number, but they are not minor in the body as they all participate in nourishing, supporting the endocannabinoid system (ECS), which is the bigger story.

**JM:** Okay. Why don't you expand on the ECS? Which implies that these cannabinoids in plants are actually working on receptors in the brain and the body that were designed there from the beginning. These are absolutely natural approaches.

**CG:** Right. While the ECS has been discovered in the decade of the 1990s, genetically it dates back over 600 million years ago. With single-celled organisms to invertebrates, humans, you have it. The 1990s was an important decade of discovery. It was a decade of discovery that we have cannabinoid receptors, and then we make compounds in our body that actually touch and influence these receptors.

Now, to understand this whole story is to look and go back to high school. We've all studied all of our physiological systems: respiratory, digestive, immune, cardiovascular, on and on and on. Well, right in the middle, orchestrating all communication between all of our organ systems and physiological functioning is this massive series of receptors touching every organ, including the skin, receptors that communicate and orchestrate massive communication throughout the body. Your ECS is like the conductor of the orchestra. The orchestra are our organ systems. We cannot be healthy. We cannot be well if our ECS does not function well.

So, what have we discovered in the 1990s? We discovered primarily two receptors: cannabinoid receptor type 1 (CB1) and cannabinoid receptor type 2 (CB2). While people have simplified this by saying, "CB1, primarily in the brain. CB2, primarily in the immune system," it's found all over

the body. Both receptors are found in every single organ, while some may be concentrated more in other areas, we find both CB1 and CB2 receptors throughout the entire body.

Now, we have these receptors that accept cannabinoids. The first question is, "With all these receptors touching every organ system and therefore influencing all physiological functioning, the body must be making something to target and influence them." In the late 1990s, we discovered we produced cannabinoids. I tell the whole world, get over it. Your body produces cannabinoids similar structurally to the cannabinoids found in cannabis. Your body feeds off of them. If you don't produce enough to feed every single receptor, various conditions and various illnesses will ensue.

Now, the two cannabinoids that have been discovered, one is called anandamide, from the word "ananda," the Sanskrit word meaning "bliss," because it touches the CB1 receptors that THC touches. Then the other is 2-arachidonolglycerol, or simply 2-AG, which is found, again, all over the body.

Now, the brains behind the discovery have been Dr. Raphael Mechoulam out of Hebrew University of Jerusalem, and all of his colleagues out of the National Institute of Mental Health: Devane, Hanus, Ulette, Ackerman. There has been a number of players, but those are the brains behind the discovery.

The ECS has been the subject of many scholarly textbooks. They talk about the endocannabidiome, the ECS, endocannabinoids. Quite frankly, this is something that should be taught from high school to college to practitioner school. Unfortunately, because of the stigma attached to cannabinoids, we were not able to study this here in the United States –

A survey by Dr. David Allen of over 150 medical schools demonstrated that less than 13 percent are teaching the ECS. I say, "Are you insane? Are you telling me –This is like me saying that for the next 70 years we will not teach the cardiovascular system, as if it never existed." We now have to dismantle the medical travesty. We just dismantled the botanical travesty by freeing up hemp. Now we have to dismantle this medical travesty of not educating not only future physicians in our country and in the world –

**JM:** Existing physicians too.

**CG:** Yeah. Absolutely. The whole thing is about education. This is critical and crucial. We have to dismantle the stigma, and we have to start educating ourselves to understand that the ECS is probably one of the most important medical discoveries in quite some time. Again, understanding the enormity of this system and what it does and what it influences throughout the entire human body.

**JM:** Terrific. Why don't you elaborate on some of the problems, complications or disease processes that occur as a result of us, A, not producing enough of our own endocannabinoids, or receiving them externally through a supplement, like a complete whole hemp product.

**CG:** There were several interesting papers published in Neuroendocrinology Letters. Ethan Russo is a part of this as well. Like anything else we produce in our body, there are times – or as we age – we don't produce enough. The cannabinoids we produce in our body, anandamide and 2-AG, are no different here. We have now been able to use these as biological markers to determine certain illnesses and conditions.

