

Clinical observations on the use of HempFlavin, a proprietary blend of twenty-three Cannflavins and flavonoids, with acute and chronic pain.

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- I. **Introduction:** Flavonoids, a group of natural substances with variable phenolic structures, are found in fruits, vegetables, grains, bark, roots, stems, flowers, tea, and wine. These natural products are well known for their beneficial effects on health. Continued efforts are being made to isolate flavonoids, and over 5,000 have been structurally identified.

The Cannabis genus of plant has been heralded as a pharmacological treasure trove of investigational medicinal products. The focus of developing cannabis-based medicinal products has largely centered around the phytocannabinoids, cannabidiol (CBD), and (-)-trans- Δ^9 -tetrahydrocannabinol (THC) due to their abundance within flower trichomes, superior knowledge of extraction and distillation techniques and much deeper understanding of their therapeutic and pharmacokinetic properties.² The cannabis plant however contains an abundance of other metabolites including phytocannabinoids, terpenes, flavonoids, stilbenoids, amino acids, fatty acids, alkaloids, hydrocarbons, carbohydrates, and phenols.

The present paper focuses on the effect of flavonoids, specifically the Cannflavins, which make up less than 0.15% of the fresh weight of cannabis. To date, a massive amount of marijuana would have to be consumed in order for the effects of this component to take place; however, a proprietary extraction technique has resulted in the production of HempFlavin, with microgram quantities dosing thereby producing an observable clinical effect.

Animals and plants have metabolic pathways, receptors, and cytokines that interact with each other in the environment. We, as humans, have a number of features in common with all the organisms placed on the earth and these common features indicate that we have a shared evolutionary history. Both animals and plants developed metabolic pathways and the flavonoid pathway is a core component enabling land plants to interact with their environment. These animal and plant pathways and cellular communications overlap and can be inhibited or promoted by medications, supplements, and diet.

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² Rea et al., 2019. Biosynthesis of cannflavins A and B from Cannabis sativa L, Phytochemistry 164 (2019) 162-171

Flavonoids were first discovered in 1930 when a new substance was separated from oranges. Albert Szent-Györgyi, a Hungarian biochemist, discovered rutin (vitamin P) and vitamin C. The role of these vitamins in the body is vast, and for his work Szent-Györgyi received a Nobel Prize in medicine in 1937. Similarly, world renowned scientist Linus Pauling and his devotion to vitamin research, and flavonoids, is continued by Oregon State University and the Linus Pauling Institute.³

Flavonoid intake has been recognized as important for decades. Riboflavin, one of the first U.S. government recommended⁴ dietary supplements, was discovered in 1920, isolated in 1933, and first synthesized in 1935. Riboflavin, also known as vitamin B₂, is found in food and sold as a dietary supplement. It is essential to the formation of two major coenzymes, flavin mononucleotide and flavin adenine dinucleotide. These coenzymes are involved in energy metabolism, cellular respiration, and antibody production, as well as normal growth and development. The amount of riboflavin a person needs depends on age and sex. Average daily recommended amounts range between 0.3 mg and 1.6 mg (milligrams) per day.

Fast forward some fifty years and flavonoids are now considered as an indispensable component in a variety of pharmaceutical, medicinal, and cosmetic applications. This is attributed to their anti-oxidative, anti-inflammatory, anti-mutagenic and anti-carcinogenic properties coupled with their capacity to modulate key cellular enzyme function.

This paper investigates the anti-inflammatory and somatic nociceptive pain-relieving clinical effects of HempFlavin, a proprietary blend of twenty-three Cannflavins and flavonoids extracted from an heirloom hemp variety which is over 2,000 years old.

Barrett and colleagues identified Cannflavins A and B and verified that these prenylated flavonoids could inhibit the production of PGE₂ in human rheumatoid synovial cells and provide anti-inflammatory benefits that were approximately thirty times more effective than aspirin.⁵

It was later demonstrated that the underlying basis for their potent anti-inflammatory properties was that Cannflavins A and B act to inhibit the in vivo production of two pro-inflammatory mediators, prostaglandin E₂ and the leukotrienes.⁶

³ <https://lpi.oregonstate.edu/>

⁴ <https://ods.od.nih.gov/factsheets/Riboflavin-Consumer/#h2>

⁵ Barrett, et al., 1985. Isolation from Cannabis sativa L. of cann-flavin-a novel inhibitor of prostaglandin production. *Biochem. Pharmacol.* 34, 2019-2024, *see also*, Barrett et al., 1986. Cannflavin A and B, prenylated flavones from Cannabis sativa L. *Experientia* 42, 452-453.

⁶ Werz et al., 2014. Cannflavins from hemp, a novel cannabinoid-free hemp food product, target microsomal prostaglandin E₂ synthase-1 and 5-lipoxygenase. *Pharm. Nutr.* 2, 53-60.

It has been well established that prostaglandins play a key role in the generation of the inflammatory response. Their biosynthesis is significantly increased in inflamed tissue and they contribute to the development of the cardinal signs of acute inflammation, rubor, calor, dolor, and tumor. The usual outcome of the acute inflammatory program is successful resolution and repair of tissue damage, rather than persistence and dysfunction of the inflammatory response, which can lead to scarring and loss of organ function. It may be anticipated, therefore, that failure of acute inflammation to resolve may predispose to autoimmunity, chronic dysplastic inflammation, and excessive tissue damage.⁷

Observation of the clinical response to prostaglandin inhibition by HempFlavin in acute and chronic pain patients is the basis for this pilot study. These observations and positive response show promising results for treating acute and chronic inflammation.

