Cannabis Therapy
Getting Healthy, Not High

INTRODUCTION

That we have an Endo-Cannabinoid System (ECS) was only imagined in the early 1990's. We now know that it is our foundational internal homeostatic regulatory system, involved in almost every physiological process. Its presence is everywhere.

Using EndoCannabinoids, short lived signaling molecules named after the Cannabis plant but produced in our bodies, the ECS initiates changes starting at the cellular level. Working through a multitude of strategies, it calls our body to action in regaining and then maintaining internal physiological balance, a healthy state of life.

To fully grasp the ubiquitous presence of the ECS we must go back in time. Researchers in 2004 found that the Sea Squirt had an ECS dating back 600,000,000 years. Sea Squirts are forerunners of vertebrate animals. We do not know what the function of the ECS was for them. But over the huge expanse of time and the crescendo of complexity of developing life, the ECS became our body's foundational language for maintaining cellular health.

Life developed and organic complexity increased. The ECS was present becoming the underlying communication foundation whose purpose is bringing balance to our bodies – homeostasis - health. Picture a house with just the framing completed. This is when the ECS made its entry into our bodies. So as the house was completed, electrical, plumbing, drywall, paint were added, it was intrinsically a part, not apart. It touches every aspect of our biological life.

Cannabinoid Therapy (CT) uses phyto or plant Cannabinoids to call the ECS into action. The list seems endless of diseases Cannabinoid Therapy (CT) can help. These diseases are just the language our bodies use to get our attention, to communicate an imbalance. They are symptoms. We have the opportunity with CT to make changes not from the outside in, invasive with side effects, but from the inside out. This is because the ECS does not primarily deal with the specific symptoms, but rather with the underlying fabric of health. Symptoms improve and can cease as balance is attained through life style changes and the intelligent use of Cannabinoids.

The ECS can slow down what is too active and stimulate what is too still. It can cool down what is heated and quiet what is noisy. It is the language at the cellular level our Innate Body Wisdom uses to keep us healthy.

Starting on a regime as low as 1mg/day, real benefit can be gained. As part of a healthier life style, CT seemingly miraculous results are available to all. All of this without needing to get high.

Life long health requires change and commitment. It requires personal participation in learning and then action. These are the elements that build a healthy and fulfilling life. Really, this is what life is about.

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ENDOCANNABINOID SYSTEM

The EndoCannabinoid System (ECS) is an internal homeostatic regulatory system that is involved in almost every physiological process occurring in the body.

Homeostasis is how a cell maintains a stable environment, a state of health, against the vicissitudes of life.

Understanding and working within ECS activity has a therapeutic potential for almost all of the diseases effecting humans.

(WOW! Please excuse me if this may seem a bit redundant. I keep saying the same thing just a little bit differently. But this fact, this observation, this knowledge is as revelatory as when the world suddenly was not flat, but round. And then on top of that, that this plant would produce an entire grocery store of molecules that would affect our physiology so deep and yet with nearly no down sided side effects. It is just amazingly unimaginable. And that this plant has been with us since we first became human and has been used by us in so many diverse ways over this huge chunk of human history continues to astound me. It is like, almost unthinkable. But here it is and here we are.)

The ECS takes its name from the cannabis plant and the molecules the plant synthesizes, Cannabinoids. These plant-produced molecules, called PhytoCannabinoids, whose structure was first defined in the 1960's, were found to be similar to compounds and a system utilizing these compounds discovered in the human body in the early 1990's. The Cannabinoids produced in our bodies are called EndoCannabinoids.

We can trace the ECS as far back as 600,000,000 years to the Sea Squirt. The ECS has been with us all the way to today. It is not found in invertebrates such as insects. It is found in all the vertebrates. It was with us on the long journey as life ever more developed in complexity. We know not what it did for the Sea Squirt, but since then it has become the underlying, foundational means by which our body speaks to itself in times of cellular crisis. We did not see it earlier because it is so ubiquitous, so pervasive in its presence and activities, so varied in its strategies. We mistook other systems that developed in our bodies physiologically later for it.

Interestingly enough, the Cannabis plant has been given a date of 34,000,000 for when it became a distinct species. Our ECS long predates the Cannabis plant.

In 1937 Cannabis became a banned substance under an edict from the newly formed Federal Bureau of Narcotics (FBN). The FBN then started to search for the active ingredient of Cannabis. Their chemist was not able to come up with anything and passed the work onto another chemist, Roger Adams. Between 1940 and 1949 he and his associates carried out 27 studies on cannabis, published in the American Journal of Chemistry. He

isolated Cannabinol (CBN), Cannabidiol (CBD) and Tetrahydrocannabinol (THC). He synthesized them. He elucidated their molecular structure.

We now had the knowledge of the molecular make up of these Cannabinoids.

The Army, looking for a truth serum, conducted the first tests using 'marihuana' (more on the history of the words marijuana – cannabis later) during the years 1942-43 at St. Elizabeth's Hospital in Washington DC. They were done under the auspices of the Office of Strategic Services (OSS), predecessor to the CIA. The goal was to invent techniques useful for questioning prisoners of war. A truth serum. The 'marihuana' was smoked as THC infused cigarettes, based on a liquid form provided by Adams' laboratory. It was tested initially on employees of The Manhattan Project, the US's ultra secret project to build an atomic bomb. They didn't find what they were looking for but had a lot of participants with bad cases of the munchies. These tests actually did not end officially until 1973.

How the ECS was discovered is an ironic story, also a byproduct of our government's misdirected research. During the Regan years, in the midst of the drug wars, millions of dollars were put into research to find out how marijuana damages the brain. They assumed that this was happening and they wanted to know how. But instead of showing how it damaged the brain, the research ended up with the discovery of the ECS and how Cannabinoids actually just might have positive health affects for us.

As part of the research, in 1988 scientists funded by the US government at St Louis Medical Center discovered the CB1 receptor. CB stands for Cannabinoid. Receptors are how the Cannabinoid message is able to get into the cell. The receptors are one of four parts that we consider to be the ECS. More on them shortly.

But the scientists did not stop there. They hypothesized that if you have a receptor it is not there to merely respond to a plant compound, it must be there to respond to something produced within our bodies. So scientists started looking for what must be an endogenous compound, a Cannabinoid made within us, which was plugging into these receptors. The first EndoCannabinoid, Anandamide, was then discovered in 1992. And so the ECS was revealed.

Dr. Raphael Mechoulam, the dean of the transnational cannabinoid research community and given credit for the discovery of the EndoCannabinoids stated, "By using a plant that has been around for thousands of years, we discovered a new physiological system of immense importance. We wouldn't have been able to get there if we had not looked at the plant."

As a side note, Opioids are an interesting group of molecules in relation to Cannabinoids. Opioid receptors, a similar G-protein coupled receptor, were first written about in published article in 1971. The first Opioid to be isolated was in 1804. We know a lot more about Opioids that Cannabinoids. Discovery of ECS lagged behind the understanding of the Endorphin system, our endogenous system that functions like and interacts with the Opioids.

Much of the positive story of Endorphins, runners' high, is actually a misunderstanding. Endocannabinoids most likely create that "well-being" feeling. Cannabinoids have so much more importance for us. One last bit of comparison, the receptors for Opioids are first found at the origin of jawed vertebrates, a mere 450,000,000 years ago.

Before we go any further a personal caveat must be given. In my understanding of health and of CT, symptoms are not really the important feature to look at. So much of the popular literature on CT consists of lists of the PhytoCannabinoids with corresponding lists of diseases they can alleviate, help, cure, whatever. While these lists are helpful to a degree, they are not giving the understandings and tools necessary for a neophyte interested in using CT for their personal health issues. Freedom comes from a broad and comprehensive understanding. Really, what good is achieved by just naming everything? Cannabinoids are intrinsic in their action to bring balance back to the body, in a foundational, systemic way. We need to strive to be the same in our relation to Cannabis and health. Our actions need to come out of seeing the big picture and not just the end expressions.

Saying the above, modulating ECS activity has a therapeutic potential for almost all of the diseases effecting humans including obesity, metabolic syndrome, degenerative disorders, cardiovascular irregularities, liver, gastrointestinal, skin, cancer, psychiatric conditions, inflammatory conditions, neurologic conditions, analgesic or pain conditions, infectious conditions, actually (and it is hard to say this without smiling) everything under the sun. Which really says it functions on the very deepest, most core level of physiological activity.

Nearly all disease involves a dis-regulation of the ECS. It is that deepest entry into the physiology of our bodies. With the sensitive and aware use of this knowledge, and the willingness to make changes to support your ECS, amazing results are achievable.

The information on the ECS is still not getting into medical or nursing schools. Their curriculums still do not generally mention ECS. Physicians will often say they've heard positive stories about taking it, usually thinking THC, but it is not part of their practice and then an "I don't know" will follow. One of the real results of Schedule 1 drug classification is fear of consequences leading to inaction. It seems that more Osteopaths are open and educated in CT than MD's. But tragic to say, there are few professional health care professionals who are able to assist a person in need.

To even further muddy up the waters, though there has been an exponential growth in the scientific studies concerning the ECS over the last 20 years, yet there is still great disagreement on what it all means. A lack of clinical trials due to the ongoing Schedule #1 classification has made relevant research on people nearly impossible. All research has been crippled by political forces around the world. This has slowed our understanding of what this incredible frontier really holds as a healing tool.

Remember the story of the blind men coming up to an elephant. Each imagined the elephant in a different way. Pillar. Rope. Wall. Hand fan. None could see the entire picture. Each had their own take that was true from their limited perspective. This is where we are with the ECS, we are enamored by the symptoms and not looking at the thing in its whole self.

A question I keep asking myself, kind of like pinching myself, is how can a plant that has been with humans longer and used in more ways than any other plant, can be so fundamental to our health, can be taken from micro to macro dosing, can affect our bodies on such deep levels for regaining balance, and in addition have no real known or documented toxicity . . . actually exist? Kind of philosophical, but back to reaching to see the biggest picture.

The ECS has four components:

1) Receptors, the avenue for getting the message from the Cannabinoid, outside the cell, to inside the cell
2) Endocannabinoids, compounds that binds to and activates the receptors that are produced in the body
3) Enzymes that are involved in the synthesis and degradation of the Endocannabinoids
4) All the other ways that Endocannabinoids can affect the body

RECEPTORS

A receptor is a protein molecule that receives messaging signals from outside a cell and passes it into the interior of the cell to initiate a cellular response. Cannabinoid receptors are in the family of G-protein coupled receptors.

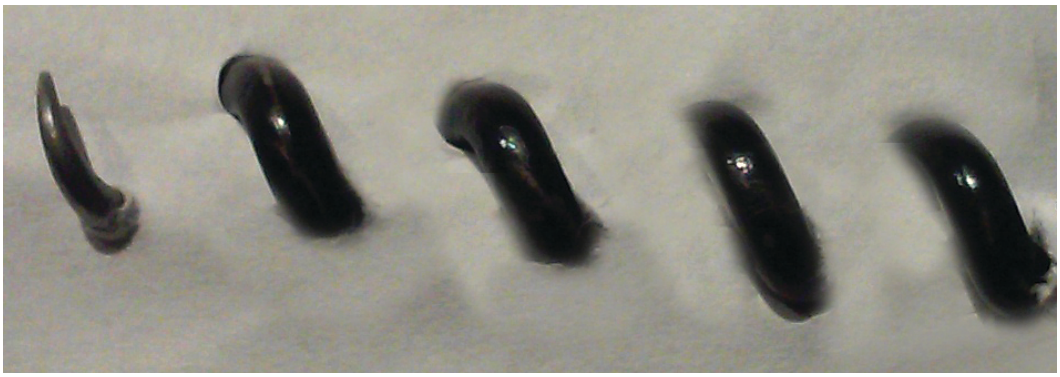
Cannabinoid receptors function as subtle sensing devices, tiny vibrating scanners perpetually primed to pick up biochemical cues that flow through fluids surrounding each cell.

Think of the receptor as a gate sitting on the surface of the cell. It is a locked pathway from outside the cell to inside. A specific key will open it so a bio chemical message or some other stimulate can be sent to the interior of the cell. This initiates the cell into some type of action.

The concept of receptors traces itself back to the early 1900's. The G-protein coupled receptor family represents the largest and most versatile group of cell surface receptors. Drugs active at these receptors have therapeutic actions across a wide range of human diseases. We still do not understand everything about how they work. It was not until around the 1980 that the mechanism of how they functioned was understood. Since 1992 eight Nobel Prizes have been awarded about work with these receptors. Approximately 1/3 to 1/2 of all pharmaceutical drugs available, and two largest selling drugs world wide all work through affecting G receptors

The Cannabinoid receptors are in the shape of a helix. Imagine it as a corkscrew that opens outside the cell and transports messenger molecules to inside the cell. But it does not go vertically through the cell wall into the

interior. Rather imagine looking at the lacing on a football. They weave in and out 6 times before opening up to the inside.



As a side, why in a helix form? And why so long a pathway for getting into the cell, the longest possible distance following the curving form of the helix? There are answers, though not in the science yet, but in the more imaginative realm of observing and listening to Nature.

When looking at a topological map of a river we always see the meandering pathway the river follows. Each unique, but always the same overall pattern. The same pattern we see when every water is flowing. What we are seeing is a two dimensional slice of a three dimensional helix form. Water always moves in this manner. It renews and enlivens itself in this sensitive chaos. Take the rhythm out, straighten the river, and it dies. Our receptors have taken the form most loved by Nature. The helix forms gives the greatest strength and allows the most encoding of information in the shortest length. Because of its circular path. This is why DNA is in this shape and the shape is continually repeated in our bodies. Following how the river flows. Following Nature's wisdom.