There is a thing called endocannabinoid deficiency states, states where we don't have enough anandamide and 2-AG hitting all these receptors, helping to control physiological functioning. We're finding endocannabinoid deficiency states in people who have migraines, fibromyalgia, irritable bowel syndrome, all the treatment-resistant conditions, inflammatory and neurological conditions as well. But it didn't stop there with Neuroendocrinology Letters of 2014 and 2008.

Another interesting paper in Translational Psychiatry looked at the levels of anandamide in the body, that when they got too low, they were statistically positive indicators for stress-induced anxiety. Again, an example of a biological marker anandamide is to determine stress and anxiety in individuals. We look at people who have migraine headaches. We look at both in the blood and in the cerebral spinal fluid. We see that the levels of anandamide are significantly decreased in people who have migraine headaches.

We look at this intimate relationship between omega-3 status. Now, we know that omega-3s are useful for two reasons to the ECS. A, it helps the cannabinoid receptors to be more active. B, those omega-3s and phospholipids are used as backbone structures to produce cannabinoids in the body. What do we see with people who have low omega-3 status? We see the same things we see in people who are endocannabinoid deficient: pain, inflammation, stress, anxiety, depression, on and on and on. It is a perfect marriage between omega-3s and phytocannabinoids, which act like a multivitamin for the ECS.

But it doesn't stop there. I mean when we look at bones. If you think calcium, magnesium, menaquinone 7, vitamin D, other accessory nutrients are important for bone health, well, when we look at post-menopausal women, we understand that the reason why we give them estrogen is because it influences the cells that buildup bone, osteoblasts, and the cells that breakdown bone, osteoclasts.

What does this have to do with the ECS? We now know – and a beautiful paper that was published in the Journal of Endocrinology talked all about this one – if you stimulate the CB1 receptors, you start to stimulate the brain-to-bone communication by slowing down the brain from releasing bone-breaking compounds, like norepinephrine. Then when you stimulate the CB2 receptors, it increases osteoblasts, the bone makers, and decreases osteoclasts, the bone breakers. You've got that aspect going for you.

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When we look at athletes – First of all, the ECS is a system of recovery. It's adaptogenic. When we look at the runner's high, we have to dismantle the runner's high being due to endorphins, because another important paper in the Journal of Experimental Biology looked at various subjects, both humans, dogs and ferrets after strenuous treadmill exercise. They noticed anandamide levels skyrocket. Then they correlated anandamide levels skyrocketing with positive feelings. The higher

the anandamide level, the better people felt. That makes sense, because anandamide hits the receptors in the brain that are involved in reward, mood.

Then we also understand that our cannabinoids we produce are quite promiscuous. They certainly touch the CB1 and CB2 receptors, but they had other receptors as well: the 5-hydroxytryptamine ($5\text{-}HT_3$), peroxisome proliferator-activated receptors (PPAR), gamma-aminobutyric acid (GABA) receptors, receptors that also control inflammation, pain, reward, anxiety and things of that nature.

What we are unravelling is as we are deficient in cannabinoids that we produce, certain conditions will ensue. The top conditions include pain, inflammation, stress, anxiety, insomnia, ocular health, bone health, neurological and inflammatory conditions. These are all conditions that can be suitably treated with giving phytocannabinoids. These are conditions that we see in people who are endocannabinoid-deficient.

**JM:** Thanks. That's a terrific answer. I really appreciate it. I'm wondering if you can help us understand the difference between endorphins being a runner for over four decades. I always thought that's why we got so high after about 20 minutes of working out. But what's the difference between endorphins and the anandamide?

**CG:** Well, as I had mentioned before, anandamide not only targets the CB1 receptor, but also influences opioid and endorphin receptors.

**JM:** It's more comprehensive.

**CG:** Absolutely. There are some interesting papers using electroacupunture. Certain key acupuncture points in the body can absolutely turn on the signaling between the ECS and opioid and endorphin output. We now know – There's a great paper on PLOS One on the care and feeding of the ECS and how herbs and nutrients and manipulation – chiropractic and acupuncture – can actually also influence endocannabinoid functioning. In this particular case, opioid and endorphin output in the body.

**JM:** Great. Earlier you mentioned the large amount of disease conditions that the hemp would be useful for. I can't imagine anyone watching this who hasn't experienced any of those conditions or one of those conditions personally themselves. If not, certainly someone they love. Let's discuss some of the specific details on how one would use that as a treatment with respect to dosing. Let's go up on dosing, then we'll talk about the quality of the product too and how you differentiate that. What is the typical dose? Then how is it possible to overdose?