- II. Materials and methods:** Doctors Hemp Solutions, Labelle, Florida, utilizing a proprietary method for extraction from a 2,000-year-old Heirloom Hemp Variety, formulated in a 100 microgram per milliliter (mcg/ml) varying amounts of Cannflavin A, B, & C, Chlorophyll, and lesser constituents of Apigenin, Pelargonidin-3-O-glucoside, Baicalin, Vitexin, Beta Sitosterol, Wogonin, Chrysin, Rutin, Fisetin, Quercetin, Luteolin, Kaempferol, and Orientin. Doctors Hemp Solutions, Labelle, Florida internal laboratory has testing capabilities for phenolics, Flavonols, Flavones, and Flavanols. They also confirm this tincture has zero (0) tetrahydrocannabinol (THC) and zero (0) cannabinoid.

The tincture has not been evaluated by the U.S. Food and Drug Administration (FDA) for efficacy or safety and is considered a dietary supplement and is distributed under the tradename HempFlavin.

Dosing is performed by the participants, utilizing a 1 milliliter (ml) dropper dispenser with 100 micrograms (mcg) per ml., participants were divided into two dosing regimens; a dosing of 300 mcg/day in the morning or 100 mcg/day in the morning was selected based on random assignment. Participants were contacted at 10 day and 30-day intervals, with a pre-study interview performed by this paper's author.

Sixty-five (65) adult volunteer patients were randomly generated for participation in the study and customary consent and waivers were obtained.

Of the sixty-five (65), forty-six (46) or seventy percent (70%) completed the full study protocol of ten (10) and thirty (30) days.

No adverse effects were reported or 'a failure to respond' as reasons for leaving or not participating in the study.

⁷ Barrett, et al., 1985. Isolation from Cannabis sativa L. of cann-flavin-a novel inhibitor of prostaglandin production. Biochem. Pharmacol. 34, 2019-2024, *see also*, Barrett et al., 1986. Cannflavin A and B, prenylated flavones from Cannabis sativa L. Experientia 42, 452-453.

Of the forty-six responders, twenty-four (24) or fifty-two percent (52%) were female, and twenty-two (22) or forty eight percent (48%) male, without transgender or self-identified gender non-specific participants (0%). The mean age was sixty (60), with a range of thirty-one (31) to ninety (90) years of age.

Participants suffered from a variety of osteoarthritic ailments, both micro-trauma (e.g., DJD) and macro-trauma (e.g., MVA fractures) in origin.

III. Results: There were no adverse effects of HempFlavin reported. Table 1 summarizes the findings of this pilot study.

TABLE 1. 30-day clinical response to HempFlavin.

	HempFlavin					
	300 mcg or 100 mcg/day		100 mcg/day		300 mcg/day	
	Clinical Response		Clinical Response		Clinical Response	
	Positive	Negative	Positive	Negative	Positive	Negative
Participants (percentage)	42 (91%)	4	6 (85%)	1	36 (92%)	3
Pain scale reported	8.5/10 to 1.6/10					

Of the forty-six (46) respondents, ninety-one percent (91%) reported a decrease in pain (8.5/10 to 1.6/10 average) and increase in activity with daily HempFlavin use, dosed at 300 mcg/day and 100 mcg/day, after 30 days of supplement use. A slightly better (92%) response to the 300 mcg/day dosing was observed.

There was also a small subset of the participants (19%) that mistakenly administered 100 mcg/day initially for 10 days with increase to 300 mcg/day for the remaining 30 days, due to poor provider communication. The present study was conducted to thirty (30) days of daily use, and on-going evaluation of the lower dosing, 100 mcg/day, is being investigated.

The overall positive response rate, for decreased pain and increased function, was observed as ninety-one percent (91%).

Our study further observed a positive response to participants suffering from unspecified migraine headaches. Participants included— female, age 48, with 100 mcg/day effective response; female age 60 with 300 mcg/day effective response; female, age 47 with 300 mcg/day effective response for 12 hours; female, age 44 experienced effective response in 20 minutes using 300 mcg/day dose; female, age 39 with 300mcg of HempFlavin pain level dropped from 8-10 to 1-2 for 12hrs.

Other noteworthy observations from patients participating in the study. Female, age 90, presented with a history of COPD and a rotator cuff tear needing surgery. Her daily pain was reported as 9 she started with 3 mL dose 100

mcg/day-- her pain relief lasted 20 hours and then a second 3mL tincture 100 mcg/day and relief lasted 24 hours. Male, age 60, presented with knee pain and was considering knee replacement surgery. After a second day of 300 mcg doses of HempFlavin he was able to sleep 8 hours without having to get up and walk due to pain. Male, age 54 with 300 mcg/day effective response for 12 hours; male, "pain level dropped from a 9-10 to 1-2 within 10 minutes," with 300 mcg/day. He was scheduled for stem cell treatment for shoulder and canceled procedure after experience significant pain mitigation with HempFlavin.⁸

IV. Discussion: This pilot study identifies a significant anti-inflammatory clinical response to Cannflavin and flavonoids. Our observations are the first known to be published with regard to acute and chronic pain, although canine positive response to cannabidiol has been reported by Verrico et al.⁹ As with animal studies of flavonoids, we did not observe any adverse effects.

The development of novel anti-inflammatory medications is of clinical importance, in the setting of the rising incidence of inflammatory and auto-immune conditions globally. Current anti-inflammatory medications are associated with significant side-effects including gastrointestinal bleeding and cardiovascular events affecting their risk-benefit profile.