Imagine the CB receptors as mountain creeks. Taking these little packets of information on the longest possible circular distance on their journey from outside the cell depositing them inside. Enlivening, charging the message with each turn of the helix and having more time to gain access to the most information.

What other "listening" part of our body is in this curved return on itself shape? The Cochlea in the ear. Though here it is more a vortex than a helix, both giving the most surface area to receive information in the least space. Both avenues of communication within the body. It only makes sense.

What makes the ECS receptors from all other receptors is that most receptors have just one substance or impulse that will stimulate it, the usual single key and lock model, with only one key to unlock functionality to do one thing. The ECS receptors do the impossible. They allow multiple keys to open the same gate entering into multiple rooms initiating a wide array of responses. The permutation of what these receptors can initiate leads to the complexity of how they affect our bodies. Or we could say the system functions below the level of specific tasks and more in an oceanic environment where all is connected.

There are currently, I stress currently, two receptors that are known and studied. CB1 and CB2. CB stands for Cannabinoid.

CB1 is primarily found in the central nervous system, but also in a wide range of other places. The more we look the more we realize they are not limited to certain tissues, but are found all over and throughout the body. So really saying they are primarily found in the central nervous system is more an historical observation, for that is where they were first found.

CB1 is the most abundant G-protein coupled receptor in the central nervous system. There are more CB1 receptors in the brain than any other G-type. It has a major neuro-modulatatory function, A neuron is an electrically excitable cell that processes and transmits information through electrical and chemical signals. CB1's role has been characterized as "relax, eat, sleep, forget and protect."

CB2 has an immuno-modulatory function, which as the name refers, is about activating the immune functions. These receptors are found mainly in the peripheral nervous system, metabolic tissue and immune cells. It plays an important role in pain and inflammation.

But all of these descriptions and classifications are like looking at a flat model of a 4 dimensional landscape. We do not know enough and our descriptions fall short of a true picture.

CB2, originally thought to be mainly limited to immune cells, but now we see it is in other parts of the body. Density is high in the liver, spleen and connective tissues.

One of the really interesting things about CB2 is that tissues that don't typically have CB2 will begin to do so after they are injured or inflamed or stressed or in some way dis-regulated. That is part of the body's way to deal with that injury.

CB receptors are virtually absent in the brain stem cardiovascular centers. This is one of the facts that explains the lack of toxicity or overdosing when taking Cannabinoids. Because there are no receptors in the brain stem they do not suppress breathing or heart rate. Opioids do have receptors in this area and so can lead to overdose and death.

The body uses endogenous Cannabinoids, speaking through the receptors, calling our body into action at the cellular level.

ENDOCANNABINOIDS
Cannabinoids made by our bodies

EndoCannabinoids are fatty neuro transmitting or messaging molecules synthesized by our bodies as an adaptive response to cellular stress, aimed at reestablishing cellular homeostasis. Or . . . cannabinoids are the language our bodies use on the cellular level to communicate states of health or dis-ease and call the body to make changes. Their main pathway of affect is the Receptors, but that is only one of many strategies of action our body uses.

These are molecules our bodies make as part of this communication system. They are synthesized on demand from precursors in the cell membrane. The precursors are derivates of Omega 6 fatty acid. Built when needed, have their affect, and then are quickly degraded and the components recycled.

These are molecules released by a cell either to regulate that cell's own (autocrine) physiology to bring it back into balance, or to do so for one of its neighboring cells (paracrine).

They are the mechanism our bodies have developed and maintained over 600,000,000 years to communicate and correct imbalances. These imbalances can be within the cell or in the environment around the cells. This is done at a core level of cellular communication. Because it is so deep in our physiology, and has been present so long, a nearly magical complexity has developed through all the strategies used in its pursuit of its function in reestablishing homeostasis.

In 1992 the first Endocannabinoid was discovered. It was named Anandamide. It was named after the Sanskrit word for Bliss, Ananda. It fits into the CB1 receptor, like a lock and key.

Anandamide is also found in the Black Truffle.

2 AG, a second Endocannabinoid was discovered a few years later. 2AG is like THC in that it binds to both Receptors.

There are numerous other Endocannabinoids besides the two, we just know very little about them at this time.

PHYTOCANNABINOIDS

Cannabinoids made by plants, primarily the cannabis plant

THC: This is the one. Endlessly written about, whose presence in human history has ranged from god-like to devil-sent. Whose persecution for possession has led individuals to lifelong suffering and even death. And this all through millennia of human history.

THC mimics Anandamide and 2-AG by acting as a partial agonist at CB1 and CB2 Receptor sites. An agonist is a chemical that binds to a receptor and activates the receptor to produce a biological response. But, THC does not stimulate the receptors all the way. And because it is a partial agonist and not a full agonist, it can at times actually block function and act as an anti-agonist. Antagonism to the receptors, both, is more likely when the ECS is down-regulated, that is, not functioning correctly.

Too high a dose of THC can actually down regulate the ECS and loose efficacy. At a weekly habit of smoking more than 1/8 oz, research has shown that the Receptors become over stimulated and the cells have the good sense of pulling them inward, closing them off. Full benefit from the Cannabinoids is then not gained.

Endocannabinoids are hydrophobic molecules. They cannot travel unaided for long distances in the aqueous medium surrounding the cells from where they are released, and therefore act locally on nearby target cells. They have much more restricted spheres of influence than do hormones, which can affect cells throughout the body.

Over the last two decade or so substantial research has gone into the medical benefits and usage of CBD. Over the last decade the amount of suffering this Cannabinoid is responsible for alleviating, without a doubt, is truly astonishing. We've all heard personal testimonies and stories and probably each know someone who has been deeply helped through this Cannabinoid. The amount of research on CBD has also exponentially increased over the last decade.

It is often repeated that CBD is NOT psychoactive. This is not true. CBD does affect the psyche, mildly, generally not impairing perceptions or creating that "stoned" high feeling. It does not affect motor coordination as THC does. It will not get you to that stoned place. But it can change a mood and bring about a psychological shift that can be felt.

Unlike THC, CBD does not attach directly to any of the receptors, but instead indirectly activates EndoCannabinoid signaling by suppressing the enzyme fatty acid amide hydroxylase (FAAH). Say it now, "FAAH."

FAAH breaks down Anandamide, so the more FAAH you have, the less Anandamide there is in the body. Turns out CBD suppresses the production of FAAH, therefore allowing more Anandamide to be present and strengthening Endocannabinoid tone. The theory being that if you have a condition associated with low levels of Anandamide, taking CBD would return it to optimum levels, which in turn could improve the symptoms.

At this time in its history of research it is still not fully understood exactly how it works on the cellular level. That is, which mechanism is having the clinical affects. But its affects are widespread as are all the Cannabinoids. Very high doses have shown no problems. And it is also effective at very low doses, as low as 1 mg.

So saying all these things is really repeating what the research is showing and anecdotal stories. Always, Less is Better. Start low. Go slow.

CBD can modulate the effect of THC. That is, CBD can affect how the THC molecule attaches to a receptor. It says, this is enough stimulation. So the THC effect is turned down. It is an antidote for consuming extremely high levels of THC and getting to that "freaking out" zone.

It seems that lower doses can be more stimulating while higher doses tend to be sedating.

CBD and THC work well together. If use just CBD alone, it will take more mg of CBD than a mixture THC and CBD at a combined lesser amount.

CBD is not sedating, it is very stimulating molecule at low and moderate doses. It is true certain cannabis plants that have CBD in them will be sedating, but it's not because of the CBD. It is more likely due to the presence of Terpenes. Some researchers think that it is Myrcene causing the sedating, narcotic-type properties. Others think it is B-caryophylene.

There are many, many more PhytoCannabinoids that have been discovered in the Cannabis plant. To name a few: CBN, THCV, CBC, CBG. Most are present in very small amounts and most we still have not done the research to fully understand what they can do in the human body.

What we do know is that using Cannabinoid products that contain as full a range of Cannabinoids as the plant produces leads to the best results. This full spectrum has been titled the Entourage Effect.

One of the most exciting forms of the PhytoCannabinoids we are working with is the Acid Form. The Acid form is how the plant produces it.

Cannabis scientists had broadly classified the Cannabinoid molecule into 3 groupings. As with everything concerning Cannabis, nothing is hard and fast and no tight and rigid definition really will hold much water, but these family groups do have value to more easily understand the complexities of this molecule.

The Cannabis plant produces all of her Cannabinoid in the Acid Form. You know it's an acid nomenclature when the name ends with an "A". It starts as CBGA in the plant. The plant then converts this to THCA or CBDA or CBCA. It is a carboxylic acid. Through some sort of oxidation process, could be temperature or chemical, smoking, vaping and baking fits into this. Then the acid turns into CO2 and we have an alcohol grouping this is called the Netural Family. This is the molecule that we love. THC. Also all the others as CBD, CBG, etc.

Through further breakdown, either in Nature as age, light, oxidation, or in our body's process of breaking complex molecules down to simpler ones, generally done in the liver. These Cannabinoids are known as Metabolites. CBN is one of these metabolites that gives the headache when cannabis is smoked that has been kept too long but when formulated with THC can be beneficial for insomnia.

So far nearly all the research has gone into Neturals. Very little on the Acids.

A 1969 study showed no psychoactive effects from THCA were seen at high doses with monkeys. Same with mice. And dogs. Nothing has come along to disprove this.

We say that THCA is not psychoactive. With the caveat, "as far as we know." It does not turn into THC in the body.

THCA suppresses inflammation that is separate from CB1 or CB2 receptors. It seems that the acid of both THCA and CBDA inhibit Cox enzyme that

produces pain and inflammation. CBDA has been shown to be a very potent Cox inhibitor

Another THCA study showed that it represses nausea in rats. WARNING: this is net the kindest treatment of laboratory animals. They gave rats lithium chloride that produces the gagging reflux. They then measured how often they gagged. It took 5mg/kg of THC to suppress gagging. THCA repressed nausea at $1/10^{th}$ of that dose. .05mg/kg. When increased the THCA dose by 10 it did not get any better. In this model, THCA is 10X more powerful as an anti-emetic than THC.

In case your interested, Cannabis tea is usually 90% THCA and 10% THC.

Another study took dosage of CBDA form mg to micrograms. They started to see a different at .1 micrograms/kg. Significant reduction in gagging was found at .005mg/kg and also very good at .001. In fact no significant difference between the two dosages was found.

The only study on THCA and seizures that was performed in 1979 found efficacy at 200mg/kg. Dr. Sulak is seeing efficacy at .1mg/kg. This is all really amazing stuff.

This is an anecdotal story from Dr. Sulak, " A boy with seizures was treated at .3mg/per day THCA, seizures stopped. Nothing else helped him. Then tried .6mg/day and seizures recurred. Went back to .3 and has been 90% seizure free.

THCA also affects tumor necrosis factor alpha. This is an inflammatory signaling protein that is produced during acute inflammation and is responsible for a diverse range of signaling events within cells, leading to sudden and normal death of cells. The protein is also important for resistance to infection and cancers. Disregulation of TNF production has been implicated in a variety of human diseases including Alzheimer's disease, cancer, major depression, psoriasis, and inflammatory bowel disease (IBD).

There is an efficacy phase for THCA that is very low.

THCA is an insecticidal.

It is also a very strong anti-inflammatory.

THCA is ¼ as powerful as an anti-convulsant as CBD.

THCA is not broken down to THC in the body. It stays as THCA, though there are different forms of THCA.

ENZYMES RESPONSIBLE FOR SYNTHESIS AND DEGRADATION OF ENDOCANNABINOIDS

Endocannabinoids have a very short life. They are created when they are needed, on demand, exist for a short time and then are broken down.

One key enzyme in this process is FAAH. Fatty acid amide hydrolase. It breaks down cannabinoids.

The reason these enzymes are important is because depending on how much we have, this could be genetically based or environmentally based, this will determine the level of our own EndoCannabinoids. For example if we have too much FAAH, it will be breaking down Cannabinoids too quickly and we will have a low level of Cannabinoids. And so will have a low level functioning ECS. Which means a weakened constitution.

Interesting enough, one of CBD's mechanism for affecting the body is by causing a lowering in the amount of FAAH and so an increase in the available amount of EndoCannabinoids.

EVERYTHING ELSE

We still do not fully understand all the ways the ECS functions in its homeostasis responsibility and all the ways that we can assist and improve on these functions.

We do know that another molecule that the Cannabis plant produces, Terpenes, has significant effects. Terpenes, commonly known as essential oils, give nearly all plants their aroma and their healing qualities. They are the main factor that gives Cannabis all its many fragrant smells. However, the smell tells you nothing about how psychoactive the plant is.

In Cannabis plants terpenes work with the plant's Cannabinoids to accentuate or modulate its healing potentials. Plants high in Myrecene are generally better as a sleeping aid, think hops. Plants high in A-pinene help soothe the lungs, think pine needles. But these are all anecdotal reports. It is also believed by some that it is terpenes that cause what is said to be the "head" high of satvia strains and the "body" high of indica strains.

We do know the ECS can be affected by many things, including terpenes, herbs, diet, life style activities, even thought. This gives us great opportunities for many strategies to improve our health. More on this further down.