**CG:** Yeah. Again, getting back to the clinical applications. When we talk about inflammation, while we think curcumin, boswellia, fish oils and quercetin are all powerful anti-inflammatory nutrients, which they are, by entering the pathways. We now understand that the ECS controls those pathways. There are several really excellent papers that talk about the mechanisms of action on analgesic and anti-inflammatory effects and the limitations to what we have today to control inflammation and pain.

We know inflammation is at the heart and soul of most disease conditions. The dosing that we look at in the literature, unfortunately, we rely on a lot of what GW Pharmaceuticals has done. But that is with single magic-bullet, isolated, purified CBD. We now know, in a paper out of Israel in 2015, showed full-spectrum oils up against isolated CBD. The group with a full-spectrum oil, from a clinical outcome point of view, was superior to the single magic-bullet isolates.

When we look at dosing, while the bulk of the literature is in the couple of hundred milligram range, there are many clinicians who are using anywhere from 10 to 25 milligrams a day. People are responding quite remarkably, which talks of the issue that you don't need a lot to jumpstart the body's ECS. This is not a numbers game. Quite frankly, when we look at the bell-shaped curve with the isolates, the higher the doses, sometimes you decrease the effectiveness of the material. When you use a full-spectrum oil and you're getting the other components, this is superior, and I'll tell you why. People have been focusing on CBD, which is the wrong message. It's the myopic message.

Think about it, CBD does not attach to the CB1 or CB2 receptors. If anything, CBD supports the CB1 receptors by preventing the breakdown of anandamide in our bodies and anandamide hits the CB1 receptor. What about the lowly CB2 receptor that controls inflammatory cycling, pain signaling, insulin sensitivity and bone building? CBD does nothing for that, so we need something of a CB2 agonist.

Luckily, the family of other phytocannabinoids in a full-spectrum oil contains all these other phytocannabinoids that complement to what CBD is not doing. We must get off this single magic bullet bandwagon. We must appreciate the full gamut of all these phytocannabinoids as a whole, and that they complement each other, because CBD is not the answer to support the ECS as a whole.

**JM:** Great. Two questions. The milligram concentrations you were referring to, I'm assuming that's the total cannabinoids. The second question, is it possible to overdose?

**CG:** The one I mentioned, 10 to 25 milligrams, yes. It's primarily CBD. In a full-spectrum oil, you'll get all the minor players in there.

**JM:** You're assaying just the CBD?

**CG:** Well, we have to get all phytocannabinoids in the plant, so we look at the full fingerprint. But since CBD is the most dominant cannabinoid in hemp, when you process it, you do have much, much higher levels of CBD naturally in the oil. Providing 10 to 25 milligrams of CBD is the sweet spot for most conditions in the trade. The other question you asked –

**JM:** Overdosing.

**CG:** Yeah. Like anything else, too much of anything can be bad.

**JM:** Makes sense.

**CG:** Luckily, with full-spectrum oils, you won't need to get there. Certainly, we've seen this using the CBD isolates and the drugs that are out there with just CBD in it. You don't necessarily overdose, but you lose effectiveness. There have been minor, at best, toxicities or adverse reactions associated with CBD, which is a good thing. I don't foresee anybody really overdosing on the standard dosages that we're recommending. Nor when we look at the data that's been published, up to 1,500 milligrams, 1,500 milligrams of CBD chronically administered – this is not an acute thing – chronically administered over time show that it was well-tolerated, minimal to no adverse reactions on physiological function, psychological functioning and other parameters in the body, including blood pressure on down. It is quite well-tolerated in humans.

**JM:** Great. Perfect answer. Let's get now to some of the practical implications of this good news. My additional understanding is that the cost of these oils are going to radically drop. Because in the past, they were required to restrict the harvesting of the CBD from the non-flowering parts of the plant. Now that they can use the flowers, which have a higher concentration, it's going to make processing much easier. Maybe I've got that confused, but can you please respond to that?

**CG:** Yeah. Absolutely. In the past, prior to the signing of this bill, we were only allowed to pull the oil from the stalk and the stem of the plant, as the leaf, flower and bud were off-limits, with the thinking that it's got more THC in it. But hemp, by definition, under the Farm Act of 2014, distinguished, differentiated and defined it as Cannabis sativa less than 0.3 percent THC. It didn't make any sense.