This paper focuses on the effect of flavonoids, specifically the Cannflavins, which make up less than 0.15% of the fresh weight of cannabis. To date, the clinical effects of flavonoids have not been studied, since a massive amount of cannabis would have to be consumed in order for effects to be observed. We tested HempFlavin, made by a proprietary extraction technique, which contains a 300-microgram dosing capable of producing clinical effect. The proprietary process (rich in Omega-3 Fatty Acid) induces the production of Cannflavins A and B and there is zero percent (0%) THC in the supplement.

A selection of Cannflavins have therapeutic properties of their own or contribute to the 'entourage effect;' however, we concentrate specifically on flavonoids and their clinical anti-inflammatory response.

Inflammation is a complex and crucial defensive host response typically induced by microbial infections; however, inflammation can also be triggered by tissue injury or trauma or micro-trauma (wear & tear) that occurs without the intervention of pathogens which is referred to as sterile inflammation.¹⁰ In most cases, inflammation is a specific, self-controlled immune response that is orchestrated in order to resolve infections or to repair tissue and wounds. A dysregulated immune response can be associated with a disruption in the homeostasis of physiological processes without a direct connection to classical inflammation triggers, which causes chronic systemic damage.

⁸ Full summary of Study Interviews attached as Appendix A to this article

⁹ Verrico, et al., 2020. A randomized, double blind, placebo-controlled study of daily cannabidiol for the treatment of canine osteoarthritis pain, *Pain*, September 01;161(9):2191-2202.

¹⁰ Behnia et al., 2016. Mechanistic differences leading to infectious and sterile inflammation. *American Journal of Reproductive Immunology*, 75, 505-518.

HempFlavin is an ingested, sublingual, tincture. Flavonoids are extensively metabolized in the intestine and consequently their metabolites are transported to the liver where they undergo further metabolization. Metabolites formed in the liver can be transported to target cells, can re-enter enterohepatic circulation by means of bile excretion being hydrolyzed to aglycones by the microbiota, or can be excreted through urine or feces. Flavonoid metabolites that do not undergo absorption in the intestine and reach the colon can be degraded by colonic microbiota and be reabsorbed.¹¹ The bioavailability of flavonoids depends on the specific subclass, but in general, it has been described to be low.¹² This emphasizes the increased need for more concentrated dosing.

The clinical observations with HempFlavin dosing are consistent with an anti-inflammatory effect and relief, specifically of joint related acute and chronic pain.

Flavonoids have anti-inflammatory properties through different mechanisms such as inhibition of regulatory enzymes and transcription factors that have a key role in the control of mediators involved in inflammation. Flavonoids are also potent antioxidants able to scavenge free radicals and to decrease their formation. Consequently, flavonoids have a deep impact on several immune cells and immune mechanisms that are important in the inflammatory processes.

In a collection of studies published during 1985 and 1986, Barret et al. studied the ability of both compounds Cannflavin A and B to inhibit prostaglandin E2 release from human rheumatoid synovial cells, demonstrating potency 30 times that of aspirin in an ex vivo setting. Arachidonic acid is released during inflammation from phospholipids contained in the plasma membranes by the enzyme phospholipase A2 (PLA2). Arachidonic acid is then metabolized by different oxygenases, such as cyclooxygenase (COX) and lipoxygenase (LOX), in order to produce prostaglandins, thromboxanes, leukotrienes and other inflammatory mediators.¹³ Flavonoids have the potential to inhibit the enzymes involved in the metabolism of arachidonic acid decreasing the release of the inflammatory mediators derived from this pathway. For example, flavonoids can inhibit the biosynthesis of prostaglandins, thromboxanes, leukotrienes by inhibition of the enzymes PLA2,¹⁴ COX,¹⁵ or LOX.¹⁶

¹¹ Thilakarathna & Rupasinghe, 2013. Flavonoid bioavailability and attempts for bioavailability enhancement. *Nutrients*, 5, 3367-3387.

¹² Hu, Wu, & Liu, 2017. Bioavailability of polyphenols and flavonoids in the era of precision medicine. *Molecular Pharmaceutics* 14, 2861-2863

¹³ Yahfoufi, et al., 2018. The immunomodulatory and anti-inflammatory role of polyphenols. *Nutrients*, 10.

¹⁴ Kumar, et al., 2017. Exploring the binding mechanism of flavonoid quercetin to phospholipase A2. *European journal of experimental biology*, 7, 33.

¹⁵ González-Mosquera et al., 2018. Flavonoids from *Boldoa purpurascens* inhibit pro-inflammatory cytokines and Cox-2 expression. *Phytotherapy research* 32, 1750-1754.

¹⁶ Hanáková et al., 2017. Anti-inflammatory activity of natural geranylated flavonoids; cyclooxygenase and lipoxygenase inhibition. *Journal of natural products*, 80 999-1006.

Protein kinases are involved in signal transduction during cell activation in inflammation. In that respect, certain flavonoids can target multiple central kinases that participate in multiple signaling pathways.¹⁷ The inhibition of kinases such as phosphoinositol kinase, protein kinase C, phosphatidylinositol kinase, tyrosine kinase or cyclin-dependent kinase-4 by diverse types of flavonoids have been reported.¹⁸

Flavonoids can inhibit phosphodiesterases such as cAMP phosphodiesterase. cAMP is a second messenger molecule key in the regulation of different cell functions during inflammation. High levels of cAMP have been associated with anti-inflammatory functions. The enzymes phosphodiesterases can hydrolyze cAMP to keep normal levels. The inhibitory effects of flavonoids on phosphodiesterases have the potential to block cAMP degradation and prolong cAMP signaling.¹⁹