REPSONSIBILITIES AND FUNCTIONS OF THE ECS

I think that the real truth is, that we don't know enough to yet fully explain all it does and how it does it. Because the ECS is deeply rooted in our physiology, the more we look the more we see. There are endless lists of diseases that Cannabinoids can positively affect. Diseases it can cure. Symptoms in can rid us of. Most of these are still at the level of anecdotal stories. But as we move forward in our applying CT in is still a very uncharted land.

Because it affects everything it is a very special opportunity that must not be abused. CT's final goal is to bring health, not just bring relief from specific symptoms.

As you read these descriptions of activities think of them as aphorisms. Short bursts of information that are to be mulled over. Thought about and perhaps made into visual vignettes that allows one to, "see what is meant." This process of imaginative seeing has even more importance to us in our healing process, for the ECS is the access of thought into our biological processes.

PAIN

In the central nervous system EndoCannabinoids are used as retrograde messengers. This means that they can slow down or stop impulses being generated from nerve cells. When there is too much pain they can turn it down. You have an injury in your leg. Pain is signaled and the body responds to this. But the pain can continue beyond its function and become in itself a problem. The ECS can send a message that we've had enough. You, pain, are becoming bothersome and please slow down your messaging. The body talks to itself in its constant state of flux through the ECS. The language of the EndoCannabinoids is one of the functional ways that the Innate Wisdom of the Body uses to direct itself in actions to regain homeostasis.

One of the functional mechanisms used by the ECS to initiate change is called "Depolarization-induced suppression of Excitation". When an excited neuron is stimulated by glutamate, calcium is released into the post synaptic cell. This then stimulates the synthesis of cannabinoids, 2AG is released. It then goes across the synapse, interacts with the CB1 receptor there to close the presynaptic calcium channel and stop the release of more glutamate. Once initiated by some type of trauma, cells will stimulate cells near them and the excitation will grow. But 2AG tells the postsynaptic cells to slow down. This is enough excitation, it is time to stop. Calm down.

The same process can happen in an inhibitory synapse. Same model, but have GABA, when enough inhibition the post synaptic cell will use 2AG to communicate back to the presynaptic CB1 receptor to close that calcium channel and prevent any more release of GABA.

All Cannabinoids reduce Glutamate excitability, Reduce seizure activity

Descending Pain Inhibitory Pathway. Our brain sends a signal down to the rest of the body. It says you are sending too many pain signals to me. You need to slow down. In that pathway there are inhibitory inter neurons, these will reduce the effectiveness of this Descending pathway. Cannabis can prevent some of the activity of those inhibitory inter neurons. A triple negative that alleviates pain signal. An inhibitory system that is inhibited by inter neurons who are then inhibited by Cannabinoids. The net effect is that the brain is more able to send this message to slow down sending pain signals to the brain.

In a seizure there is a lot of glutamate released, it becomes toxic to the surrounding cells in the rest of the brain, leads to neuronal disfunction and

further seizure activity. Same thing in a stroke. When an area of the brain is injured or destroyed by a lack of oxygen, then those cells start releasing their contents, some of that is glutamate and that can become toxic to the cells surrounding that area, and that area can spread to surrounding areas over hours or even days. The Cannabinoids have been shown to stop the release of Glutamate and stop the spreading of that damage

Local effects at the site of an injury. Every time we sustain blunt trauma, an injury, cells release and if not in check will increase sensitivity and cause hyperalgesia, exaggerated response to pain.

The functioning of the ECS at the peripheral terminal of the pain nerve provides the first line of defense against pain.

Multiple different tissue types all speaking the same language, this Cannabinoid language, all for the purpose of responding to the injury, preventing peripheral sensitization to pain and helping to get the pain under control. We want pain we are injured, to take our hand off a hot stove, what we don't want is for that pain to persist after the dangerous event is over

The CB2 receptor itself can have direct activity on pain. They are found in human peripheral nerves after injury particularly in painful neuromas and in the central nervous system as well. So cells that generally do not express CB2 receptors can after injury develop them in order to protect themselves.

CB2 receptor agonists produce anti nociceptive pain (caused by damage to body tissue and usually described as a sharp, aching, or throbbing pain) effects.

NERVE

Cannabinoids can have a major affect on modulating Neural Plasticity. This is the pruning and sprouting, the densification, the comings and goings of dendrites and neural pathways amongst cells in the brain and the nervous system. Synaptic plasticity is the biological process by which specific patterns of synaptic activity result in changes in synaptic strength and is thought to contribute to learning and memory. It gives rise to every type of adaptive learning: recovering from a stroke and regaining function, the conscious act of gaining a new skill or getting better at a skill that you've done so many times (where you can go into autopilot mode because you have set up neural pathways through repetitive actions), central sensitization to pain (when pain itself modifies the way the central nervous system signals from long term firing, and you actually becomes more sensitive and gets more pain with less provocation), and deep seated fears. Get the picture? And this is only one small shot of all that is going on. Is the elephant a wall? Whatever it is, its level of functioning is at the cellular quantum level, where there is some leap in dimensionalities.

Here is a shocker. In 1999 the US Dept of Health and Human services applied for patent, granted in 2003, using Cannabinoids as anti oxidants and neural protectants. What we have here is a failure to communicate in the Body Politic. We have one branch of the government saying Cannabis is so dangerous and has absolutely no medical value, that you can not even use it under your doctors care, and then there is this other branch of the

government that has already claimed ownership of it, and are planning on in one way or another control the use of Cannabinoids for certain diseases such as recovering from a stroke, multiple sclerosis, Alzheimer, Parkinson's and more.

Cannabinoids can act as neuroprotective, That is protecting nerve cells against degeneration. They are also involved in the creation of new neural cells. Promotes neuroplasticity, the brain's ability to respond to trauma. Like after a stroke.

Both Anandamide and 2AG are produced by the nervous system upon chemical and mechanical trauma, head injury, stroke. Neurons will start producing Endocannabinoids to help them respond to that injury.

The anti-inflammatory, antioxidant, and antispasmodic properties of THC and cannabidiol in cannabis reduce the symptoms and slow the progression of multiple sclerosis. These properties also benefit patients with Huntington disease and amyotrophic lateral sclerosis. Dampening of glutamate excitotoxicity prevents epileptic attacks and limits infarct size post-stroke. Both AEA and 2-AG thwart Alzheimer disease by blocking microglial activation and β-amyloid plaque formation. They also prevent Parkinson disease symptoms by rebalancing neural activity in the striatum.

It has been shown to have a role in Autonomic Tone. Heart rate, breathing, organ function, those things our bodies do that we do not have to think about. In Sympathetic Nervous system there are CB1 receptors. Fight or flights. Will decrease norepinephrine release. Sympathetically mediated nervous pain is one of toughest types of pain to treat. Cannabis seems to dampen that.

Can modulate the HPA and HLA access, these are pathways by which the hypothalamus communicates with the rest of our body

Sympathetic nervous system is the rest and digest nervous system also and Cannbinoids can reduce elevated activity which is what we attribute the anti-emetic or anti nausea effects of Cannabis.

Vascular and Cardiac effects are also part of Autonomic Tone. Controlling blood pressure and heart rate. CB1 Receptors in the muscle tissue of the heart can cause bi-phasic effects in heart rate. There is an increase in heart rate and blood pressure followed by a lowering. In activation the CB1 causes the blood vessels to dilate that is cause of decreased blood pressure. There have been anti hyper tension effects documented, but seem to be greater in magnitude to people what have high blood pressure than if you have normal blood pressure.

It is a homeostatic system whose job it is to bring the body back into balance

STRESS

Cannabinoids are very key to stress response. After stress event and response, ECS turns down the thermostat, brings you back to normal, so the stress response just does not keep playing out.

But there are different types of stress that Cannabinoids use different strategies to bring back balance.

There is acute Stress, like when drinking alcohol, which is a poison, a toxic. it stresses the body. In studies with rats, give them alcohol and there is a spike in the signaling of the ECS, EndoCannabinoids can modulate this, to turn down the bodies' stress reaction and bring it back to normal.

With Chronic Stress it is just the opposite. It results in a lowering of the bass line Cannabinoid signaling. This makes you more vulnerable to disease for this is your first line defender. Chronic Stress deflates Endocannabinoid tone. Elevates cortisone levels that leads to inflammation. Hormonal imbalances. Cognitive impairment. Heightened blood sugar and susceptibility to disease. Not a healthy way to be. Again, Cannabinoids can modulate this. But always remember, this is just one part of the actions you can take to bring greater health. This is a good time to look at them all and see where you know you can bring changes that would be positive. The trick is they have to be changes you enjoy making. Not fighting with. Doing what you like in itself strengthens the ECS.

In particular the ECS really gets thrown out of whack by industrial toxins. Like PCBs. They are not water soluble toxins and are really, really unhealthy for us.

In heart attacks, even very small amounts of THC have been shown to protect the heart.

ECS has a lot of potential for pain. And probably what it is most used for. Activating this system, the ECS, can have anti pain effects in acute pain, persistent inflammatory pain, neuropathic pain. Due to multiple mechanisms of action in different parts of our nervous system and in our connective tissues.

It is everywhere.

INFLAMATION AND CONNECTIVE TISSUE

More than 4000 years ago, the Chinese physician Shen Nung recommended cannabis for rheumatic pains. More recently, patients with myofascial pain and arthritis are among those who most often use cannabis medicinally. Activation of CB2 suppresses proinflammatory cytokines (substances secreted by certain cells of the immune system) that have an effect on other cells) while increasing anti-inflammatory cytokines. Although THC has well-known anti-inflammatory properties, CBD also provides clinical improvement in arthritis via a cannabinoid receptor–independent mechanism. Many connective tissue related cells express CB1, CB2, and EndoCannabinoid metabolizing enzymes.

The endocannabinoid system also protects against Crohn disease—a TH1-mediated inflammatory bowel condition—and also perhaps ulcerative colitis.

SKELETAL SYSTEM

An "animal model" of osteoporosis, for example, was created in normal mice and in knockout mice lacking CB receptors. When a synthetic cannabinoid drug was given to both groups of osteoporatic mice, bone damage was mitigated in the normal mice but had no effect on rodents sans CB receptors —which means that CB receptors are instrumental in regulating bone density.

A German research team would later prove that CB2 receptor activation re-strains the formation of bone reabsorbing cells, known as osteoclasts, by down- regulating osteoclast precursors, thus tipping the balance in favor of osteoblasts, cells that facilitate bone formation.

There seems to be Endocannabinoid activity in Bone. Stimulating CB2 tends to decrease Osteoclass activities that are the processes that break down bones and increase Osteoblast activity that has a bone building effect, therefore offering a potential treatment option for osteoporosis. CB1 stimulation may help prevent scoliosis in children by turning off bone building in the restrictive way that leads to scoliosis. The EndoCannabinoid system is essential for the maintenance of normal bone mass.

EndoCannabinoids are very active in our remodeling process of skeletal system and in the process of breaking down and rebuilding our connective tissues. The efficacy of us being able to do this greatly affects our ability to move and function. They can prevent cartilage destruction by inhibiting inflammatory signals that are active in rheumatoid arthritis and Lyme's Disease. Decrease connective tissue inflammation and dampen the inflammatory component of hardening of the arteries. There is connective tissue on the inside of the blood vessels that are susceptible to injury and inflammation and by preventing or helping to repair that injury or inflammation we can reduce one of the underlying causes of heart disease.

Immune System

The ECS modulates the Immune System. They don't enhance or suppress bit modulate and the net overall result tends to be a decrease in inflammation.

The human immune system, an amazing physiological wonder, kicks on like a furnace when a fever is required to fry a virus or bacterial invader. And when the job is done, endocannabinoid signaling turns down the flame, cools the fever, and restores homeostasis. (Cannabinoids —endo, herbal, and synthetic— are anti-inflammatory; they literally cool the body.)

TUMORS

Neoplasm: Cannabinoids have been shown to inhibit tumor growth in multiple cell lines. Tells the cancer cells it is time to die. Much better way

than necrosis or killing the cell with chemotherapy drugs which kill the cell, but then releases its contents and becomes a toxic burden on the organism, that then needs to be detoxified. Suppresses new capillaries from growing to tumors to feed them. Interferes with migration and adhesion of cancer cells. Their effect is selective and does not seem to effect healthy cells. Not a single pathway, many different ways it affects and stops the spread of tumors.

Already has proven to be so beneficial in cancer treatment and recovery in many different ways.

Pain from cancer. 3 groups: Placebo, just THC, THC and CBD
10mg three times a day moderate dose
It took slightly more combined than just THC, but more combined reach the 30% pain reduction

Cannabinoids can be part of an effective treatment for cancer. For nausea and vomiting they can be calming. Help with insomnia. Help tolerate treatments so can help strengthen to deal with your healing. Very low likelihood of a drug interaction. Offer numerous benefits at end of life for people with terminal cancer. Can achieve most of these goals with low dose in most cases. Start cancer treatment with low dose. Get anxiety under control. Improve sleeping. Then depending on the cancer increase. In cases as these always be under the care of a suitable health care provider.

Anxiety is a huge part of all of human's suffering. Cannabinoids have been used for millennia to ease Anxiety.

Cannabinoids are involved in the cell cycle and the fate of the cell. Not just in cancer, but also during embryology.

EMBRYOLOGY

For EndoCannabinoid receptors to survive 600 million years, they must serve evolutionarily important functions. The CB1 receptors have been detected in mouse embryos as early as the second day of gestation. The implantation of the Blastocyst, a small group of cells that find their way to the endometrium and implant themselves, starting to receive nutrients from the inner lining of the womb, and become the developing embryo requires suitable levels of Anandamide. So this first suckling function, nutritive experience, requires suitable presence of Anandamide. This is the first nutrition received.