Nevertheless, now that that's all gone and the Farm Bill of 2018 opened up the ability for processors to now use the leaf, flower and bud, where the cannabinoids are more concentrated, it's more economical now. What this will translate to are more economically priced products for the consumer, which is a good thing.

**JM:** Great. Just like in food, we know that it's much better to grow your own vegetables. You can be sure that it's organic, and it's properly nurtured and harvested. Similarly, even though the price is going to drop pretty dramatically, the other implication of that law that I neglected to mention is that it is now legal in every state of the United States to grow hemp in your backyard or in your apartment.

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If one is doing that – this is something I wanted to do for such a long time, and I've got an acre of land that I can plant and harvest food from. I'm definitely planning on doing this. I'm wondering if you could provide us with instructions on how much you would harvest, and the timing of that, to put into a smoothie.

**CG:** Well, that's interesting because the whole plant can be used to juice or to put into smoothies, what have you, as a plant itself. But it's interesting that while this bill has now allowed U.S. farmers to grow, process and to cross state lines – In Europe, we've been doing this for the past few decades, where we didn't have those restrictions. One of the things that is immediately coming out of the gate is that the U.S. is going to want to make sure that growers here in the United States are using certified seeds.

What we mean is that seeds that have been used for products for human use for a very long time. Since we've been doing it in Europe for decades, certified seeds from Europe are going to be preferred to be used here in the United States until things kind of settle out.

Growing it for yourself would be wonderful. It is a weed. It has a short period of harvest. It grows very rapidly. July, August and September, we're looking at that we do in Europe. Yes, the whole plant can be used rather than just extracting the oils from it, which all the phytocannabinoids and lipids – they're found in the oils, but the leaf, flower, bud, stalks and stems can be juiced and put into smoothies as well – or the oil can be used as well. But in terms of your growing it and processing it, it's a rather easy plant to grow, because it is a weed and –

**JM:** Imagine that. But what type of dose would you take? Would you take like a bud? Would you weigh it out of the plant material? I imagine it's not very much, maybe for just a few grams.

**CG:** Yeah. You don't need much.

**JM:** I don't know the concentration to get 25 milligrams of the CBD or cannabinoids in that. Would you need a gram, 5 grams, 10 grams, 30, an ounce?

**CG:** Well, the thing is when we talk about the raw plant, a lot of these cannabinoids are in their acidic form. CBD is in CBDA, cannabidiol acid. To convert it to its useable form, the acid has to be decarboxylated. It has to be removed. The plant itself, while you may benefit from a lot of the phytocannabinoids, it's going to be reliant on the body's ability to kind of process from the acidic forms that are in there. The exposure to heat, light, moisture and air will decarboxylate a lot of them as well. The more you kind of process it yourself, the more useable some of those phytocannabinoids will be.

**JM:** What does a home processing look like?

**CG:** Well, you can take the leaf, flower and bud. You can blend it and store it in the refrigerator. Over a day or two of exposure to air, light, moisture and what have you, it'll decarboxylate and you'll benefit more from that. Again, how much do you get? Twenty-five milligrams of CBD. That's a hard thing to do with just juicing alone.

**JM:** Yeah. What's your best guess? I mean assuming you're using a concentrated form in the flowers. Would it just be an ounce? Would it just be half an ounce? I'm sure it's a relatively small amount.

**CG:** Yeah. It would be a small amount. I don't want to misquote myself and say the wrong thing. But yeah, probably an ounce or two, which would do the trick. Again, you don't need a lot to jumpstart the body's ECS. Again, it's not a numbers game. Small doses, you would definitely respond to.

**JM:** Now you seem to be quite literate with the literature on this. I'm particularly curious on the anti-inflammatory component, because inflammation is really a central part of aging. It's typically – There are a lot of things that contribute to inflammation, but we're finding out now that senescent

cells, these senile cells that stop reproducing for a variety of reasons have these inflammatory profiles that produces inflammatory cytokines and NF-κB and a whole variety of other inflammatory mediators. I'm wondering what the mechanism is for CBD and the other cannabinoids in lowering inflammation.