Lastly, tissue injury during inflammation produces free radicals such as oxygen-derived radicals (or reactive oxygen species, ROS), nitrogen derived radicals (or reactive nitrogen species, RNS), that have detrimental effects in cell function.²⁰ Free radicals have unpaired electrons that make them highly reactive and detrimental for lipids, proteins, and DNA. Free radicals' impact on cellular membranes by lipid peroxidation and on proteins and nucleic acids by oxidative damage. High production of free radicals together with low sequestration of transition metal ions and low free radical scavenging activity result in oxidative stress.²¹ Flavonoids have antioxidant activity due to their inhibitory effects on the production of free radicals and their scavenger activity for ROS, RNS, and other reactive species. The antioxidant properties of flavonoids are derived from their chemical structure, the specific substitution patterns within the structures and the phenolic hydrogens that enable them to act as hydrogen-donating molecules.²²

This pilot study identifies a significant clinical response to HempFlavin, with a decrease in inflammatory related symptoms. Given the current literature, more likely than not, Cannflavin A and B are inhibiting prostaglandin E2 release from joint synovial cells with a potency some 30 times that of aspirin. A further robust study is recommended.

¹⁷ Hou & Kumamoto, 2010. Flavonoids as protein kinase inhibitors for cancer chemoprevention. *Antioxidants & Redox Signaling*, 13, 691-719.

¹⁸ Lolli et al., 2012. Inhibition of protein kinase CK2 by flavonoids and tryphostins, *Biochemistry*, 51, 6097-6107.

¹⁹ Guo et al., 2018. Prenylated flavonoids as potent phosphodiesterase-4 inhibitors. *European Journal of Medicinal Chemistry*. 144, 758-766.

²⁰ Mittal et al., 2014. Reactive oxygen species in inflammation and tissue injury. *Antioxidants & Redox Signaling*, 20 1126-1167.

²¹ Nimse & Pal, 2015. Free radicals, natural antioxidants, and their reaction mechanisms. *Rsc Advances*, 5, 27986-28006.

²² Chen, et al., 2019. Antioxidant and anti-inflammatory properties of flavonoids from lotus plumule. *Food Chemistry*, 277, 706-712.

APPENDIX A
CLINICAL STUDY RESULTS INTERVIEWS

1. Male, Age 73

Vietnam vet presented with: History of Multiple leg fractures and back fractures. Pain level is 8-10 without controlled substances or interventions. Dosage: started taking 1mL HempFlavin in morning and 2mL HempFlavin an hour before going to bed. Results: Relieved pain for about 6 hours but when he took nighttime dose it allowed him to sleep for first time in 10 years with no bad dreams. He increased dose to 3mL in morning and 3mL at night. Results: Pain relief lasted 12 hours and he is no longer taking controlled substances. He still reports improved sleep with no bad dreams, loves the product and recommends it to everyone.

2. Male, Age 70

Presented with: History of rotator cuff issues in right shoulder and unable to lift right arm above his shoulder in past five years. Previously has treated with medical marijuana and various controlled substances. Dosages and results: Started with 3 mL of HempFlavin daily and reported pain relief lasted for 18 hours. Second day, he took 3mL of HempFlavin and reported pain relief lasted 20 hours. After those initial doses he changed to 2mL and after 10 days he switched to 1mL of HempFlavin per day with 24-hour pain relief. After first dose he could lift his Right arm over his right shoulder and can still do so. He recommends the product to anyone in pain or restricted mobility.

3. Female, Age 90

Presented with: History of COPD and needing rotator cuff surgery but due to COPD she is unable to have surgery. Pain level: 9, and she does not like taking controlled substances for pain. Dosage & Results: She started with 3mL first day and the pain relief lasted 20 hours. Second day, she took another 3mL and pain relief lasted 24 hours. The first time she took the HempFlavin her pain decreased from a 9 to a 5. After second dose it was a 4. She was able to sleep for an entire night for first time in ten years. She continues to take 3mL every day and recommends product to everyone.

4. Female, Age 79

Presented with: History of arthritis in hands and fingers. Pain level: 9, and she uses many therapies to help with her hands for mobility. Dosage & Results: She started taking 3mL HempFlavin and within 12 hours she noticed improved mobility in her hands and fingers. Within 24 hours, the pain started coming back. She took another 3mL and pain went from 9 to 4 and continued to improve each day. She then used 1mL every day with current results of no arthritis pain and can use her hands like she did ten years ago.

5. Male, Age 43

“Blue collar worker” who owns his own grading and sod company. Presented with: history of “that he beats his body up in his equipment” and has tremendous back pain. Pain level: 8-10, which makes it hard to get up in the morning and he never was able to get 6 hours of sleep in the last 4 years. Dosage & Results: 3mL of HempFlavin and for the first 8 hours he had immediate relief of pain from a 9 to a 6. He took another 3mL within 12 hours as his pain was going back up. After second dose he received relief of pain for 20 hours. His pain averaging a 3 of max relief. He continued to take 3mL every 12 hours for four days, then began taking 3mL every night. “Highly recommends HempFlavin to others”.

6. Female, Age 44

Presented with: severe migraines and pre-menstrual pain. Has taken “pain killers”/prescription medications and other remedies to try to combat both issues. Pain level: for migraines is 10 and she is down and out for 12-24 hours after suffering from the migraine. Dosage & Results: Participant took 3mL

daily for ten days, and then reduced to 2mL for next five days. She had two migraines beginning to present and she took 3 mL as soon as migraine started and the pain subsided. She “Never approached a 7 pain level”. Throughout the entire 30 day trial, she had five migraines and took 2mL daily and 3mL when the migraine began and the migraine never turned into her severe level 10 migraine. In fact, never went above a level 3 pain level and she was able to work and interact when the migraine cleared up. First month she can remember that she did not have any pre-menstrual pains. She normally has level 8 menstrual pain for three to four days. She recommends product to anyone with migraines and pre-menstrual pains. She continues 2mL a day dosage and then using 3mL when her pain begins to kick in and within 20 minutes the pain is gone.