Blastocysts express CB1, CB2, and FAAH. In fact, the EndoCannabinoid system organizes a broad array of developmental processes in the embryonic brain. Proliferation and differentiation of neural stem cells are shaped by extracellular cues provided by EndoCannabinoids. Once stem cells commit to neuronogenesis, EndoCannabinoids regulate neuronal migration and synaptogenesis. Also, axon guidance is shaped by axon growth cones, and EndoCannabinoids are part of the molecular "soup" that guides growth cones to their destinations as the brain develops and complexifies.

Adult neurogenesis is regulated by many of these "embryonic" mechanisms and primarily arises in neural stem cells within the subependymal layer lining the cerebral ventricles and the dentate gyrus of the hippocampus. Neural stem cells in both of these brain regions express CB1, and neurogenesis by these cells is driven by the EndoCannabinoid system.

DIGESTIVE SYSTEM

The ECS is active in the Digestive System. CB1 receptors are in our digestive track and interacts with the central nervous system. The health of the gut affects the health of the brain. CB1 receptors inhibit gastric acid secretion. Relaxes the lower esophageal sphincter. Alters intestinal motility, visceral pain and inflammation. Delays gastric emptying. By slowing activity, persistalsis, and less acid, it can reduce nausea. Opiate addicts (slows activity) are not nauseous until they withdraw from the opiates

CB2 also found in digestive system, more the immune components. Inhibits inflammation, visceral pain.

There are an expression of receptors and EndoCannbinoids in the liver and the enzymes to degrade EndoCannabinoids. The liver is using Endocannabinoids to regulate its function. Hepatic stimulation of CB1 can make scaring of liver worse. Leads to Cirrhosis. CB2 agonists counter acts the process of fibrosis, scaring of connective tissue. If have active liver disease use the smallest amount of cannabinoids to control your symptoms and lean much more heavily on CBD. CBD, not using either receptor can also alleviate liver scaring.

HUNGER AND FEEDING

Hunger is modulated by ECS. Breast milk contains Endocannabinoids. And thought can stimulate the hunger in the infant. New born mice that were given a CB1 blocker stopped suckling and died. EndoCannabinoids modulates all the other hormones of metabolism. Obesity can leads to the excessive production of EndoCannabinoids by the fat cells that can drive CB1 to a feed forward dysfunction. Their fat tissue may be producing more Cannabinoids than they actually need and this can desensitize and down regulate the CB1 receptor undermining the function of the ECS and creating a vicious cycle that will drive Metabolic Syndrome and more obesity. Some Cannabinoids may help prevent that affect.

Low and acute doses of THC can upregulate the ECS. Explains why often the first or first couple time a person tries cannabis they do not feel anything. It was second or third time that they experienced the THC effect. Perhaps they were expecting something else and were not keyed into the effects of THC. But more likely the acute dosage of THC actually caused an up regulation of the CB1 receptors. THC up regulates the ECS, increases the production of Endocannabinoids in brain cells.

But high and repeated doses down regulates the ECS. The CB1 receptors are pulled into the cells and no longer are available. Often experienced cannabis uses are using too much. Need to reduce dose to bring back more

of the therapeutic actions they've lost and actually enhance the efficacy of the cannabis, save money, get better results, less side effects,

Cells use CB1 receptors to tell itself it has had enough excitation. And this can happen in an inhibitory synapse.

Homeostatic function: if there is too much excitation or too much inhibition, cannabinoids can bring either scenario back to balance.

Cannabinoids in nervous system do a lot more than just balancing excitation. Involved in Neurogenesis, the birth and growth of new nerve cells.

The ECS also functions at a level where thought enters the body. This is really the quantum nature of living organisms. The basis to the Placebo Effect. How what we think and feel affects our biological physiology. They can also be effected by other substances and actions that we can take

Some questions to ask yourself, what is the diagnosis and what is the prognosis? Are you seeking this is an adjunct to conventional treatments or as an alternative. Where is this decision coming from? Look within to determine what goals are. How comfortable are you with death? This is metaphoric to the disease happening. A cell that will not confront its death is cancer.

The protocol that Dr. Sulak follows for the Elder is to always start with a very low dose. That is 1mg per day. Then increase till something is felt. Not that all is better. But you should feel something. Stay with that dose. Then do it for 3 days 3 times a day. Then increase till find dose that has therapeutic effects being looked for. Or go to high and have mild side effects and come back down again.

Start low, go slow but don't be afraid to go all the way.

CANNABINOID-OPIOID SYNERGY

This is one of the greatest potential for health benefit. Cannabinoids potentiates or enhance the pain relief that the Opioids give. Can decrease dosage. Not just an additive effect, but by a power, 30 plus 30 equals 100. Morphine alone 30% reduction in pain. THC alone 30% reduction. When combined in same amounts gave 100% reduction. This is with rat tail flick test.

People combine Cannabinoids with Opioids the pain relief felt is much greater. While it lowers dose to get pain relief, dose not lower the lethal dose, so less chance of OD because need to use less to get results. So creates better safety profile for the Opioids with wider safety window.

Retention of efficacy. When use both of them actually have an up regulation in Opioid receptors. This is unheard of. Usually with extended use builds higher tolerance, this creates down regulation, so more is needed over time to get same effect.

CLINICAL ENDOCANNABINOID DEFICIENCY (CED)

In 2004 the term Clinical Endocannabinoid Deficiency (CED) was first use by Dr. Ethan Russo.

Russo doesn't just limit Clinical Endocannabinoid Deficiency to IBS, migraines and Fibromyalgia. He believes it could be at the root of may other conditions such as MS, Parkinson's, Huntington's disease, depression, neonatal failure to thrive, cystic fibrosis, causalgia, brachial plexopathy, phantom limb pain, infantile colic, glaucoma, dysmenorrhea, hyperemesis gravidarum, unexplained fetal wastage (repetitive miscarriages), post-traumatic stress disorder (PTSD) and bipolar disease

PTSD is considered to be an Endocannabinoid deficiency.

Certain diseases, migraine, fibromyalgia, irritable bowel syndrome, can be traced to low base line cannabinoid signaling

PTSD, Alzheimer, Alcoholism, Clinical Depression, all could be caused by CED

What causes CED? Can be genetically based. 1-2% of diseases can be directly connected to gene disorders. But more likely most disease is lifestyle oriented. Accumulated stress. Genes can direct proclivities toward specific disease but that has to be brought out by stress. Chemical stress. Life style stress.

So many neurodegenerative diseases are age related. As you get older. So many chronic diseases, as we age we are more prone to get them. The ECS gets worn out.

Tones down an excess. An excess can be too much or too little.

What we consider placebo effect is actually our ECS working, stimulated by thought. About 1/3 of medical conditions respond to placebo. You would think that the placebo effect would be consistent. Some people respond really well to placebo effect. Has to do with gene that controls the production of FAAH. At least part of it.

It is the cannabinoid receptors, especially in the brain, where the mind and the body meet.

All the different holistic disciplines, chiropractic, osteopathy, massage, acupuncture, diet, all working through the same mechanism, the cannabinoid receptors. Cannabis is not this other thing way out there. It is with us right down to our core.

Long term potentiation and long term depression of neuro pathways are mediated by cannabinoids.

The body uses endogenous Cannabinoids to stimulate the receptors.

DELIVERY METHODS

THROUGH THE LUNGS

Smoking cannabis-the most common method of application-is problematic. Smoking is very wasteful of THC. Research shows anywhere from 55% to 73% of Cannabinoids destroyed by heat of the flame, then about 15% of the THC is actually drawn into he lungs. Although smoking cannabis alone, without tobacco, has not been linked to the development of lung cancer, it does produce polyaromatic hydrocarbons, which are carcinogens. The body has to process them, which puts an unnecessary metabolic demand on the liver. Irritants in he smoke cause bronchitis.

There is also the real danger of inhaling toxic pesticide residue. In a test the pesticides Diazinon, Paclobutrazol, Bifenthrin, and Permethrin where applied to cannabis. Then when smoked through a bong (with and without filters) and a glass pipe, between 40 and 70% came through. Labs queried in California said that between 15 and 35% of their samples from growers and dispensaries had pesticide residues.

Bioavailability differs widely. To get any handle at all on dosage would have to talk about how many puffs

Varporization is preferable to smoking as a delivery system for cannabis, but it's not perfect. Still polyaromatic hydrocarbons.

THROUGH THE MOUTH

Edibles
Anything that goes through the stomach is going to loose a whole lot, up to 60% of Cannabinoids in the acidic environment of the stomach. In addition dosing is difficult for you do not know if the material was mixed well enough for even distribution of the Cannabinoids. But sweet edibles can be the preferred way to work with Seniors who may be fussy about drops but have no problem with a sweet treat. Edibles are generally more toward the Recreational market.

Tinctures
Tincture is a bit of incorrectly used term. By definition a tincture uses alcohol as the base. Starting with herbal medicinal remedies tinctures now include any liquid filler. Coconut oil is most common with Cannabis. Because Cannabinoid molecules are fat based, they are not soluble in water. So either alcohol or some oil needs to be used. Olive oil, sesame, even ghee. Glycerin, made from plant oils, is also used.

Generally tinctures are medicated from dropper bottles and then dosed in the drop. This is then sub lingual, or held under the tongue. The Cannabinoids can be directly absorbed through the mouth's under tongue tissue. This keeps the initial absorption out of the stomach, where stomach acids are very corrosive to the Cannabinoids and as much as 60% of the Cannabinoids are destroyed.

Tinctures under tongue bring quick results, not quite as quickly as smoking, but within 20 minutes or so.

Typically there are 20 drops to 1 ml. This generally equals 1 dropper full. In a 15 ml bottle there would be approximately 300 drops. But this is somewhat an approximation, depending on viscosity of the material, (an alcohol based tincture would have more drops, less volume per drop because it is less viscous, than a coconut oil tincture), temperature and the nature of the bulb on the dropper. Our experience shows that in a coconut oil tincture the number of drops in a bottle is more in the 400 drop range. But to know the amount of Cannabinoids you must know how many mg of Cannabinoids per bottle and the size of the bottle. Generally the bottle size is 15ml (1/2 oz) and it has either 300 mg or 200 mg of Cannabinoids. See Appendix 4 for Dosing Chart.

In comparing prices of different brands it is not dollar to dollar. Rather it is mg/$ to mg/$. So a 15ml bottle that has 300mg of cannabinoids and costs $60, the cost is $.20/mg. As compared to a 15ml bottle that has 200mg of cannabinoids and costs $50 where the cost is $.25/mg. The better buy is the $60 bottle with 300mg of Cannabinoids.

Oil

Pure oil is what comes directly out of the Extraction process. It is similar to honey in color and viscosity. It is usually sold in a syringe. Usually by the gram. It is usually 65-70% Cannabinoids by weight. That is as high a density that you will find naturally. It is the most cost effective way to get Cannabinoids. It is often used by individuals in a very Cannabinoid heavy regime of up and beyond a gram a day. But it is very sticky and harder to exactly dose. Best way to take it is on a rice paper, that you then toss it all down the gullet.

Capsules

Capsules are a very good way to get a known amount of Cannabinoids into your system. Each capsule will have a given amount of total Cannabinoids and know Formulation. Capsules usually start with 5 mg of cannabinoid. Most common is 10mg.

The problem with most capsules is the same as any Cannabinoid eaten. A great amount of the Cannabinoids, up to 60%, will be destroyed in the acidic environment of the stomach.

Delayed Release Capsules

These are capsules that have all he pluses of regular capsules, but in addition have the feature that they do not dissolve in the acidic environment of the stomach, but wait for the alkaline environment of the small intestines. The medication is delivered to the organ meant to handle absorption with a very high Cannabinoid density intact. Both the Bioavailability and Bioabsorption of the Cannabinoids are maximum.

UP THE BUTT: SUPPOSITORIES

Suppositories are more and more in the CT conversation with divided opinions. We feel that for getting the most cannabinoids to the abdominal region for issues as IBS, Crohn’s disesase, Prostate, for women, Endometriosis. Reports that all have greatly benefited with CT therapy and the use of suppositories.

DERMAL: QUITE HONESTLY I KNOW REALLY NOTHING ABOUT HOW EFFICACIOUS THEY ARE WITH CANNABINOIDS. YOU'LL NEED TO DO YOUR OWN RESEARCH HERE

DOSAGE

Dosing is a crucial issue therapeutically. 2.5mg of THC is a threshold dose. 5mg is usually effective and tolerated. 10mg is too much for many people

Because with Cannabis Therapy the dosage can vary so widely and affect each individual in very different ways, it is really impossible to dose, even for a trained provider.

But Cannabis is truly unlike other plants. The effective dosing range is from .15mg per day to 3g/ per day. With adults it does not seem that body weight makes all that much difference. There are so many variables. You don't see this range in else where in medicine and the body tolerates.

Monkeys survived 9 grams
In addition, Cannabinoids are unique medicine in that you can't just dose as you can with a pharmaceutical, That is, take x mg so many times a day, and this will be the result. There are huge individual variances. There is a real need for patient education to walk them through their experience of relating to this plant, this teacher, this healing herb, and finding out what is the optimum relation for each individual.

Following Dr. Sulak's Protocols, 1 mg at first is a perfect place to enter your CT.

But don't forget that many professional health care providers specializing in CT work with grams a day with great outcomes. If you have such a provider of course follow them. But as novice to CT and on ones own, this 1 mg/day minimum is a great place to start.