**CG:** Yeah. As I mentioned the common anti-inflammatory nutrients we have in the marketplace, none will compare to what cannabinoids will do in the body, phytocannabinoids from the plant. There was an initial paper in Current Opinions in Clinical Nutrition and Metabolic Care of 2014 that talked about the ECS being the emerging player in inflammation, because it's intertwined with all of the inflammatory pathways, including the eicosanoid ones that the omega-3 fish oils influence.

But then in 2017, in the International Journal of Neuropsychopharmacology, they talk all about targeting the ECS for both inflammatory and neuropathic pain, as well as the mechanisms of action of how these cannabinoids and your ECS act as analgesics, anti-inflammatory agents to deal with, again, pain and inflammation.

It does so by a number of mechanisms, not just inflammatory pathways, but various neurotransmitters that are released in these pain pathways, reducing inflammatory signaling, both at the cell and signaling to the brain. It has a number of mechanisms, but you cannot contend with any inflammatory conditions unless you're supporting the ECS. They can be used interchangeably phytocannabinoids along with curcumin and boswellia and fish oils would be remarkable, as they are complementary to each other by doing different things.

Again, we must address the ECS in any inflammatory condition, whether it be irritable bowel syndrome to injuries. Even inflammation in the brain, which is one of the hallmarks of all neurological diseases.

Look, in 2003, the United States government got issued a patent on the neuroprotective effects of cannabinoids. At that time, while the government has been telling us that phytocannabinoids are like lysergic acid diethylamide (LSD) and heroin – have no medical value – they go out and get a patent on the medical value. But that was followed up, and there are many papers that talk all about the anti-inflammatory effects in the brain, in the nervous system, of these cannabinoids and your ECS, which are useful in treating neurological conditions and can be useful, "Let's get out of the clinic, Larry, and look at the athlete, to prevent further brain damage."

I mean that patent in 2003 talked all about how non-psychoactive phytocannabinoids can reduce further damage to the brain if the stroke or trauma, and is useful for neurodegenerative diseases. The athlete and why WADA, the World Anti-Doping Agency, took CBD off their banned list, because of the context for it, whether it be football, martial arts or what have you to reduce further damage neurologically. It is a physiological system that we cannot ignore anymore. It comes to all these inflammatory and pain conditions. There is nothing else like supporting the ECS with phytocannabinoids.

**JM:** Well, thanks. I'd like to research this more and plan on going to PubMed and looking it up. I'm wondering if you could recommend the keywords. Would it be "endocannabinoid system,"

“phytocannabinoids,” or “endocannabinoids and inflammation?” What are the keywords that you use to search?

**CG:** I would just put in “endocannabinoid system and pain,” and “endocannabinoid system and inflammation.”

**JM:** Okay.

**CG:** You’ll see many many.

**JM:** I’ll find it out. Yeah. Because I’m really curious about the mechanism, because I think it ties in well. I’m really aggressively reviewing the anti-aging literature. I haven’t seen any reference to this at all. I think it’s something that may have been missed, so I’m particularly curious.

**CG:** Yeah. That’s the tragedy. Again, we’ve just dismantled the botanical travesty with the signing of the law. Now, we have to dismantle the medical travesty. We have to study more of this here in the U.S. We have to educate students from high school to college to practitioner school. You can’t ignore this anymore. It’s just absurd.

**JM:** Yeah. I couldn’t agree more. One of the pervasive problems and conditions that you have mentioned earlier that it’s useful for is insomnia. We know very clearly that if you’re not sleeping well, you are just inevitably going to suffer in your health. It’s going to deteriorate in some way, shape or form. It’s just almost a guarantee. I’m wondering if you could recommend doses, and more importantly, the timing on a full-spectrum hemp oil supplement.

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**CG:** Yes. In using the full-spectrum hemp oil for insomnia, I would go to the higher end of the dose range we spoke about before. That is looking at the 25-milligram range. Now, CBD at that range does a number of things. Number one, it reduces excitability in the brain. It can reduce glutamate toxicity and any excitatory conditioning.

Secondly, CBD is involved in various neurotransmitters that are involved with a normal sleep cycle. While it has a calming effect and helps to establish a normal sleep cycle, it’s not necessarily a sedative. You can use it with melatonin. You can use it with lavender. You can use it with chamomile and passionflower, what have you. But that’s the dose. I would do that towards the latter part of the day. Whereas lower doses of CBD are more stimulating, so to speak, and more upregulating. That would be low doses.