7. Male, Age 34

Works all day with in a “blue collar” position. Presented with: After work he is “always in pain and cannot do anything Except rest, try to get some sleep and start over next day.” Dosage & Results: He used 3mL before going to bed for first dose, and he was able to sleep for at least 6 hours, which was more than he had slept in last several years. He continued with work the same and instead of his daily pain level at 8-9 for the first week it was at 6. The next week following same routine he was able to sleep 6-8 hours and his pain was a 3 to 4 and that is where it has continued to stay. “Love the product.”

8. Female, Age 55

Presented with: History of Bilat. hip replacements and severe pain in her back. Dosage & Results: She started with 3mL of HempFlavin daily and after ten days went to 1mL daily. She reported during the study that she believes the HempFlavin was helping her and reducing her pain from 8 to 5-6. She ended the study and did not have any HempFlavin for four days. She called in to order HempFlavin as she was in 8-9 pain. She could feel her pain getting worse every day she was not on the HempFlavin and she is amazed how subtly it helped with her chronic pain.

9. Female, Age 70

Presented with: pain related to AMD. Dosage & Results: She was taking 1mL every 24 hours at night to help her pain so she could sleep. When she has her injection for AMD she is “out of commission” for 12 to 24 hours because of the intense pain from the injection into her eyeball. She took 3mL of HempFlavin ten minutes after the AMD injection and her pain reduced from 10 to 6 in 5 minutes and then reduced to a 2 within 10 minutes. She continues to use 1mL every day and recommends it to everyone.

10. Female, Age 65

Presented with: arthritis and what she calls “basic old person” pain. Dosage & Results: She took 3mL for ten days and then 1mL for the remainder of the study. She called us two days prior to this study ending and she believed it helped but not greatly. She called back ten days later wanting to buy HempFlavin immediately. Her pain level was at an 8 after the study concluded. She said she could feel her pain and arthritis pain increasing two to three days after running out. After five days pain was back to where it was prior to the study. She called again four days after being back on the HempFlavin and she stated her pain was “non-existent” to a three and she recommends the product to everyone she talks to and tells them to “don’t stop taking it because your body feels better and you think you don’t need it, because the HempFlavin is working without you even knowing it.”

11. Female, Age 39

Presented with: History of femur and pelvis fractures, ganglion cyst removals(x5), gastrointestinal inflammation, sciatic nerve pain, bulging and herniated discs, migraines, inflammation behind eyes and ears from/post Covid-19, and bacterial meningitis as an infant in 1989, resulting in deafness/hard of hearing and vision complications. Pain level: 8-10, and she stated, “would be higher if possible”. Previously

on gabapentin, baclofen, Diflucan, and other pain medications “just to be able to function” from the pain. Dosage & Results: 300mc, within 15-25mins she stated her pain level dropped to a 1-2. She takes 300mcg of HempFlavin every 12hrs, due to her pain level creeping back up after 12 hrs. She states this is the first product that she has ever taken that controls her pain and allows her to live her life fully. She highly recommends HempFlavin to everyone looking for a natural source to pain relief.

12. Female, Age 55

Presented with: History of L4-L5 chronic back pain, nerve pain, autoimmune disease dermatomyositis. She was previously taking steroids for her pain and inflammation. Dosage: 300mcg daily. Reports no ASE while taking Hempflavin. Results: After taking her first dose of Hempflavin she reported immediate relief in nerve pain, then after 1 week completely pain free. She stopped taking the Hempflavin for three days and her pain returned. She went back on Hempflavin at 300mcg and again received immediate relief and continues to take Hempflavin routinely without any issues. She also reports that her muscles and overall body is more relaxed than before and that she had some routine blood work done that resulted in increased muscle enzymes that is in the normal/good range and prior to Hempflavin they were below average range due to autoimmune disease.

13. Female, Age 58

Presented with: history of Bilat. Shoulder and hip replacements. Experiencing chronic pain, inflammation, and overall soreness. Dosage & results: 300mcg once daily. Reported no ASE while taking Hempflavin. She stated after taking her first dose she noticed pain relief “almost immediately”. She stopped taking it and her pain came back immediately. She continues to take 300mcg daily and remains pain free, without breakthrough pain.

14. Male, Age 52

Presented with: History of Arthritis (chronic) to knuckles/hands, Bilat. Knees and elbows. He also suffers from scoliosis. Pain Level: 6-8. Prior to starting Hempflavin he reported that he used Joint Support Vitamins and pure C4S-Sulfate. Dosage- 300mcg 1-2x daily. Reports no ASE while taking Hempflavin. Results- After starting Hempflavin he noticed relief within 30-45mins. He reports that he would notice it wearing off approx. 5-6hrs after use and therefor would take another does in the evening. He now continues 300mcg twice daily and remains pain free. “Recommends it to family/friends”.

15. Female, Age 48

Present with: History of chronic lumbar and leg pain. She also suffers from occasional migraines and previously using acupuncture for relief. Dosage: 100mcg daily. Reports no ASE while taking Hempflavin. Results: After consistently taking 100cmg daily after 3-4days she was pain free and no migraines. She reports 100mcg was effective for her and did not need to increase to 300mcg. She continues taking Hempflavin daily.