Here come some background informational musings.

Within this wide dosing range we have a non-linear dose response curves. This is typical for bi-phasic dose response. If you start with a low dose you can gradually increase the dose and see more and more benefit. Up to a certain point. And then above that point, people generally feel a decrease from the benefit or an increase in unwanted side effects if consuming THC. Diminishing returns. Somewhere in the middle is an optimum dose. And when find that optimum dose they are getting the most benefits with the least side effects and it is sustainable. They don't build tolerance. Don't need dose escalation over time. This optimum dose is different for each person, but there are some guidelines.

At very low doses they can get a benefit, but go up can lose that benefit and sometimes at very high doses can get that benefit back. But at the very high doses the symptoms reduced was not as great as in tiny low doses. Plus at the high dosage there is the emergence of a side effect. Catalepsy. Staying still for a long time.

In comparison tests with European pharmaceutical anti-psychotic drugs both performed about the same. The big difference, there were way less side effects with the CBD medicinal.

CBD has been studied in social anxiety disorder and has been shown to have benefit.

Lots of research needs to be done to understand how it can help and optimum dose in mental health world.

The placebo effect is dependent on the ECS. A very profound thought. If it is actually true, this is a singular junction between mind, molecule, and body.

In regimes a little THC with CBD brings greater efficacy at lower doses.

Really surprisingly good results can happen at very low dosages.

When we go beyond the optimum dose people build tolerance. The receptors are getting overwhelmed and the cell decides to pull them inside and make them unavailable for further stimulation.

A wonderful phenomena that happens with THC, or a mix THC/CBD: the widening of the therapeutic window. It is the space between the lowest effective dose and the dose that is going to cause intolerable side effects. For someone new to it, especially with THC, if they do a little

Build tolerance to the adverse effects faster that the beneficial effects.

For beginners, by starting with a very low dose and slowly building up to their optimum dose, they stop being naïve and the adverse effects take even higher dose, as build tolerance to the adverse effects.

As you should expect by now, the dosage for CT is all over the playing field. Not only in the amount, and results, but in that effects differently at different dosages and differently over time. Truly a Zen Koan of the most original kind. What is what it is not except when it may be.

Bi-directional effects, very common in Cannabis. Experiencing the opposite effect. The same medicine can cause opposite results if different people. Anxious people are likely to become less anxious while the less anxious people are more likely to become anxious when given THC. Same with appetite suppression. The same material causes opposite responses in the same person with the same or different doses. Depending on the environment. Relaxing environment, more likely relaxing. Stressful environment, more likely stressful.

Combining CBD with THC will temper some of the bi-directional effects. Will mitigate some of the unpleasant effects, toxification, while accentuating the analgesic, anti-nausea, and anti cancer

CBD can change affinity of the CB1 receptor for THC, but that is not all it is doing. It is antagonizing receptors, agonizing others, preventing uptake of neural transmitters. More neural transmitter activity for the brain.

THC works on both CB1 and CB2. CBD rarely does anything to either of them. Is an inverse agonist or is an antagonist. Does not fully block CB1 or CB2 but it does decrease their activity.

Use Cannabinoids to promote balance in the nervous system then we can help many things as the over use of pharmaceutical drugs to alter brain activity to get rid of pain and fears.

POINTS OF MIS OR INCORRECT UNDERSTANDINGS

The conversation is CBD is not psychoactive. It is not that CBD is not psychoactive; rather it is more psycho deactivating. It is psychoactive, just in a less and more subtle way than THC. It generally does not lead to inebriation. It is not motor skill disrupting. But it can be mood altering.

Calling Cannabis or Cannabis products Organic. Untill Cannabis is moved from its DEA #1 classification; Organic certification cannot be given out. When any company states this, ask them how. There are smaller, usual region entities that give a certification for certain growing practices. Usually in sync with the FDA in their Organic Certification laws. It has not shown itself to be like the Chinese herbal import issue of poor and even dangerous levels of toxins. But it is a young industry without yet all the standards and proof of standards it needs to be following.

Cannabis/marijuana nomenclature. The DEA calls in Marihuana. Marijuana is a racist term that has all kinds of baggage in its meaning. Should be dropped. This is Cannabis. And Cannabis Therapy. (Please see Appendix 1, 1937 for more on this.) The term pot also is based on a Mexican slang phrase, again racist connotations)

You'll hear a lot about sativas and indicas, most of which is nonsense, because even the taxonomists can't agree. Taxonomists are the people who define what species is what in botany and they are constantly changing their minds. There's no uniformity of opinion at all. The prevailing notion is the Cannabis is one species with varieties. Three basic types, Type 1 is a high THC plant. Type 2 is a mixed THC and CBD, the way cannabis frequently was in the past. And Type 3 is a CBD predominant.

Some consider what really distinguishes one Cannabis variety from another is their Terpene content.

STRENGTHENING THE ECS

Herbal Medicines have ECS activity

Cannabis, Echinacea, and other plant products that stimulate resistance to infection and fatigue have been described as "adaptogens"—natural products that work "osteopathically" by enhancing health rather than fighting disease. The alkylamides in *Echinacea* potently agonize CB2 and

stimulate phagocytosis. The lack of psychoactivity caused by *Echinacea* can be attributed to the relative lack of CB2 in the brain.

Cumin (tumeric)
Copal incense, beta caryphyilinene (black pepper) is a CB2 agonist

Caring for your ECS. Exercise that you enjoy. Medium and high intense that is voluntary.
Social Play.
Electro-acupuncture CB2.
Manipulation and bodywork.

Good feeling after work out is not endorphin but ECS.

Diet is a life long exploration. You should experiment, change, re assess over time. Always pay attention to what your body is telling you. It is your best source for what to do.

Cease: sugary drinks, processed foods, corporate made foods, eating out
Decrease: meats, dairy products
Increase: fruits, vegetables, grains, fresh water.

Generally speaking good health comes from the simples actions we take daily to consciously improve ourselves. Hard to say, but the greatest contributor to long life and good health is . . . LUCK. Yup. You know, you could cross the street tonight and be hit by a truck and it ruins you health but is just plain old bad luck.

Saying that, in maintaining optimum health, each and every day we consciously do the healthy things for ourselves, this positions us in the best place to meet whatever the vicissitudes life throws our way.

This information has been gleaned from lectures of primarily Dr Dustin Sulak and Martin Lee. To this has been added my research and years pursuing good health. None of this narrative is meant for the diagnosing or treating diseases. It is for informational use only for opening the Imaginative Eye. Remember, "Pay Attention"

Excellent information website:

Society of Cannabis Clinicians http://cannabisclinicians.org

O'shaughnessey's on Line http://www.beyondthc.com

One of the best overviews available
The Endocannabinoid System: an Osteopathic Perspective
By Dr. John McPartland
http://jaoa.org/article.aspx?articleid=2093607

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APPENDIX 1: HISTORICAL PERSPECTIVE

No plant has had a longer and more complex relation with humans than Cannabis. Of any plant, cannabis has most cradled humans within a symbiotic relation of supplying whatever was needed at that time: food, shelter, clothing, writing materials and healing compounds, to name a few. Just to be able to be around us and for us to transport and propagate her to all corners of the planet.

In 1977 Carl Sagan proposed that cannabis may have been the world's first agricultural crop, leading to the development of civilization itself. He said, "It would be wryly interesting if in human history the cultivation of marijuana led generally to the invention of agriculture, and thereby to civilization."

More so, its use as rope made possible exploration of the world from antiquity, from horse to wagon and to sailing ship. The history of human exploration and development would be very much different without the cannabis plant.

The plant is indigenous to central Asia and the Indian subcontinent. It is currently, with studies based on DNA sequencing, considered in the same family as stinging nettle and hops.

How far back do you know of the Cannabis story? Here is a brief retelling from present day back, with an amazing start date at the beginning.

2016: Cannabis usage is legalized in California

2016: 7,296 citations in PubMed.gov search for “Endocannabinoid”

2013: Dr. Sanja Gupta brings the efficacy of medical cannabis to the American public.

2002: The classification family Cannabaceae is created which hemp and hops both belong in. This is in the order Rosales or the rose plant.

1999: US National Institute of Health files for patent titled “Cannabinoids as antioxidants and neuroprotectants.” Granted 2003

1996: The Compassionate Care Act is passed in California making cannabis available to the general public for medicinal usage.

1993: 10 citations in PubMed.gov search for “Endocannabinoid”

1992: The first Endocannabinoid is discovered. Anandamide

1988: Scientists funded by the US government discover the CB1 receptor. CB stands for cannabinoid.

1964: THC isolated (questionable, may have been 1942)

1942: CBD and THC isolated

1942: Experiments by US government on cannabis oil infused cigarettes as a truth serum.

1937: Cannabis becomes a banned substance in the US with claim it has no medicinal value.

So why was Cannabis, that had a long history of medicinal value, banned so quickly? Conspiracy theorists have a field day here. Consider these factors: (1) the ending of Prohibition and the need to vilify some other substance and keep the policing engines turning, (2) racism (Mexican immigrants, black Jazz musicians) (3) the greed of rising modern monopolistic cataclysmic capitalism that infected the medical industry and (4) a few greatly misinformed but committed zealots for the ban. This led to a whole lot of tragic trials, troubles and tribulations for millions of individuals caught up in the drug wars and witch hunts that resulted.

Why Cannabis and not Marijuana or Marihuana (name used by DEA)? In a mere years a medicinal that had been used in this country for centuries suddenly had to become stigmatized, vilified, iand neutralized. To do this they had to change the name so all the positive association would end. The perfect change was Marijuana. A name from another language and culture that could be associated with addiction, immigrants, low life. Sound familiar? Overnight what once was, was no longer and what now is, is really bad. Which goes to prove that a name is more than a name.

Even the nickname Pot comes from the Spanish word Potiguaya, which means Marijuana Leaves. It's a Mexican-Spanish word that is a contraction of ***potación de guaya****, which referred to an alcoholic drink made of marijuana leaves soaked in Brandy or Wine.*

1850-1915: Cannabis is widely used throughout the United States as a medicinal tincture. It could be purchased in apothecary shops and general stores. During this time most of our now major brands of pharmaceuticals had medicinal tinctures with Cannabis as the key ingredient. This included Pfizer, Eli Lilly, Squibb, Merck, Upjohn, Abbott, and more.

1850: Cannabis is added to The U.S. Pharmacopoeia

1764: Medical Cannabis appears in The New England Dispensatory

1606-1632 French and British cultivate Cannabis for hemp at their colonies in Port Royal (1606), Virginia (1611), and Plymouth (1632).

1545: Cannabis spreads to the western hemisphere when Spaniards imported it to Chile for its use as fiber

1171-1341 During the Ayyubid dynasty of Egypt, Cannabis is introduced by mystic devotees from Syria.

950: Cannabis seeds found in remains of Viking ships

500-600: The Jewish Talmud mentions the euphoriant properties of Cannabis.

130-200 Greek physician Galen prescribes medical marijuana.

70: Dioscorides, a physician in Nero's army, lists medical cannabis in his Pharmacopoeia.

23-79 Pliny the Elder's The Natural History mentions hemp rope and marijuana's analgesic effects.

440 BCE: The oldest written record of cannabis usage in the West is the Greek historian Herodotus's reference to the central Eurasian Scythians taking cannabis steam baths. His (c. 440 BCE) *Histories* records, "The Scythians, as I said, take some of this hemp-seed [presumably, flowers], and, creeping under the felt coverings, throw it upon the red-hot stones; immediately it smokes, and gives out such a vapour as no Grecian vapour-bath can exceed; the Scyths, delighted, shout for joy."

700-600 BCE: The Zoroastrian Zendavesta, an ancient Persian religious text of several hundred volumes, refers to bhang as the "good narcotic."

2,737 BCE: First recorded use as medicine by Emperor Shen Neng of China

4,000 BCE: Cannabis textiles used in China and Turkestan

6,000 BCE Cannabis seeds and oil used as food by Chinese

10,000 BCE: Hemp cord found in pottery in present day Taiwan

27,000 BCE: Hemp rope found in Czechoslovakia, making it the oldest known object to be associated with cannabis.

100,000 BCE: Anecdotal stories that horn pipes and ashes of cannabis have been found in caves.

34,000,000 BCE: The Cannabis plant evolved as a distinct species

NOW THIS IS WHERE IT REALLY BECOMES REVELATORY

600,000,000 BCE: The Sea Squirt has Cannabinoid Receptors, discovered through gene sequencing in 2004.

Let this sink in, SIX HUNDRED MILLION YEARS AGO animals had an Endocannabinoid System. SIX HUNDRED MILLION YEARS AGO.

The ECS developed very early in animal evolution. Whatever functional role it took on initially we do not know, but the function was important enough that as complexity of life developed, moving to vertebrates and mammals and man, the system became the fundamental way that the living body could maintain itself in healthy balance, in homeostasis, to an ever changing and invasive environment.

Its functions are foundational, it does not have a singular, specific way it affects the body. It was in the body before that specialization developed. So it almost acts as a magical panacea, a true elixir, or as the Philosopher’s Stone, doing whatever is needed at that moment to bring the body back to balance. It is truly an amazing way the body responds to perturbations. This is a fundamental biological, cellular system that we had no idea about, no idea at all, till recently. Its total function and value is still not fully understood. It is not taught in medical schools. In the future it will alleviate suffering and return health as no substance ever has.

This is a 6-day protocol for individuals who are over medicating. It is designed to allow them to come back from over usage to a daily regime that gives the optimum benefits with minimum dosage from their Cannabinoid intake.