**JM:** We’re looking at one hour, two hours, three hours or four hours before bedtime?

**CG:** Yeah. At least an hour or two before bedtime. Absolutely.

**JM:** Okay. Well, thanks. That’s perfect.

**CG:** Yeah.

**JM:** Again, in trying to identify optimal sources of supplementation, I'm wondering if there's a difference in the hemp or the CBD supplements that are available now advertising CBD that are extracted from hemp. Will there be any difference in the newer ones that come out that are actually doing the processing from the hemp flowers, which have a higher concentration, other than the cost? Or are they going to be essentially the same product?

**CG:** Well, the good news, again, using the leaf, flower and bud, is that there are more of the terpene family in there, where you didn't have much at all in the stalk and stem. You have the phytocannabinoids there. We will have a more concentrated source of not just phytocannabinoids, but terpenes, which are very complementary to the phytocannabinoids and the activity of the plant.

Again, that was all spoken to with Dr. Ethan Russo's paper in the British Journal of Pharmacology, and talking about this entourage effect, where we need all the phytocannabinoids and the terpenes present. The consumer is benefiting the most – reduced pricing, a more full spectrum of not just the phytocannabinoids, but also the terpenes in the plant that are clinically relevant.

**JM:** I believe terpenes are a polyphenol. I'm wondering if you could expand on the biological actions of terpenes.

**CG:** People have to understand that phytocannabinoids are all terpene-like structures in the plant. The fact that they influence, touch or attach to the CB1 and CB2 receptors in the body, they were reclassified as phytocannabinoids. The terpenes are all important, because many of them are phytocannabinoids. While they give rise to the smell and odor and taste of plants, they have some really potent effects in the body, from anticancer to anti-inflammatory, and again, all complementing the phytocannabinoids in the plant.

**JM:** Okay. Great. Are there any recommendations on how to identify a high-quality product? I mean, obviously, it should be organic. But are there anything on the label that we need to look for to say, "This is a product that's good," other than growing it yourself, which I think is probably the ideal.

**CG:** Yeah. Some of the attributes that I tell consumers to look for is being organic, being Kosher-certified and being non-GMO. We also have to look at the fact that whether or not the material has been tested for pesticides and herbicides. Was it grown on either organic or eco-certified land? Because that's a major issue plaguing the marijuana sector. It's no different here with hemp, in that the use of pesticides and herbicides are going to be an issue. The use of GMO here in this country is going to be an issue as well.

Looking for non-GMO, organic, Kosher-certified, looking for the full-spectrum, trying to get an idea of where these materials are coming from, get to know your companies, because there has been a lot of characters in the trade right now. People who don't even understand the dietary supplement industry, don't understand DSHEA Law, blatantly breaking the law in terms of labelling.

I look for companies that are doing the right thing also. That is they don't mention CBD. They talk about phytocannabinoids. They talk about hemp oil. They talk about nourishing the

endocannabinoid system. This is a superior story to just CBD. Those are the more reputable companies that are telling the right story, that should have unraveled years ago, not just isolated CBD.

**JM:** No question about it. That is really the key. Thank you for expanding on that. Are there any other insights you'd like to share? Something that we left out?

**CG:** Well, there are two particular areas of interest to me. Number one, the brain-gut-immune connection. We know how important this connection is in the body, this triad of organ systems, of the brain pushing out the neurotransmitters, the immune system pushing out immunotransmitters, and then the heart and soul, the gut, who no longer is a system of digestion; it's also your largest immune organ.

Going deeper into the cellular structure, we find out hundreds of millions of neurons – your second brain. We now understand how the gut is involved with communicating with the brain and the immune system, because it has brain cells and immune cells in it.

What does this have to do with the endocannabinoid system? Well, right smack in the middle is your endocannabinoid system, orchestrating this tri-directional communication. In a beautiful article in the Gastroenterology, 2014, the role of the ECS in the brain-gut access, it now unraveled that the ECS controls motility in the gut. It controls intestinal inflammation. It controls abdominal pain. It reduces the activity of the stress pathways, the hypothalamic-pituitary-adrenal (HPA) pathways.