16. Female, Age 59

Presented with: History of chronic pain related to Rheumatoid Arthritis to hand and feet. Dosage: 100-300mcg. Was not taking properly due to miscommunication. Results- Was unable to complete trial and did not receive results. he ran out of Hempflavin after 5-6weeks due to alternating doses and did not feel it was adequate amount of time for clinical study. She reported no ASE while taking Hempflavin.

17. Female, Age 60

Presented with: History of chronic severe migraines, neck pain, and LUE/humorous fracture. Prior to starting Hempflavin she received Botox injections with relief as well as routine OTC pain/anti-inflammatories. Dosage: 300mcg daily. Reported no ASE while taking Hempflavin. Results: She reported “positive results and migraine relief” without the need of other interventions previously using for relief. She continues taking Hempflavin daily.

18. Male, Age 52

Presented with: History of cancer 6yrs ago, has been a ballroom dancer for 40+years with chronic right leg pain/soreness. Reports he has had multiple corrective surgeries that have left him with nerve damage and pain. Previously was taking Tramadol 50mg routinely. Dosage: 300mcg Daily. Reports no ASE while using Hempflavin. Results: He reported after consistently taking Hempflavin daily after 1 week he received desired results. He also reported that “this sublingual was tasteless, odorless, and easy to use”. He continues to take Hempflavin and occasionally Tramadol and recommends Hempflavin to family/friends.

19. Female, Age 70

Presented with: History of L eye macular degeneration and receives eye injections for treatment that causes her much discomfort even hours after injection which she would have to rest and wait till it passed. Previously was using Advil routinely without desired results. She also reported coincidentally she had a cold while clinical trial started that left her with chronic cough/congestion and fatigue. Dosage: alternating 100mcg and 300mcg doses daily depending on how she felt. Reports no ASE while taking Hempflavin on alternating doses. Results: After starting Hempflavin she felt immediate relief and no longer suffers from the discomfort after her eye injections for macular degeneration. Also, amazingly reported that it cleared/broke up her cough/congestion she was suffering from better than the anti-congestion medication (OTC) she was taking and resolved her “fatigue and ill-feeling”. She reports she continues to take Hempflavin routinely and recommends it to all family/friends.

20. Female, Age 57

Presented with: History of chronic nerve pain to neck. Prior to taking Hempflavin she was using OTC pain/anti-inflammatories. Dosage: 300mcg and reports no ASE while using. She did not take every day and reported she personally does not like taking the sublingual oil. Results: When she was taking Hempflavin she noticed “some relief” and after trial she switched to the topical Hempflavin cooling cream per her preference and reported complete relief and continues to use topical Hempflavin daily with no pain and recommends it to family/friends.

21. Male, Age 70

Presented with: History of Diabetes Type 2, Knee, back, shoulder, and neck pain. Described his pain as chronic muscle/joint arthritic pain. Prior to Hempflavin he was taking high dose Advil routinely. Dosage: Alternated between 100-300mcg depending how severe his pain was. He said he usually only took 100mcg but on “severe pain days” took 300mcg. Reports no ASE while taking Hempflavin. Results: After starting Hempflavin he reports his pain relief was immediate with all day relief. On days he would have more severe pain and anticipating completing more physically challenging tasks he would take 300mcg and noticed improvement in his severe pain and able to complete tasks in ample amount of time and previously was unable to do so. He also reported that due to his many years of using Advil in higher doses he received abnormal kidney function and concerns related to his DM2 diagnosis. After starting

Hempflavin and completing trial his kidney function improved from being able to stop taking Advil. He reports he continues to take Hempflavin 100mcg routinely and that its all he needs for all his aches/pains.

22. Male, Age 47

Presented with: history of chronic abdominal pain, suffers from MS that attributes to his chronic lumbar pain. Pain level 7-8 on daily basis. Prior to starting Hempflavin he routinely took Gabapentin and OTC extra-strength Tylenol. Dosage- 300mcg. Reports no ASE while taking Hempflavin. Results: after starting Hempflavin he noticed immediate desired effect and reduced his pain greatly but not completely. He stated he noticed it wearing off after a couple of hours and did not receive further instructions r/t increasing the frequency to more than once a day. He said he would like to continue taking Hempflavin more than once a day as well as recommends it to family/friends.

23. Female, Age 47

Presented with: History of chronic back pain, PMS, and migraines. Prior to starting Hempflavin she was using Excedrin Migraine/Dual Action Advil. Dosage: 300mcg Daily. Reports no ASE while using Hempflavin. Results: After taking first dose of 300mcg she reported immediate relief that lasted for 12hrs generally. She stated she never noticed in wearing off. She said the pain was gone and no longer a chronic issue. She continues to take Hempflavin routinely and recommends it to family/friends. Reported she has concerns about the affordability of the product. She also expressed concerns with the taste slightly bitter but not terrible and easy to take.

24. Female, Age 53

Presented with: History of chronic BLE/knee pain from arthritis. Pain level: 5. Prior to starting Hempflavin she was not taking any medications or OTC. Dosage:300mcg Daily. Reports no ASE from Hempflavin. Results: After starting Hempflavin she noticed overall pain relief after 1 week without issues and did not notice it wearing off. She reported after clinical study the pain came back immediately once she stopped Hempflavin. She restarted taking Hempflavin and remains pain free. She continues to recommend it to family/friends.

25. Female, Age 54

Presented with: History of chronic hand pain as she is an avid tennis player. Dosage: 100mcg daily. Reports no ASE while taking Hempflavin. Results: Reported she received desired results and hands improved greatly. She would continue to use Hempflavin and recommends to family/friends.