It is recommended if smoking more than 1/8 oz per week. Or patients who feel they have built a tolerance to Cannabis. And anyone who seems out of balance in their relationship to Cannabis.

Heavy Cannabis users have less CB1 activity. They have stopped getting the maximum benefit. With over stimulation the receptors are drawn back into the cell and cease functioning. After 2 days of cannabis cessation CB1 activity returns.

All drugs, substances put into our bodies from outside to create some change, have a danger of interfering and stunting our WILL. The inner strength we depend on for the greatest freedom in our lives. Following a regime as this helps to build our will and positively effects all aspects of how we move in our lives. It can help us become more sensitive to Nature.

Results are decreased consumption. Improved benefits with less side effects. Especially less fatigue. Saves money. And following the protocol develops new self-awareness pathways.

Smoking is the least efficient way to use Cannabis. 60 to 70% of the Cannabinoids are destroyed in the combustion. Though Cannabis has not been found to be carcinogenic, as tobacco, it is an irritant to the lungs and has other negative health effects. It is also impossible to accurately dose. For maximum benefit knowing dosage is crucial.

Try moving to a tincture. When held under the tongue the effects are nearly as quick as smoking, dosing can be exact. And it does not have the negative side effects that comes with smoking.

Central to the process is taking the Inner Inventory. This is taking a moment, closing your eyes and looking inside. Asking your self, “How am I feeling?” Going through, from top to bottom, inside to out, and really checking in. What feels good? What is in pain? What part of my inner being is speaking to me? What is it saying? What do I need to change? Stay with this for 1-5 minutes each time.

Just doing this makes most people feel better. When you reach something that is hurting, that feels out of sorts, try giving it an Inner Smile. This practice strengthens the placebo effect, or how our thoughts affect our bodies. Turning into your inner world, which is incredibly rich, helps us feel more connected, feel better. Doing this

several times a day, you'll emerge from the program with more self-awareness.

Keep a journal during this time. Each time you take the Inner Inventory write down your experience. This will prove to be invaluable.

Day 1 and 2: Absence days. Days to work on yourself. Exercise, massage, walks in Nature, healthy food, enjoying friends, feeling gratitude. These are all activities that stimulate, in a very positive way, the EndoCannabinoid system. Whenever you have thoughts of needing to ingest Cannabis do the Inner Inventory.

Day 3 – 5: Reintroduce Cannabis to the minimum therapeutic effect. Take a puff, wait 5 minutes. Do Inner Inventory. If feel a change, that is it. If no change another take another puff. Wait 5 minutes. Do the Inner Inventory. If still no effect take one more puff. But that is all. Stop after three puffs.

If using tincture, a 1-1 THC–CBD ratio is a good place to start. If it is a 15ml bottle with total 300mg of Cannabinoids, then one drop will have 1 mg of Cannabinoids. Start with 5 drops. Wait 15-30 minutes. Do the Inner Inventory. If no affect 5 more drops. Again, wait 15-30 minutes. Do the Inner Inventory. If no effect one more time. But then that is all for the day.

Day 6: Start from the minimum dose from Day 5. Increase to what gives you the best feeling and relieves your symptoms. On the average this can reduce your ongoing optimum maintenance dose by more than 50%. And receive greater all around health benefits.

Remember. Try switching from inhalation to oral mucosa, drops under the tongue. Smoke less. Realize that excessive smoking can be a compulsive act and just chasing the symptoms. Not maximizing the healing potential available from this very special plant.

It is a spirit plant. If we respect it, it will respect us.
The goal is to feel great. Be healthy.

If under a physician's care,
ask first if a reduction in cannabis is right for you.

This article was based on protocol developed by Dr. Dustin Sulak www.healer.com

You Want me to Put That WHERE?

By Nicholas Fraleigh

This is a common reaction to the suggestion that cannabis can be used as a suppository. Rectal administrations (suppositories) have an unfairly bad reputation in North America, despite the diverse benefits they offer. This article aims to educate about the advantages associated with the rectal application of cannabis and provide a simple set of guidelines for the effective use of suppositories.

There are many advantages to the rectal administration of cannabis not afforded by other routes. Medicine may still be administered even if the oral route is impaired (e.g., due to vomiting, an injured jaw or throat, or gastrointestinal difficulties) or disallowed due to the oral intake restrictions that are frequently required both before and after surgery. Avoiding the gastrointestinal tract also prevents first-pass metabolism by the stomach and liver, which break down many different molecules into their constituent parts (including Δ9-tetrahydrocannabinol, otherwise known as THC), and allows the active constituents to reach the blood in much higher concentrations.

In the case of THC, the liver transforms around half of what is ingested into the significantly more psychoactive metabolite 11-Hydroxy-Δ9-tetrahydrocannabinol. While not harmful in and of itself and potentially of therapeutic benefit, this molecule causes much more intense cognitive effects than THC. Rectal administration not only avoids these effects, but also allows a much greater proportion of THC to eventually reach the blood stream. This increase in overall efficiency is also shown in the different levels of bioavailability that different administration routes afford, as seen in Fig. 1.

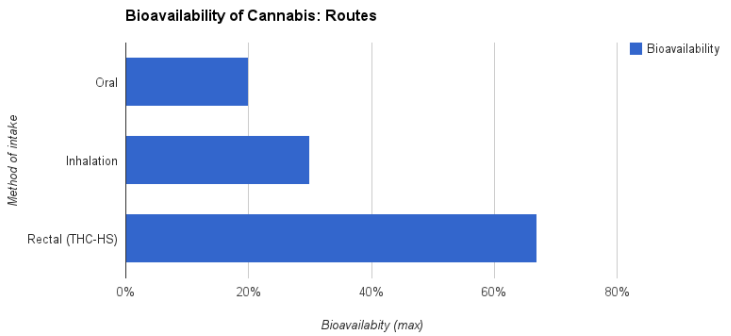


Fig. 1 – Comparative bioavailability of different administration routes

<u>Inhalation</u> : 10 – 25% efficiency, highly variable, depends largely on the individual's level of experience

<u>Oral</u> : around 20% efficiency, highly variable, even between doses within a single individual

<u>Rectal</u> : around 50% – 70% efficiency, with predictable effects even between different individuals

Due to the large surface area available for absorption, rectal administration provides the most effective way for your body to take in the medicinal compounds.

Rectal administration also allows for medicine to exert effects over localized ailments (e.g., hemorrhoidal tissue, inflammation of the rectum, or tumours in the rectal cavity). This form of use also has a much faster uptake than oral

administration (around 10 minutes, on average) and leads to more consistent blood concentrations of the active constituents. The speed and reliability of their uptake combined with their circumvention of many of the issues surrounding both ingestion and inhalation make rectal applications an excellent addition to both new and pre-existing therapeutic regimens.

When designing a personalized medication regimen, it is important to know the various timings involved with a given administration route. With suppositories, most people will begin to notice initial effects within the first 10 – 15 minutes after insertion. These effects usually last for between 4 – 8 hours, depending on the individual's physiology and tolerance to cannabis. This swift increase in effect allows for acute dosing in many cases, although this depends both on the situation and on specific individual needs.

There are several issues that can slow absorption from the rectum to the blood stream. Diarrhea and fecal matter can slow or prevent the active ingredients from reaching the rectal wall and being absorbed. Tumors or cysts on the rectal wall can also slow or prevent absorption. In this case, less medicine would reach the blood, but as the tumors are likely the intended target(s) of the suppository, the direct delivery of the active constituents may help prevent an overall reduction in efficacy.

Finally, rectal dehydration can drastically reduce the effectiveness of suppositories. Staying well hydrated by maintaining a healthy consumption of both water and electrolytes should prevent this in most cases, but specific medical conditions may cause it as well, in which case the solution may not be as simple. As always, if there are concerns, a medical professional should be consulted.

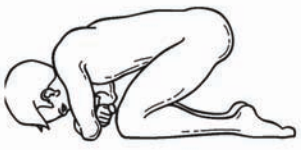
Anyone who decides to take advantage of the benefits provided by suppositories should do so with a good understanding of the process involved. Although not overly complex, the few simple instructions outlined below will enable their effective use.

The unique properties provided by the rectal administration of cannabis have the potential to empower many individuals. Suppositories can be used to refine existing therapeutic regimens to greater effect. Individuals who have been prevented from using cannabis due to an inability to administer via either inhalation or ingestion can potentially derive benefit from this wonderful plant for the first time.

Administration of Rectal Suppositories

1. Gently squeeze the suppository to determine if it is firm enough to insert. Chill a soft suppository by placing it in the refrigerator for a few minutes or by running it under cool running water.
2. Remove the suppository from its wrapping.
3. Dip the suppository for a few seconds in lukewarm water to soften the exterior.
4. Lie on your left side with knees bent or in the knee-to-chest position (see drawings A and B). Position A is best for self-administration of a suppository. Small children can be held in a crawling position.
5. Relax the buttock just before inserting the suppository to ease insertion. Gently insert the tapered end of the suppository high into the rectum. If the suppository slips out, it was not inserted past the anal sphincter (the muscle that keeps the rectum closed).
6. Continue to lie down for a few minutes and hold the buttocks together to allow the suppository to dissolve in the rectum. The parent/caregiver may have to gently hold a child's buttocks closed.
7. Remember that the medication is most effective when the bowel is empty. Try to avoid a bowel movement after insertion of the suppository for up to 1 hour so that the intended action can occur.

A



B

C

APPENDIX 4: DOSAGE PER DROP

Approximate MG/2 drops
300mg Cannabinoids/15ml bottle

Name Ratio	THC	CBD	THCA
Balanced 1:1	.5	.5	
Plentiful 10:1	.1	.9	
Abundant 20:1	.05	.95	
Robust 1:5	.8	.2	
THCA 1:5		.2 (CBDA)	.8
Evie's 20:1	.2	3.8	

HEALER

Introduction to Cannabis
4 Day Program — Tincture

- **Have a positive first experience with cannabis.**
  This program is designed to allow your body to become sensitive to cannabis and to ensure you achieve the optimal therapeutic benefits at the lowest effective dose. **With cannabis it is important to remember that less is more.**

- **Understand and determine the right cannabis dosage for you.**
  Using the correct dose of cannabis is the single most important factor in having a successful therapeutic relationship with cannabis. Unlike most medications, cannabis cannot be prescribed at a certain quantity and frequency based on body weight and age. This program helps you find your optimal cannabis dosage.

- **Prevent negative side effects.**
  For most patients, using less cannabis can provide superior medical benefits. Using too much cannabis will often decrease its effectiveness and increase the unwanted side effects. Our patients report that by using less cannabis they achieve maximum therapeutic benefits while having more energy, feeling more clear-headed, with little to no paranoia or anxiety.

Before you get started...

During these first few days, the goal is for you to begin to feel some of the therapeutic effects from cannabis. I know that you're excited to experience all that cannabis has to offer you. You're excited to get symptom relief or control of your condition - and you will be able to achieve these goals by following this procedure. Over the next four days, you are going to sensitize your body to cannabis, allowing you to use a much lower dose with greater efficacy, and maintain those great effects for the long run.

Using the correct dose of cannabis is the single most important factor in having a successful therapeutic relationship with cannabis. Unlike most medications, cannabis cannot be prescribed at a certain quantity and frequency based on body weight and age. We all have a unique internal chemistry, and the cannabinoid system is very complex, so different dosages will be best for different people. **With cannabis it is important to remember that for most people, less is more.** Many of the benefits of cannabis actually diminish with increased dosage, and very high doses can actually worsen the symptoms one might be trying to alleviate.

Thousands of patients have reported that when they first try cannabis at low to moderate doses, they do not feel any effects at all after the first 1-3 uses. Then, they suddenly begin responding to cannabis at the same dosage previously tried. Animal research gives us clues to understand this "sensitization" effect: THC can trigger production of more cannabinoid receptors[1], increase the sensitivity of existing cannabinoid receptors[2], and increase the production of the body's own endocannabinoids[3], at certain doses. On the other hand, high doses of THC have been shown to have the opposite effect, decreasing the number of available cannabinoid receptors.[4] By following this protocol, you can improve the tone of your endocannabinoid system, an integral component of our capacity to adapt to stress and restore balance at a cellular level. Not only will you achieve better results with cannabis, you will also enhance your capacity for self-healing.

Considering its broad therapeutic effects, cannabis is an incredibly safe medicine, with most side effects described as mild, perhaps bothersome, but rarely dangerous[5]. The most commonly reported side effects include changes in balance and fine-motor control, tiredness, anxiety, dry mouth, increased appetite, and short term memory loss. Luckily, when using this protocol, patients usually build tolerance to the negative side effects of cannabis within the first 3-5 days, while the positive effects continue to increase!

The most common cause of adverse effects experienced by new users can be found in the interface between the patient's state of consciousness (what they are thinking) and their surrounding environment[6]. You can prevent these side effects by paying attention to your mindset and surroundings before using low doses of cannabis.

Prior to administering cannabis, take 1-5 minutes to observe and evaluate your current Inner Inventory. While cannabis can help patients "turn the page" on stuck emotions and unhealthy thought patterns, it can also amplify these uncomfortable states. Patients often will not know which outcome to expect, and amplification of certain emotions or thoughts can be uncomfortable or distressing, though often therapeutic after these feelings are addressed with love and acceptance.