Then in the Proceedings of the National Academy of Science of the United States of America in cannabinoid research, that unraveled how anandamide participates in the immunological response in the gut, how the ECS reduces inflammation and disruptions in permeability in the gut and how it controls various aspects of tolerance to foreign antigens.

What was really unraveled, which is interesting, is that the communication of the endocannabinoid system, we call the endocannabidiome, and your microbiome, the probiotics, all had an interplay here with this mass communication between these three organ systems.

The other interesting area, which is fascinating and is unravelling as we speak, is the role of the endocannabinoid system in controlling consciousness. We could look at consciousness in a variety of ways, the classical view, the thoughts, the sensations, the feelings that one has, the neuroscientists' point of view, all this communication is due to our awareness and our experiences and how they influence these neural pathways. Well, there have been several papers that have been published looking at this very subject.

In a paper in CNS and Neurological Disorders – Drug Targets talked all about how the endocannabinoid system modulates levels of consciousness, emotions and like the dream states.

There are other papers that show that under anesthesia, where you knock out consciousness in manipulating the endocannabinoid system, bringing animals out of the unconscious state, how in a sense, every thought, every feeling, every perception that we have, in one way, shape or form, is

influenced by our endocannabinoid system, because we know the endocannabinoid system controls neurotransmission in the brain. It's heavily concentrated in the brain, controlling so many other aspects of our well-being, our perceptions, our awareness and our thoughts.

The endocannabinoid system, quite frankly, is an internal reflection of who we are. These are the two areas that are really exciting, that are unravelling as we speak.

**JM:** From your review of the literature, has there been any research that you're aware of that looks at the endocannabinoid system where phytocannabinoid supplementation on the different stages of sleep?

[-----50:00-----]

**CG:** Not so much the different stages of sleep, although I can tell you that I have worked with a couple of firms. One in particular has actually produced an app for your phone, that when you put it in airplane mode, so there's no signaling, when you put this app on, you put it under your pillow, it measures your sleep cycle. They work with insomniacs. You could see the disruptions of the sleep cycle in those with insomnia.

With the application of hemp oil rich in CBD, you could see a normalization of the sleep cycle. With just in our beginning stages to look at how it influences various states – alpha, beta and gamma states in the brain – and its regulation of the sleep cycle.

**JM:** I haven't thought that there were any studies. I actually wear a device. It's a relatively new device. That's a four-lead electroencephalography (EEG) every night, which is far superior to lacing up a phone onto your head and your pillow at night.

**CG:** Yes.

**JM:** It very accurately assesses rapid eye movement (REM), deep sleep, light sleep and when you're awake. I'll be able to do some research. I'll let you know. We'll probably have you back on again. Because what I neglected to mention at the beginning of the interview is that you've actually written a book. It's not published yet. You've invited me to write the foreword. I haven't read your book, so I can't answer that question yet. What's the name of the book? What does it discuss? When will it be published?

**CG:** Yeah. The name of the book is called *Road to Ananda.* "Ananda" is the Sanskrit word for "bliss," which is the word used to describe our first cannabinoid discovered, anandamide. *Road to Ananda: The Simple Guide to the Endocannabinoid System, Phytocannabinoids and Hemp.* I'm ecstatic to announce that the person who wrote the introduction to the book is Dr. Raphael Mechoulam.

**JM:** Wow. Congratulations.

**CG:** Yeah. The discoverer of the endocannabinoid system. He is well-known in the scholarly circles. There are certainly plenty of scholarly work out there, but we need to get this message, this story, which is enormous, out to the layman and practitioner out there who is really unaware

still. It was written with a lot of illustrations. I brought on an illustrator. Again, Dr. Mechoulam wrote the intro and I need to get his work out there to become a household work for all of us.

**JM:** Great. I'll likely write the foreword, but I look forward to reviewing it. When is it going to be published again?

**CG:** We are publishing the book at the end of January. It will be available –

**JM:** January of 2019?

**CG:** Yeah. It'll be available at the beginning of February.

**JM:** Okay. Great.

**CG:** Thank you.

**JM:** Wonderful. Anything else you'd like to add?

**CG:** Well, all I can say is I've been in this industry for over 35 years. I'm a clinical nutritionist by trade. I have not seen any compounds, natural compounds this clinically relevant since the inception of this industry. I can tell you that targeting the endocannabinoid system, supporting it, will dominate medicine and nutrition of the next couple of decades.