26. Male, Age 57

High school coach, Presented with: Bilat knee pain from arthritis. Prior to starting clinical study was taking Aleve routinely. Dosage: 300mcg daily. Did not experience any ASE while taking Hempflavin. Results: After taking Hempflavin for one week consistently he noticed 100% complete relief of pain and did not notice it wearing off as he still takes it to this day. He stated he could not think of any recommendations or negative aspects of this product and continues to recommend it to family/friends.

27. Female, Age 39

Presented with: History of Fibromyalgia, Bilat. Knee pain, and plantares fasciitis to R foot. Dosage:300mcg. No ASE while taking Hempflavin. Results: After taking Hempflavin for a couple of days she received all day pain relief and did not return or have breakthrough pain. She reports she continues to take Hempflavin and recommends it to family/friends.

28. Male, Age 73

Presented with: history of back pain (previous back surgery) fractured Kneecap, (Motorcycle accident) Vietnam-broke ankle, chronic shoulder pain from (osteo)Arthritis and neuropathy. Pain level: 7-8. He is Bedridden. Prior to starting Hempflavin he was taking Gabapentin, Tramadol, Hydrocodone and OTC Tylenol. Dosage: 300mcg Daily. No ASE while taking Hempflavin and other routine medications. Results: After taking Hempflavin he noticed an immediate desired effect and calmed his pain greatly but not 100%. He reported he noticed it wearing off after approximately 5 hours. He is working on weaning off all narcotics and does not want to be addicted to anything. He also stated "I liked the products, and it works, but when it wears off the pain comes back. I took two droppers at night and got better sleep. I have PTSD and this product helped with nightmares and restlessness. I achieved increased sleep to 6-7hrs instead of 3hrs and waking up multiple times at night." "I highly recommend this product to others".

29. Male, Age 60

Presented with: History of multiple surgeries to L hand and R shoulder, 3 major R knee surgeries related to torn ACL, surgeries caused scar tissue resulting in arthritis (Severe). He was recommended a knee replacement but opted out of it. Prior to starting Hempflavin he was taking CBD from another manufacturer. But stopped taking it for clinical study. Dosage: 300mcg and reports no ASE while taking Hempflavin. Results: He reports after taking Hempflavin for 3 days he noticed complete pain relief that lasted all day with no breakthrough pain. He reports his pain did not return and he continues to routinely take Hempflavin and recommends it to family/friends. He states "Other oils I have tried have had not had ANY effects except for one. Your product is very beneficial! The taste it pleasant, not bitter, Simple. Straight forward product and ingredients".

30. Male, Age 51

Presented with: History of general back/spine pain that is a chronic issue for him. Prior to starting Hempflavin he was using Aleve/Naproxen. Dosage: 300mcg Daily. No ASE while taking Hempflavin. Results: Reports he noticed positive results after just one day of 300mcg dose. He did notice it wearing off at night and just did not take another dose before bed. He reported "I have tried many different CBD oils and yours stands out as a higher, more premium product. No bitter taste effect and gave me good relief of my pain and I recommend it to all."

31. Male, Age 61

Presented with: History of chronic pain related to Rheumatoid Arthritis and previously was not taking anything for his pain. Dosage: 300mcg daily with no ASE while taking Hempflavin. Results: After taking Hempflavin he noticed positive effects shortly after taking first dose, but it did not completely take his pain away and that the results varied on how severe of pain he was experiencing and unsure if he should take more than one dose. He stated he would recommend it to family/friends.

32. Male, Age 55

Presented with: History of nerve pain-Quadriplegic. Prior to starting Hempflavin he has been taking many different medications r/t nerve pain and diagnosis of Quadriplegia. Dosage:100mcg twice daily. Reported he was not taking proper dosing likely for his pain. Results: He reported noticing minor results after two days that lasted throughout the day. He did not increase the dosage (which would've been recommended to the 300mcg 1-2x Daily). He stated he obtained a butterfly rash to his face but unsure if it was related to Hempflavin or other medications he was on. But stated it did not bother him much and that he

continues to use Hempflavin and trying increased dosage. He stated that he likes that it helped with his breakthrough pain at night.

33. Female, Age 54

Presented with: History of thumb, arthritic pain and Bilat. Knees. Prior to starting Hempflavin she was not using any medications to tx her pain. Dosage: 300mcg QD AM. No ASE from Hempflavin. Results: She reports that she noticed results about an hour after taking her first dose but didn't feel pain free till two days later. She stated she continues to take Hempflavin with positive results and recommends it to family/friends.

34. Male, Age 50

Presented with: History of RTC pain, lifting weights- General soreness and Bilat knee pain. Dosage: 300mcg. Reports no ASE from taking Hempflavin. Results: He reported that he noticed pain decrease after 15 minutes of first dose and that he has had consistent pain free results since he started taking Hempflavin and he continues to take it daily. "Recommend it to my family and friends".

35. Male, Age 48

Presented with: History of Bilat. Shoulder surgery- Has had chronic shoulder pain despite the surgery. Prior to taking Hempflavin he was taking Motrin. Dosage: Started on 100mcg and then increased to 300mcg. No ASE reported on Hempflavin. Results: He states he received instant relief after 1hour of the first dose and did not notice it wearing off. He states "Great product and great result. It did not 100% take my pain away but it helped greatly". And that he would continue to recommend to family/friends.

36. Female, Age 53

Presented with: History of general back pain and aches, recent diagnosis of Nephrolithiasis. Pain level: 8-10. Prior to Hempflavin she was taking OTC anti-inflammatories. Dosage: 300mcg daily. No ASE from Hempflavin reported. Results: She stated she noticed full relief 1-2 days after starting the Hempflavin and now only taking 100mcg for maintenance.

