HB3785 Testimony

By Nishi Whiteley
Curator of the medical cannabis website MyChronicRelief.com

I'm testifying in support of HB 3785.

Cannabis is a highly versatile herb that provides relief for many different ailments with a high degree of safety. There are few cannabis receptors in the part of the brain that control heartbeat or breathing (Donald Abrams 2009). This is why no one has died from its overconsumption – unlike the situation with opiates.

The reasons that cannabis benefits so many different ailments boils down to the fact that a class of chemicals produced in the cannabis plant - known as cannabinoids - mimic chemicals in the human body called endocannabinoids – or the cannabinoids within.

These endocannabinoids along with a series of enzymes and receptors throughout the body make up the Endocannabinoid system or the ECS, which serves as a primary biological harm reduction system tasked with bringing the body back into balance or homeostasis whenever it is challenged by stress, infection, injury or lifestyle.

It regulates, modulates or plays role in every major biological function of the human body including but not limited to:

- pain control
- mood
- immune function
- newborn suckling
- appetite reward
- temperature regulation
- memory
- inflammation regulation
- neuroprotection

(Marzo 1998)

The ECS is critical to human survival.

When it is no longer able to regulate itself, cannabinoids and other chemicals from the cannabis plant, when properly used, may help stimulate the ECS in a safe, therapeutic and non-toxic way.

The country's foremost expert in cannabis science, and my mentor is neurologist Dr. Ethan Russo. He explains in the document I am providing for you, that the ECS has a network of chemicals that when coupled together result in what is known as an *"entourage effect"* or a boosting effect that provides an enhancement for the management of pain, inflammation or other problem (Russo 2015).

The same is true for cannabis. The major and minor chemical components of the plant are vastly more therapeutic **together** than when isolated and together have fewer side-effects (John M. Mcpartland 2001).

It is for this reason that **whole-plant cannabis is almost always a more effective medicinal agent than a single isolated product** such as CBD-only products or the synthetic THC drug, Marinol® (Russo 2001).

Most pharmaceutical drugs are designed to address a primary problem and bring comfort. Cannabis is much more dynamic, stimulating the ECS to address many problems at once in multiple biological layers, not only bringing comfort but restoration in many cases. **And, its safety profile is superior to any modern pharmaceutical medicine – including aspirin.** We have more scientific data about cannabis than 95% of all FDA approved drugs (Carter 2014).

It is time that we bring science to the forefront of our cannabis policy and dissolve the cloud of shame, secrecy, and fear around the use of this potentially SAFE and legitimate medicine.

Please vote YES for HB 3785.

Carter, Gregory T. "Cannabis in the Management of Neuormuscular Disorders." *The Eighth National Conference on Cannabis Therapuetics - The Endocannabinoid System and Age-related Illness.* Portland: Patients Out of Time, 2014. NA.

Donald Abrams, Andrew Guzman. "Cannabinoids and Cancer." In *Integrative Oncology*, by Andrew Weil Donald Abrams, 147-170. New York: Oxford University Press, 2009.

Ethan B. Russo, Jo. "Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects." *British Journal of Pharmacology*, 2001: 1344-1364.

John M. Mcpartland, Ethan B. Russo. "Cannabis and Cannabis Extracts: Greater than the Sum of Their Parts?" *Journal of Cannabis Therapuetics*, 2001: 103-132.

Marzo, Vincenzo Di. "'Endocannabinoids' and other fatty acid derivatives with cannabimimetic properties: biochemistry and possible physiopathological relevance." *Biochemica et Biophysica*, 1998: 153-175.

Russo, Ethan B. *Introduction to the Endocannabinoid System.* subject overview, Los Angeles: PHYTECS, 2015.

Introduction to the Endocannabinoid System

Ethan Russo, MD

Medical Director, PHYTECS

The endocannabinoid system (ECS) is an essential regulator of bodily function in its many facets. There is hardly any physiological process that is not affected by it to some degree. It is surprising then to realize that the ECS was totally unknown prior to one generation ago. The name derives from the fact that the bodies of all higher animals harbor natural chemicals within that resemble in many respects the activity of tetrahydrocannabinol (THC), the phyto- (plant) cannabinoid that is the main psychoactive component of *Cannabis sativa,* sometimes derisively labeled as marijuana. Despite the prominence and importance of the ECS as an essential regulatory mechanism in the body's biochemistry and physiology, the basic machinery of everyday life, knowledge of it remains quite limited among American physicians due to a dearth of appropriate education in medical schools. This is a knowledge deficit that must be filled in order to benefit the public health as a whole.