We just gave the viewers a glimpse, a very brief glimpse of the enormous effects of the ECS on the body, not only internally, but to end with – There are topical applications for phytocannabinoids, because, again, our skin is one of our largest organs. It also has about 5 to 10 times more cannabinoids in it than we have in our brain. The CB1 and CB2 receptors are there as well.

When we look at the global picture of what is the subcutaneous endocannabinoid system doing, it's helping to maintain normal cell proliferation, differentiation and immune competence. Oncologists are going to be interested in that aspect.

But then if you disrupt the endocannabinoid in the skin, there are three targeted areas for topical applications. One, obviously, is pain and inflammation, because the CB2 receptors are there that control that. That is something that will blow away any of these compounds in the marketplace today for topical pain relief. Then we know that certain cannabinoids strangle the sebaceous gland for acne. Certain cannabinoids also influence monolysis, so age spot development, anti-aging. [There are] some very interesting things going on in the topical application area.

**JM:** Very exciting, very exciting. I can't thank you enough for sharing your wisdom with us, and your understanding of the literature as it relates to the endocannabinoid systems and the potential benefits that it offers each and every one of us.

Magnificent news with the Farm Bill. Who would have known that it would be legal in 2019 and that we could have access to this? And it's even less expensive. Actually, one of the questions I

asked you earlier but I didn't get an answer was the cost of the GW Pharmaceutical's product? How much does that thing cost per month?

**CG:** Tens of thousands of dollars per year.

**JM:** Tens of thousands of dollars. You could treat yourself for multiple lifetimes.

**CG:** Exactly, exactly.

**JM:** It's crazy. A month's worth of the pharmaceutical. I bet you GW Pharmaceutical was not pleased with the Farm Bill.

**CG:** Well, there are rumblings behind closed doors that they want to get into the dietary supplements space. They probably will at some point. I mean having drugs approved by FDA, they can petition the FDA at lower doses than the drug doses for dietary supplement and food use. They have that capability of doing that if we really want this CBD on the label in the future.

**JM:** Okay. It won't change the product that we're able to purchase, but it will change the manufacturers', who are selling the products, ability to advertise that as an approved indication.

**CG:** Correct, correct.

**JM:** Alright. Hopefully they make the investment and we can tell the truth, because as you well know, and I certainly know and most people watching this, many of the supplements – we are handcuffed. We cannot say a fraction of the things it does, otherwise we're shut down or we go to jail.

**CG:** Right. Well, that certainly would open up at least what we can say. But whether GW does that and gives us the ability to put CBD on a front panel and call it a dietary supplement, I still am behind the story that CBD is the minor player.

**JM:** Right, right. Yeah.

**CG:** It doesn't matter.

**JM:** It doesn't matter. Right. I guess one last question too is, "Do you think that there is research going on now that will further elaborate or identify perhaps other endocannabinoids other than CBD that are particularly potent and effective?" I mean it's just an intellectual curiosity because it doesn't really matter in the end, because you want to full spectrum.

**CG:** Yeah. Absolutely. First of all, CBD is going to be hitting the marketplace soon. That's cannabigerol. Cannabigerol is like the stem cell phytocannabinoid, which others are made from, THC to CBD. Cannabigerol has more potent effects than CBD in certain conditions. Then we look at something like beta caryophyllene, which is a minor phytocannabinoid. But beta caryophyllene is a potent CB2 agonist.

Going back to this whole story that I was telling about, how people who take CBD think they're nourishing the endocannabinoid system, well, again, we know that CBD does nothing for the CB2 receptor. Having beta caryophyllene present is critical to give full CB1 and CB2 support in the human body. People are going to have to wake up. That CBD is not this whole story. It needs some of the phytocannabinoids, which either are more potent or complementary to its activity in the body, because CBD does not touch all the receptors.

**JM:** Wonderful summary. I thank you for sharing that. That is brilliant. Beautiful. Beautifully well stated. Thanks again for all your help. I look forward to reading your book, actually.

**CG:** Thank you.

**JM:** *Road to Ananda.*

**CG:** Thank you so much. It's a pleasure to be here.

*[END]*