Taking time for pre-cannabis introspection will empower you to participate in your response to cannabis, and increase the likelihood of "turning the page" if that is what is needed. While 1-5 minutes does not sound like a long time, it will probably feel like a long time. Be intentional. Make a ritual out of your cannabis use. Notice how you feel, and think of what you hope to get out of this experience.

In addition to optimizing your sensitivity to cannabis, this program will empower you to develop simple and incredibly effective ways to improve your health and augment the power of cannabis. The Inner Inventory is a selfawareness tool that can be used to better integrate one's mind and body, assess the benefits of other health care activities, and take control of the neuroplastic forces unlocked by cannabis. Enjoyable exercises included in this program and specific foods, such as omega3 fatty acids and dark chocolate, have also been shown to enhance the endocannabinoid system.[7,8]

While performing this program I also recommend that you review my "Strategies to Use Cannabis Without Getting High" if that is one of your intentions.

IMPORTANT NOTE

*Use Caution. The goal is to use the minimal amount of cannabis to achieve the maximum benefits. If at any time you notice that you are developing tolerance to cannabis (needing a higher dose to get the same effect), then you have likely exceeded your optimal therapeutic dosage. I recommend you try our Sensitization Protocol. I advise patients to avoid smoking joints or eating edibles. Both of these methods predispose patients to inhale or ingest too much cannabis. Vaporizers and tinctures are preferred methods and allow patients to dose correctly with the right amount of cannabis.

- Dr. Dustin Sulak

Research supporting program:

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[2]Oviedo, Angelica, John Glowa, and Miles Herkenham. "Chronic cannabinoid administration alters cannabinoid receptor binding in rat brain: a quantitative autoradiographic study." Brain research 616.1 (1993): 293-302.

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[4]Hsieh, C., et al. "Internalization and recycling of the CB1 cannabinoid receptor." Journal of neurochemistry 73.2 (1999): 493-501.

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[6]"surrounding environment"
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Naliboff BD, Rickles WH, Cohen MJ, and Naimark RS (1976) Interactions of marijuana and induced stress: forearm blood flow, heart rate, and skin conductance. Psychophysiology 13:517–522.

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[8]Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. British Journal of Pharmacology. 2011;163(7):1344-1364. doi:10.1111/j.1476-5381.2011.01238.x.

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DAY 1 - Tincture

Your Introduction to Cannabis

Today, your goal is to **feel the slightest or minimal effect** from cannabis.

- Do not be concerned if you do not feel any effect today.
- During the next three (3) days, your body's sensitivity to cannabis will increase allowing you to experience therapeutic results.

STEP 1:

Check your "Starting Inner Inventory" before your administration of cannabis and write it down on the worksheet under Day 1.

Rate each using a scale of 1-10: (1 challenging and 10 easiest)
Breath: How easy and smooth is your breath?
Body: How comfortable and calm does your body feel? How easy is it to remain still and comfortable?
Mood: How easy is it for you to feel a sense of contentment and appreciation? How easy is it for you to smile right now?

STEP 2:

- **Take 1/2 of your recommended dosage (approx. 1-2 mg's)**
- **Wait 30-45 minutes.**
  - If you can feel any ***minimal effect*** from the administration and there is even **a slight change in your inner inventory, stop** and go about your day.
  - If you can feel ***absolutely* no effect, and found no change in your inner inventory,** then repeat the cycle.
    - Take another administration.
    - Wait 30-45 minutes.
    - Check your inner inventory.
    - Stop once you feel the slightest effect or change in your inner inventory.

***IMPORTANT NOTE: Listen to your body and don't over do it. Less cannabis is more.**
Limit yourself to only 1-3 administrations per session and remember to follow the process of only taking 1 administration, waiting 30-45 minutes, and checking your inner inventory to determine if there is a slight change.

Todays Focus:

- To only feel the slightest or minimal effect each time.
- Listen to your body and don't over do it.
- You may use cannabis, following this procedure **up to 3 times per day** based on your health and condition.
- Follow our recommended cannabinoid enhancing exercises, suggested foods, and drink water.

DAY 1

Goal: To feel only the slightest effect from cannabis

Date: _____

Remember to try the cannabinoid enhancing foods, exercises, and drink water regularly.

Session 1:	**Session 2:** (Optional)	**Session 3:** (Optional)
Starting Inner Inventory:	**Starting Inner Inventory:**	**Starting Inner Inventory:**
Breath Body Mood	Breath Body Mood	Breath Body Mood
Rate Each: 1-10	Rate Each: 1-10	Rate Each: 1-10
Start Time: _____	**Start Time:** _____	**Start Time:** _____
Take 1 administration Wait 30-45 minutes Check inner inventory	Take 1 administration Wait 30-45 minutes Check inner inventory	Take 1 administration Wait 30-45 minutes Check inner inventory
Stop: Slightest Effect	**Stop: Slightest Effect**	**Stop: Slightest Effect**
Post Inner Inventory:	**Post Inner Inventory:**	**Post Inner Inventory:**
Breath Body Mood	Breath Body Mood	Breath Body Mood
Rate Each: 1-10	Rate Each: 1-10	Rate Each: 1-10
*After 30-45 minutes, if you feel NO Effect, try eating an organic apple or other healthy snack, wait 10 minutes, take 1 additional administration	*After 30-45 minutes, if you feel NO Effect, try eating an organic apple or other healthy snack, wait 10 minutes, take 1 additional administration	*After 30-45 minutes, if you feel NO Effect, try eating an organic apple or other healthy snack, wait 10 minutes, take 1 additional administration
Perform up to 3 administrations. Wait 30-45 minutes in between.	Perform up to 3 administrations. Wait 30-45 minutes in between.	Perform up to 3 administrations. Wait 30-45 minutes in between.

DAY 2 - Tincture

Increasing Your Sensitivity to Cannabis

Today, your goal is to continue to feel the slightest or minimal effect from cannabis. You may notice more effects today as your body creates cannabinoid receptors and becomes more sensitive to cannabis.

- Check your inner inventory and write it down on the worksheet.
- Take 1 administration, wait 30-45 minutes, check inner inventory and write it down on the worksheet.
  - **Stop. If you can feel any *minimal effect*** or change in your inner inventory and go about your day.
  - **If you can feel *absolutely* no effect,** try eating an apple or other healthy snack, wait 10 minutes, if you still feel nothing, repeat the cycle.

***IMPORTANT NOTE: Less cannabis is more.**
Limit yourself to only 1-3 administrations per session and remember to follow the process of only taking 1 administration, waiting 30-45 minutes, and checking your inner inventory to determine if there is a slight change.

Todays Focus:

- To only feel the slightest or minimal effect each time.
- Listen to your body and don't over do it.
- You may use cannabis, following this procedure **up to 3 times per day** based on your health and condition.
- Follow our recommended cannabinoid enhancing exercises, suggested foods, and drink water.

DAY 2

Goal: To feel only the slightest effect from cannabis

Date: _____

Remember to try the cannabinoid enhancing foods, exercises, and drink water regularly.

Session 1:

Starting Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

Start Time: _____

Take 1 administration
Wait 30-45 minutes
Check inner inventory

Stop: Slightest Effect

Post Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

*After 30-45 minutes, if you feel NO Effect, try eating an organic apple or other healthy snack, wait 10 minutes, take 1 additional administration.

Perform up to 3 administrations. Wait 30-45 minutes in between.

Session 2: (Optional)

Starting Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

Start Time: _____

Take 1 administration
Wait 30-45 minutes
Check inner inventory

Stop: Slightest Effect

Post Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

*After 30-45 minutes, if you feel NO Effect, try eating an organic apple or other healthy snack, wait 10 minutes, take 1 additional administration.

Perform up to 3 administrations. Wait 30-45 minutes in between.

Session 3: (Optional)

Starting Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

Start Time: _____

Take 1 administration
Wait 30-45 minutes
Check inner inventory

Stop: Slightest Effect

Post Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

*After 30-45 minutes, if you feel NO Effect, try eating an organic apple or other healthy snack, wait 10 minutes, take 1 additional administration.

Perform up to 3 administrations. Wait 30-45 minutes in between.

DAY 3 - Tincture

Building More Cannabinoid Receptors

Your body is continuing to build more cannabinoid receptors. You are becoming sensitive to these small doses, you are feeling more confident in your control of cannabis use, and you are gaining an understanding of how cannabis affects you.

- Check your inner inventory and write it down on the worksheet.
- Take 1 administration, wait 30-45 minutes, check inner inventory and write it down on the worksheet.
  - **Stop. If you can feel any *minimal* effect** and go about your day.
  - **If you can feel *absolutely* no effect.** try eating an organic apple or other healthy snack, wait 10 minutes, if you still feel nothing then repeat the cycle.

***IMPORTANT NOTE: Less cannabis is more.** Limit yourself to only 1-3 administrations per session and remember to follow the process of only taking 1 administration, waiting 30-45 minutes, and checking your inner inventory to determine if there is a slight change.

Todays Focus:

- To only feel the slightest or minimal effect each time.
- Listen to your body and don't over do it.
- You may use cannabis, following this procedure **up to 3 times per day** based on your health and condition.
- Follow our recommended cannabinoid enhancing exercises, suggested foods, and drink water.

DAY 3

Goal: To feel only the slightest effect from cannabis

Date: _____

Remember to try the cannabinoid enhancing foods, exercises, and drink water regularly.

Session 1:	Session 2: (Optional)	Session 3: (Optional)
Starting Inner Inventory:	**Starting Inner Inventory:**	**Starting Inner Inventory:**
Breath Body Mood	Breath Body Mood	Breath Body Mood
Rate Each: 1-10	Rate Each: 1-10	Rate Each: 1-10
Start Time: _____	**Start Time:** _____	**Start Time:** _____
Take 1 administration Wait 30-45 minutes Check inner inventory	Take 1 administration Wait 30-45 minutes Check inner inventory	Take 1 administration Wait 30-45 minutes Check inner inventory
Stop: Slightest Effect	**Stop: Slightest Effect**	**Stop: Slightest Effect**
Post Inner Inventory:	**Post Inner Inventory:**	**Post Inner Inventory:**
Breath Body Mood	Breath Body Mood	Breath Body Mood
Rate Each: 1-10	Rate Each: 1-10	Rate Each: 1-10
*After 30-45 minutes, if you feel NO Effect, try eating an organic apple or other healthy snack, wait 10 minutes, take 1 additional administration.	*After 30-45 minutes, if you feel NO Effect, try eating an organic apple or other healthy snack, wait 10 minutes, take 1 additional administration.	*After 30-45 minutes, if you feel NO Effect, try eating an organic apple or other healthy snack, wait 10 minutes, take 1 additional administration.
Perform up to 3 administrations. Wait 30-45 minutes in between.	Perform up to 3 administrations. Wait 30-45 minutes in between.	Perform up to 3 administrations. Wait 30-45 minutes in between.

DAY 4 - Tincture

How to Find Your Therapeutic Dosage?

Today, you'll be using this procedure to increase the dose of cannabis, beyond the minimal effect, to the optimal effect. Think of the symptomatic relief you want to achieve using cannabis. Today you should experience that level of relief, using a very low dosage.

- Check your inner inventory and write it down on the worksheet.
- Take 1 administration, **wait 30-45 minutes,** check your inner inventory and record it on the worksheet.
- **If you do not feel the desired relief from your symptoms, you may increase your dosage by:**
  Repeating the process:
  - Take "1 administration", wait 30-45 minutes, check your inner inventory.

****Important Note:** 2 administrations will be administered in a 1 to 1.5 hour time period. 3 administrations will take 1.5 hours to 2 hours and 4 administrations will be completed over 2-2.5 hours.

Stop the process once you feel the optimal benefits (relief from your symptoms) and write the number of administrations required on the worksheet.

- **"How do I know when I reach the optimal dose?"**
  One of two things will occur:
  - You feel enough symptom relief that you are no longer limited by whatever was bothering you. Your session is over, mark down your findings and go enjoy your day!
  - You notice a decrease in your inner inventory 30-45 minutes after administration. This actually means that you have slightly exceeded your optimal dose. Don't worry if this happens, it's an important part of the learning process!

You have found your new **maximum dose for cannabis.**

- Use the next 2-3 sessions to confirm your dosage by repeating the process and waiting 30-45 minutes between administrations. Moving forward you do not have to wait the 30-45 minutes between each administration.
- I recommend you try taking one administration less than your maximum dosage to determine its effect. You can always take another administration if needed 45 minutes later.

IMPORTANT NOTE:
* Use Caution. The goal is to use the minimal amount of cannabis to achieve the maximum benefits.

If at any time you notice that you are developing tolerance to cannabis, (meaning you are needing a higher dose to get the same effect), then you have likely exceeded your optimal personal therapeutic dosage. I recommend you try our Sensitization Protocol. I advise patients to avoid smoking joints or using edibles because it predisposes them to use too much cannabis and build tolerance.

- Dr. Dustin Sulak

DAY 4

Goal: To discover the lowest therapeutic dose of cannabis you need to achieve the optimal benefits.

Date: _____

Remember to try the cannabinoid enhancing foods, exercises, and drink water regularly.