The basic functions of the ECS have were summarized in 1998 by Professor Di Marzo as, "relax, eat, sleep, forget and protect." There are two primary endocannabinoids, arachidonylethanolamine (AEA), nicknamed anandamide from the Sanskrit word for "bliss," and 2-arachidonylglycerol (2-AG). CB_1 is best known as the neuromodulatory receptor in the brain where THC exerts its effects on short-term memory, pain, emotion, hunger, etc. Receptors may be thought of as locks, to which a corresponding chemical (natural or synthetic) will fit like a key, if it has the proper structure to conform to it. CB_1 is actually the most abundant G-protein coupled receptor in the brain, and this certainly attests to its importance in cerebral function in health and disease. Both endocannabinoids bind to cannabinoid receptors in a similar manner to THC in the brain, but are actually produced on demand in post-synaptic neurons (nerve cells) and travel in a retrograde fashion (backwards) to inhibit the release of various neurotransmitters (chemical messengers). As one example, neuropathic (nerve-based) pain is an all too common condition associated with multiple sclerosis, diabetes and HIV/AIDS, and which is notoriously difficult to treat with conventional pharmaceuticals. Glutamate is one of the primary stimulatory neurotransmitters, but when present at excessive concentrations, it perpetuates neuropathic pain and may even provoke cell death after head injury or stroke. The endocannabinoids are naturally secreted after such insults and act to inhibit glutamate release, thereby alleviating neuropathic pain and reducing cell death. THC, and cannabidiol (CBD), a non-psychoactive component of some cannabis strains, have similar neuroprotective benefits.

AEA and 2-AG are merely the star players in a larger group of endocannabinoids. Some of the others are seemingly inactive molecules when tested on their own. When combined with AEA and 2-AG, however, many experiments have demonstrated that these entourage compounds produce prominent enhancement of the overall effect on pain, inflammation or other function. This synergy (boosting) of effect due to an ensemble of ingredients has been termed the

"entourage effect," and is paralleled by similar attributes in the cannabis plant, whose minor components modulate (modify or influence) the effects of THC.

Beyond the brain, CB_1 receptors are abundant in the spinal cord and peripheral nervous system, where they have a key role in regulation of pain, itch and muscle tone. The ECS also influences the gastrointestinal tract, where CB_1 modulates two important aspects of digestion: propulsion and secretion. The endocannabinoid system also regulates endocrine function and fertility, as well as factors in cellular function, whether developmentally or in the uncontrolled growth and spread of cancer (see below).

CB_1, however, is not the only cannabinoid receptor. Less studied, but extremely important is CB_2, a non-psychoactive receptor that is mostly found in the periphery (outside the brain) and which is a key immunomodulatory mediator with additional activity on pain and inflammation. It, too, is expressed in the brain under conditions of insult, whether it be traumatic injury or degenerative diseases. Many disorders characterized by fibrosis (development of scar tissue), such as liver cirrhosis, and certain heart and kidney disorders may be targets for drugs that affect CB_2.

A third receptor, TRPV1 (transient receptor potential vanilloid-one) is also considered part of the ECS, and is best known as the site of action of capsaicin, the active ingredient of chile peppers, but is also a target of anandamide and cannabidiol, but not THC. TRPV1 mediates pain signals through a mechanism distinct from that of the endogenous cannabinoids and opioids, but the receptor is subject to desensitization: this means that if continuously stimulated, the pathway will eventually slow down or even stop. This raises therapeutic possibilities for agents to effectively treat certain kinds of neuropathic pain.

The third component of the ECS along with the endocannabinoids and their receptors are the biosynthetic and degradative enzymes that respectively produce or breakdown AEA and 2-AG. These have also become targets for new drug development, and interestingly cannabidiol, among its many activities is capable of inhibiting AEA breakdown by the enzyme fatty acid amidohydrolase (FAAH), thus strengthening and prolonging its effects, much like selective serotonin reuptake inhibitors (SSRIs) increase serotonin activity to treat depression.