37. Female, Age 78

Presented with: History of Osteoarthritis to hands, Disfigured fingers and pain from disease. Pain level: 10 and chronic. "Weather greatly affects the pain and frequently has Night-time pain, making it difficult to sleep and/or stay asleep". Dosage: She started on 100mcg, then 200mcg, then 300mcg daily. Results: Prior to Hempflavin she was taking naproxen often and stopped taking it when she started trial and has not needed it since. Reported no adverse side effects. She prefers to not take anti-inflammatories r/t possible liver damage after long-term use and appreciates that hempflavin is so effective without that effect on liver. 1 dropper was not effective for her. When she switched to 3droppers she noticed immediate difference and relief. She continues to take Hempflavin and recommends it to family/friends.

38. Male, Age 52

Presented with: History of pain and inflammation to hands and wrists. Dosage: 300mcg daily. Results: He stated he was completely pain free after the first 2 days of taking Hempflavin. Now he is switching to 100mcg for maintenance dosing. He continues to use product and recommends Hempflavin to family/friends.

39. Female Age 68

Presented with: Injured low back in 1985, and now has two blown discs, two bulging discs, severe spinal stenosis, and arthritis spurs on the spine. Recently, diagnosed with rheumatoid arthritis. She was on strong narcotics for years to deal with the pain but couldn't function with all of the side effects. Pain level: 9-10. Dosage: 300mcg of HempFlavin. Results: "within 10 minutes my pain level was down to a 1-2." After dosing 300mcg once a day, for ten days, she lowered her dose to 100mcg. 100mcg lasts for 24hrs and keeps her pain level at 1-2. She's now exercising and ballroom dancing again. She recommends it for everyone.

40. Male, Age 60

Presented with: "farmed and raised cattle my entire life. This lifestyle certainly takes a toll on your body." He's had 3 surgeries on his right knee, one on his left hand, and one on his left shoulder. He states over the past 30 years the arthritis, swelling, and pain has had him considering knee replacement surgery. Dosage: 300mcg. Results: After his second day of taking 300mcg of HempFlavin, he states that the swelling and pain was "completely under control". He was able to sleep the first night, for 8 hours in his bed, without having to get up and walk due to the pain. He states "HempFlavin should be kept in every farmer's kitchen because I guarantee everyone will use it."

41. Male, Age 31

Active-duty soldier. Presented with: Injury to his knee while running drills. He stated that he had been placed on restricted duty, until he saw a surgeon before deployment. Pain level: 10+, and he was refusing narcotics due to history. He first applied HempFlavin Cooling Cream to his knee, and he said his pain level dropped to a five within two minutes. He also took 300mcg of HempFlavin orally, and he said his pain went to 0 within 15-20 minutes. Within 45 minutes to an hour, the swelling reduced in his knee substantially. He stated he continued applying the HempFlavin Cooling Cream twice a day and taking 300mcg of the HempFlavin tincture once daily. His pain level remained at 0, and the swelling in his knee went back to normal. After three weeks of maintaining this regiment of HempFlavin, he was taken off restricted duty and back to work at 100%. He said HempFlavin and HempFlavin Cooling Cream should be an option for everyone, and not just doctors pushing narcotics. Recommends HempFlavin 100% for pain needs.

42. Male, Age 71

Presented with: Neuropathy of the lower legs and feet caused by chemical exposure, nerve pain in the right hip and right calf. Pain level: 8-9 Dosage: 0.5-1mL twice daily and sometime three times daily as needed. Results: Within minutes pain level went down to 0-1 that lasted 4-5 hours. If the pain is not too bad, I will drop back to 1/2 ml instead of a whole mL.

43. Female, Age 64

Presented with: Chronic Hip pain due to bursitis and Arthritis to hands. Previously was getting Steroid injections, Recent R hand Anchovy Surgery- chronic Hand pain despite surgery. Dosage: She started on 300mcg Hempflavin daily. Results: She was completely pain free "pretty immediately" after a couple of

days. She states, " I love this product and it has helped me avoid another hand surgery (to L hand) with no side effects at all". She reported she forgot to take a dose one day and her pain came back that same day but when she restarted the Hempflavin it was relieved almost as fast as she took it. She continues to use Hempflavin 300mcg a day and plans on switching to 100mcg for Maintenance dose. She highly recommends this products/all product.

44. Female, Age 53

Presented with: History of osteoarthritis causing Chronic hip, knee and back pain. Dosage: She started on 300mcg Hempflavin daily and stated she had a "significant and immediate reduction in pain."

Pain scale: dropped from 8 to 3 within 24 hours and relief lasted 12 hours. She reported an interest in continued use of the product. She highly recommends this product and experienced no side effects from product.

45. Male, Age 54

Presented with: History of left shoulder pain, osteoarthritis and previous slight tear in the rotator cuff.

Dosage: 300mcg Daily. Results: immediate relief within 2 hours sustained for 12-14 hours. Pain level: dropped from 9-10 to 1-2 within 2 hours of taking HempFlavin. He highly recommends product. He was schedule for stem cell treatment and cancelled due to relief he experienced with 300 mcg daily and continues to use product.

46. Male, Age 58

Presented with: History of osteoarthritis causing chronic back and knee pain. Dosage: She started on 300mcg HempFlavin daily and stated he realized a significant reduction in pain. Pain level: dropped from 8.5-3 within 24 hours and relief lasted 10-12 hours. He reported an interest in continued use of the product and recommends it.

ⁱ note 1 ml = 100 mcg and 3 ml = 300 mcg.