Session 1:

Starting Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

Start Time: _____

Take 1 administration
Wait 30-45 minutes
Check inner inventory

Stop: Optimal Effect

Track - Post Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

***Continue to take 1 additional administration, waiting 30-45 minutes and checking your inner inventory in between until you reach the Optimal Therapeutic Effect.**

Number of drops: _____

Session 1:

Starting Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

Start Time: _____

Take 1 administration
Wait 30-45 minutes
Check inner inventory

Stop: Optimal Effect

Track - Post Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

***Continue to take 1 additional administration, waiting 30-45 minutes and checking your inner inventory in between until you reach the Optimal Therapeutic Effect.**

Number of drops: _____

Session 1:

Starting Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

Start Time: _____

Take 1 administration
Wait 30-45 minutes
Check inner inventory

Stop: Optimal Effect

Track - Post Inner Inventory:

Breath	Body	Mood

Rate Each: 1-10

***Continue to take 1 additional administration, waiting 30-45 minutes and checking your inner inventory in between until you reach the Optimal Therapeutic Effect.**

Number of drops: _____

APPENDIX 6

The Discovery of the Endocannabinoid System
by Martin Lee

Up until the late 1980s, Cannabis research remained a rather esoteric field involving a small number of scientists in the United States and abroad. Their efforts were circumscribed by the politicized agenda of the National Institute of Drug Abuse, which subsidized studies designed to prove the deleterious effects of cannabis while blocking inquiry into its potential benefits.

Rather than discrediting cannabis, NIDA inadvertently facilitated a series of major discoveries about the workings of the human brain. These breakthroughs —among the most exciting developments in brain chemistry of our time— spawned a revolution in medical science and a profound understanding of health and healing.

"By using a plant that has been around for thousands of years, we discovered a new physiological system of immense importance," says Raphael Mechoulam, the dean of the transnational cannabinoid research community. "We wouldn't have been able to get there if we had not looked at the plant."

In the two decades following the identification and synthesis of THC by Mechoulam and his colleague Y. Gaoni in Israel in 1964, scientists learned a great deal about the pharmacology, biochemistry and clinical effects of cannabis. But no one really knew how it worked —what it actually did inside the brain on a molecular level to alter consciousness, stimulate appetite, dampen nausea, quell seizures, and relieve pain. No one understood how smoked marijuana could stop an asthma attack in seconds, not minutes. No one knew why it lifted one's mood.

When American researchers at Johns Hopkins University identified receptor sites in the brain capable of binding with opioids (such as morphine and heroin) in 1973, some scientists expected that the discovery of receptor sites for marijuana would soon follow. But 15 years would elapse before a U.S.-government- funded study at the St. Louis University School of Medicine determined that the mammalian brain has receptor sites — specialized protein molecules embedded in cell membranes— that respond pharmacologically to compounds in marijuana resin.

Initially identified by Allyn Howlett and William Devane, cannabinoid receptors turned out to be far more abundant in the brain than any other type of neurotransmitter receptor.

A potent THC analog synthesized by Pfizer (CP55,940) enabled researchers to radioactively tag and begin mapping the precise locations of cannabinoid receptors in the brain. Not surprisingly, they are concentrated in regions responsible for mental and physiological processes: the hippocampus (memory), cerebral cortex (higher cognition), the cerebellum (motor

coordination), the basal ganglia (movement), the hypothalamus (appetite), the amygdala (emotions) and elsewhere.

On July 18, 1990, at a meeting of the National Academy of Science's Institute of Medicine, Lisa Matsuda announced that she and her colleagues at the National Institute of Mental Health (NIMH) had achieved a major breakthrough — they had pinpointed the exact DNA sequence that encodes a THC-sensitive receptor in the rat's brain.

People have the same receptor, which consists of 472 amino acids strung together in a crumpled chain that squiggles back and forth across the cell membrane seven times. Cannabinoid receptors function as subtle sensing devices, tiny vibrating scanners perpetually primed to pick up biochemical cues that flow through fluids surrounding each cell.

Matsuda also disclosed that she had successfully cloned the cannabis receptor. This electrifying news was the curtain raiser for "the Decade of the Brain," as it was proclaimed at the National Academy of Science meeting. During the 1990s, there would be more advances in neuroscience than in all previous years combined.

The cloning of the cannabis receptor was crucial. It opened the door for scientists to sculpt molecules that "fit" these receptors like keys in a slot. Some keys —"agonists"— turned the receptor on others —"antagonists"— turned it off.

Scientists also developed genetically engineered "knockout" mice that lacked this receptor. When administered to knockout mice, THC had virtually no effect; the THC had nowhere to bind and hence could not trigger any activity. This was further proof that THC works by activating cannabinoid receptors in the brain and central nervous system. Finally, after 50 centuries of medicinal usage, the scientific basis of cannabis therapeutics was coming into focus.

Researchers soon identified a second type of cannabinoid receptor, dubbed "CB2," which is prevalent throughout the immune system and the peripheral nervous system. CB2 receptors are also present in the gut, spleen, liver, heart, kidneys, bones, blood vessels, lymph cells, endocrine glands and reproductive organs.

The CB1 receptor mediates psychoactivity. CB2 regulates immune response. Cannabis does so much and is such a versatile medicine because it acts everywhere, not just in the brain.

Just as the study of opium resulted in the discovery of endorphins, the brain's own morphine-like substance, so, too, marijuana research would lead to the discovery of a natural, internal, THC- like compound, our "inner cannabis," so to speak. In 1992, Raphael Mechoulam, in collaboration with NIMH research fellow William Devane and Dr. Lumir Hanus, found a novel neurotransmitter, a naturally-occurring "Endocannabinoid," which attaches to the same mammalian brain-cell receptors as THC. They decided to call it "anandamide," deriving from the Sanskrit word for bliss.[6]

In 1995, Mechoulam's group discovered a second major Endocannabinoid — 2-arachidonoylglycerol, or "2-AG" — that "locks on" to both the CB1 and CB2 receptors.

By tracing the metabolic pathways of THC, scientists stumbled upon a unique and hitherto unknown molecular signaling system that is involved in regulating a broad range of biological functions. Scientists call it "the Endocannabinoid System," after the plant that led to its detection. The name suggests that the plant came first, but in fact, as Dr. John McPartland has explained, this ancient, internal signal system started evolving over 600 million years ago (long before cannabis appeared) when the most complex life form was sponges.

Endocannabinoids and their receptors are present in fish, reptiles, earthworms, leeches, amphibians, birds and mammals —every animal except insects. Given its long evolutionary history, scientists surmised that the Endocannabinoid System must serve an important and basic function in animal physiology.

The effects of cannabis have drawn scientists to the still unfolding saga of the Endocannabinoid System, which has only recently begun to reveal its profound mysteries. Endocannabinoids and their receptors emerged as a hot topic among scientists who shared their findings in highly technical peer-reviewed journals and at annual conclaves hosted by the International Cannabinoid Research Society (ICRS). Formed in 1992, the society and many of its members (mainly university-connected scientists) were supported by U.S government research grants.

ICRS proceedings piqued the interest of big pharmaceutical firms. Drug company investigators paid close attention to cutting-edge developments in cannabinoid science, which few people outside the scientific community were privy to. Advances in the burgeoning field of cannabinoid studies would pave the way for new treatment strategies for various pathological conditions —cancer, diabetes, neuropathic pain, arthritis, osteoporosis, obesity, Alzheimer's, multiple sclerosis, depression and many other diseases that seemed beyond the reach of conventional cures.

CB1 and CB2 receptors recognize and respond to three kinds of cannabinoid agonists (turn-on keys): endogenous-fatty-acid Cannabinoids; Phytocannabinoids concentrated in the oily resin on the buds and leaves of the marijuana plant; and synthetic cannabinoids concocted in university and drug company laboratories.

For Big Pharma, cannabinoid research became a tale of knockout mice and men. Using genetically engineered rodents that lacked CB receptors, researchers were able to prove that cannabinoid compounds can alter disease progression and attenuate experimentally induced symptoms.

An "animal model" of osteoporosis, for example, was created in normal mice and in knockout mice lacking CB receptors. When a synthetic cannabinoid drug was given to both groups of osteoporatic mice, bone damage was mitigated in the normal mice but had no effect on rodents sans

CB receptors —which means that CB receptors are instrumental in regulating bone density

A German research team would later prove that CB2 receptor activation re- strains the formation of bone reabsorbing cells, known as osteoclasts, by down- regulating osteoclast precursors, thus tip- ping the balance in favor of osteoblasts, cells that facilitate bone formation.

Other experiments would establish that CB-receptor signaling modulates pain and analgesia, inflammation, appetite, gastro-intestinal motility, and sleep cycles, along with the ebb and flow of immune cells, hormones, and other mood-altering neurotransmitters such as serotonin, dopamine, and glutamate.

Glucose metabolism in every cell of the human body is regulated by the Endocannabinoid System. Formed "on demand" from fatty acid precursors in areas of need, Anandamide and 2-AG impact the organism in ways that are "predominantly local and specific," says Mechoulam. "Their actions are ubiquitous. They are involved in most physiological systems that have been investigated."

When tickled by THC or its endogenous cousins, cannabinoid receptors trigger a cascade of biochemical changes on a cellular level that puts the brakes on excessive physiological activity. Endocannabinoids are the only neurotransmitters that engage in "retrograde signaling," a form of intracellular communication that inhibits immune response, reduces inflammation, relaxes musculature, lowers blood pressure, dilates bronchial passages, and normalizes over stimulated nerves. Retrograde signaling serves as an inhibitory feedback mechanism that tells other neurotransmitters to cool it when they are firing too fast.

"Endocannabinoids are central players in life's multidimensional biochemical balancing act known as homeostasis," says biologist Robert Melamede, who describes the Endocannabinoid System as "the Ur-Regulator," the master modulator, which is constantly multitasking, adjusting and readjusting the complex network of molecular thermostats that control our physiological tempo.

The human immune system, an amazing physiological wonder, kicks on like a furnace when a fever is required to fry a virus or bacterial invader. And when the job is done, Endocannabinoid signaling turns down the flame, cools the fever, and restores homeostasis. (Cannabinoids —endo, herbal, and synthetic— are anti-inflammatory; they literally cool the body.)

But if the feedback loop is out of control, if the pilot light burns too high, if the immune system overreacts to chronic stress or mistakes one's body for a foreign object, then the stage is set for an autoimmune disease or an inflammatory disorder to develop.

Prior to the discovery of the Endocannabinoid System, retrograde signaling was known to occur only during the embryonic development of the brain and nervous system. Endocannabinoids choreograph "a broad array of developmental processes in the embryonic brain," as McPartland put it,

including neural stem cell proliferation and differentiation, a process guided by extracellular cues conveyed via CB receptors.

By the time the Decade of the Brain had run its course, scientists would learn that CB receptor signaling also regulates adult neurogenesis (brain cell growth) and stem cell migration.

High Endocannabinoid levels in the brain are triggered by strokes and other neurological insults —attesting to the neuroprotective properties of the Endocannabinoid System, which can be viewed as part of the body's "general protective network, working in conjunction with the immune system and various other physiological systems," according to Mechoulam. His Nobel-worthy discoveries posed a direct challenge to scientific orthodoxy by revealing that the brain has a natural repair kit, an in-built mechanism of protection and regeneration, which can mend damaged nerves and brain cells.

The discovery of the Endocannabinoid System has breathtaking implications for nearly every area of medicine, including reproductive biology. Dr. Mauro Maccarrone at the University of Teramo, Italy, describes the Endocannabinoid System as the "guardian angel" or "gatekeeper" of mammalian reproduction.

Endocannabinoid signaling figures decisively throughout the reproductive process —from spermatogenesis to fertilization, ovuductal transport of the zygote, embryo implantation, and fetal development. CB receptors proliferate in the placenta and facilitate neurochemical "cross-talk" between the embryo and the mother.

A misfiring of the Endocannabinoid System could result in serious problems, including ectopic pregnancy and miscarriage. (A deficiency of anandamide, the bliss molecule, can cause spontaneous abortions in mammals.) High levels of Endocannabinoids in maternal milk are critically important for the initiation of suckling in newborns. Infant colic has been attributed to a dearth of Endocannabinoids.

Israeli neuroscientist Ester Fride observed that knockout mice missing CB receptors resemble babies who suffer from "failure to thrive" syndrome. (Without CB receptors, mice wither and die prematurely.) This is one of many enigmatic conditions that may arise because of a dysfunctional Endocannabinoid System.

Endogenous cannabinoid deficiency could result from too few cannabinoid receptors or the insufficient presence of Anandamide and/or 2-AG. Individuals have different congenital Endocannabinoid levels and sensitivities.

Whether the result of poor diet, lack of exercise, drug abuse, environmental toxins or genetic factors, Endocannabinoid deficits are associated with a reduced ability or inability to adapt to chronic stress. Prolonged exposure to stress depletes Endocannabinoid tone, and this, in turn, has an adverse impact on a plethora of physiological processes. University of Washington neurologist Ethan Russo postulates that "clinical Endocannabinoid

deficiency" underlies migraines, fibromyalgia, irritable bowel disease, and a cluster of other degenerative conditions, which may respond favorably to cannabinoid therapies.

Ironically, the U.S. government's unending search for marijuana's harmful properties yielded astonishing scientific insights that validate the herb's therapeutic utility. By stimulating CB1 and CB2 receptor signaling, marijuana functions as a substitute "retrograde messenger" that mimics the way our bodies try to maintain balance. Cannabis is a unique, natural medicine that taps into how we work biologically on a very deep level. Thanks to this plant, scientists have been able to decipher the primordial language that nerves and brain cells use to communicate. From womb to tomb, across countless generations, the Endocannabinoid System guides and protects.

But a big disconnect existed between the world of science and the general public during the Decade of the Brain. Aside from certain segments of the scientific community, few people knew about the Endocannabinoid System. Doctors, journalists, public officials —hardly anyone was clued into the latest scientific research that went a long way toward explaining why marijuana is such a versatile remedy and why it is, by far, the world's most popular illicit substance.

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