Taken together, the three components of the ECS, the endocannabinoids, their regulatory enzymes and receptors, can be thought of as a key mediator of physiological homeostasis, thus ensuring that various bodily systems function within tight parameters with neither a deficiency nor excess of activity. Just as the immune system deals with invasive proteins from bacteria and viruses, Professor Raphael Mechoulam has hypothesized that the ECS serves an analogous role in the body to neutralize and rectify non-protein insults, such as trauma or oxygen lack.

What if the ECS itself is out of balance? How might this be manifested? Recent discoveries have provided some insights. Ideally, if the ECS is functioning normally, a person might enjoy a normal mental state, without pain, have good digestive function, etc. In contrast, morbid obesity is accompanied by a metabolic syndrome with increased inflammation, insulin resistance and even diabetes. The ECS has been observed to be hyperactive in such states. Similarly, an excess of CB_1 activity can be associated with hepatic (liver) fibrosis. Such

problems led to the development of drugs such as rimonabant (aka Acomplia® or SR141716) to combat this excess. This drug is an inverse agonist at CB_1. That means that it antagonizes the receptor so avidly that it drives down the baseline activity of the ECS, thus lowering what is termed "endocannabinoid tone." While this might be effective to reduce hunger and weight gain, and improve laboratory findings of the metabolic syndrome, the widespread effects of this drug also spilled over to other systems to produce undesirable adverse events (side effects) such as depression and suicidality that led to its removal from the market. Other liabilities of CB_1-inverse agonists would include nausea, an increased likelihood of seizures and even development of malignant tumors. In contrast, CBD is a milder neutral antagonist at CB_1 that may be capable of addressing similar medical needs without the attendant risks.

What if endocannabinoid levels are too low? It has been theorized and subsequently borne out in subsequent research that numerous mysterious disorders fit the description of "clinical endocannabinoid deficiency" (CED). Noteworthy among these are migraine, fibromyalgia and idiopathic bowel syndrome (IBS or "spastic colon"). These disorders affect millions of otherwise healthy people who are plagued by chronic pain and other symptoms, leading to extensive medical tests and attempts at treatment, often to limited benefit. The three conditions tend to affect the same individuals at various times of their lives, and are therefore termed "co-morbid." All three are characterized by "central sensitization," the concept that normal sensations in the brain are magnified to the point of becoming painful when they would not be to a person free from the affliction. The three disorders also benefit from treatment with cannabinoids according to patient testimonials. Available data confirm that the target organs (brain, gut, musculoskeletal system) seem to express lower than normal levels of anandamide, thus providing credence for the concept that they would benefit from treatments that would upregulate the ECS back to normal levels. Similar putative (theoretical) deficiencies have been highlighted in the ECS for numerous other conditions including intractable depression, post-traumatic stress disorder (PTSD), neuropathic pain conditions such as complex regional pain syndrome, causalgia, post-herpetic neuralgia, interstitial cystitis, and even certain forms of infertility and early miscarriage.

Finally, many forms of cancer are accompanied by increases of CB_1 and/or CB_2 expression, felt to be part of the body's effort to combat the disorder. Interestingly, the phytocannabinoids demonstrate the potential to treat cancer in high doses without harming the normal cells of the body. Some of the mechanisms are mediated through CB_1 and/or CB_2, but others seem to work through independent, non-receptor means. Cancer arises due to a loss of ability for malignant cells to undergo apoptosis, a normal process of programmed cell death whereby the body remolds and renews itself. Instead, cancer cells become immortalized, divide and grow in an uncontrolled fashion, invade surrounding tissues, stimulate their own blood supply, and even metastasize (spread remotely to distant sites). The endo- and phytocannabinoids, particularly CBD, have the ability to reverse or prevent many of these effects, as demonstrated in experiments in many cancer cell types and even in a growing number of case reports in humans. Beyond the issue of eliminating the malignancy itself, properly constituted cannabinoid treatment may hold the promise of additional "side benefits" by

to sustain themselves, grow and spread. This discovery offers great promise for the treatment of brain and other types of cancer.

THC is also a bronchodilator, anti-spasmodic, muscle relaxant, a powerful neuroprotectant and antioxidant. **In fact, it has 20 times the anti-inflammatory power of aspirin and twice that of hydrocortisone**.

Cannabinol (CBD)

CBD is the second most common cannabinoid in cannabis and the most common in hemp plants. CBD can generally represent 0.1-12 percent of the cannabinoid content of the plant. CBD rich cannabis (4% or more) provides potent therapeutic benefits for many different ailments. While THC is widely known for its psychoactive properties, CBD may be best known for its ability to ability to help control severe forms of epilepsy and its ability to counterbalance anxiety, tachycardia (rapid heartbeat), hunger and sedation caused by high levels of THC. **CBD and THC have a synergistic effect. This means that when they are both present at therapeutic levels, they are more effective together than they are alone.**

CBD is as beneficial and versatile a cannabinoid as THC in addressing many hard to manage conditions such **as diabetes, rheumatoid arthritis, cancer, epilepsy, antibiotic-resistant infections, alcoholism, PSTD and neurological disorders.** CBD has very strong anxiolytic (reduces anxiousness), anti-convulsant, anti-emetic (reduces nausea), anti-inflammatory, antioxidant (**stronger than vitamins C & E**), anti-depressant and anti-psychotic properties. One of the most exciting aspects of CBD is its combined strong anti-inflammatory, anti-oxidant and neuro-protective properties which yields great promise for the treatment of Alzhiemer's, Parkinson's disease, and all neurodegenerative-related diseases. CBD also helps regulate blood pressure and is **cytotoxic to breast cancer and certain other types of cancer cells while protecting healthy cells.**

THE CANNABIS IRONY

Although possession of cannabis is illegal under federal law, twenty-three states have some form of a medical cannabis law and more are expected by the end of 2015. The synthetic form of isolated THC, the component of cannabis that the federal government claims is the offending compound that makes cannabis illegal, is available with a doctor's prescription under the brand name Marinol. It is a Schedule III drug.

HOW IS HEMP DIFFERENT FROM CANNABIS?

Hemp and medicinal cannabis are in the same genus – cannabis, (*Cannabis sativa, Cannabis indica*, and hybrids), and both have psychoactive components but the hemp plant has so little that its flowers are not effective to use for medical or recreational purposes. The difference is in breeding/growing methods – hemp is grown for its seed, oil and fiber, which is used to make food, health products, body care items, clothing, rope, paper, etc., and medicinal cannabis is bred to have larger buds and more psychoactive and therapeutic compounds. Hemp seed and oil are highly nutritious packed with protein, and high quality essential fatty acids that are an important nutrient for our endocannabinoid system.

GET INFORMED

"Cannabis is the single most versatile herbal remedy, and the most useful plant on Earth. No other single plant contains as wide a range of medically active herbal constituents."

- Dr. Ethan Russo, Neurologist, Ethnobotanist, Former President of the International Association for Cannabinoid Medicine, Medical Director of PHYTECS, and leading global medical cannabis expert.

The following are some of the premier resource about cannabis science and politics.

Organization	Website	Organization	Website
Chronic RELIEF	MyChronicRelief.com	Marijuana Policy Project	mpp.org
cannabinoid medicilles International Association for Cannabinoid Medicines	cannabis-med.org	Project CBD	projectcbd.org
O'Shaughnessy's The Journal of Cannabis in Clinical Practice	beyondthc.com		medicalcannabis.com
Journal of Cannabis Therapeutics	cannabis-med.org	Medical Marijuana 411.com	medicalmarijuana411.com
AmericansFor SafeAccess	safeaccessnow.org	Leaf Science	leafscience.com
Cannabinologist	cannabinologist.com	MedicalJane	medicaljane.com
THEWEEDBLOG	theweedblog.com	NORML Working to reform marijuana laws	Norml.org

The true crime regarding cannabis is doing nothing, when we know it can help millions of people safely. Please do your own homework and speak with your colleagues and constituents about this issue. It is time we dissolve the cloud of shame, secrecy and controversy about the use of this legitimate medicine and make it legal in Texas!

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