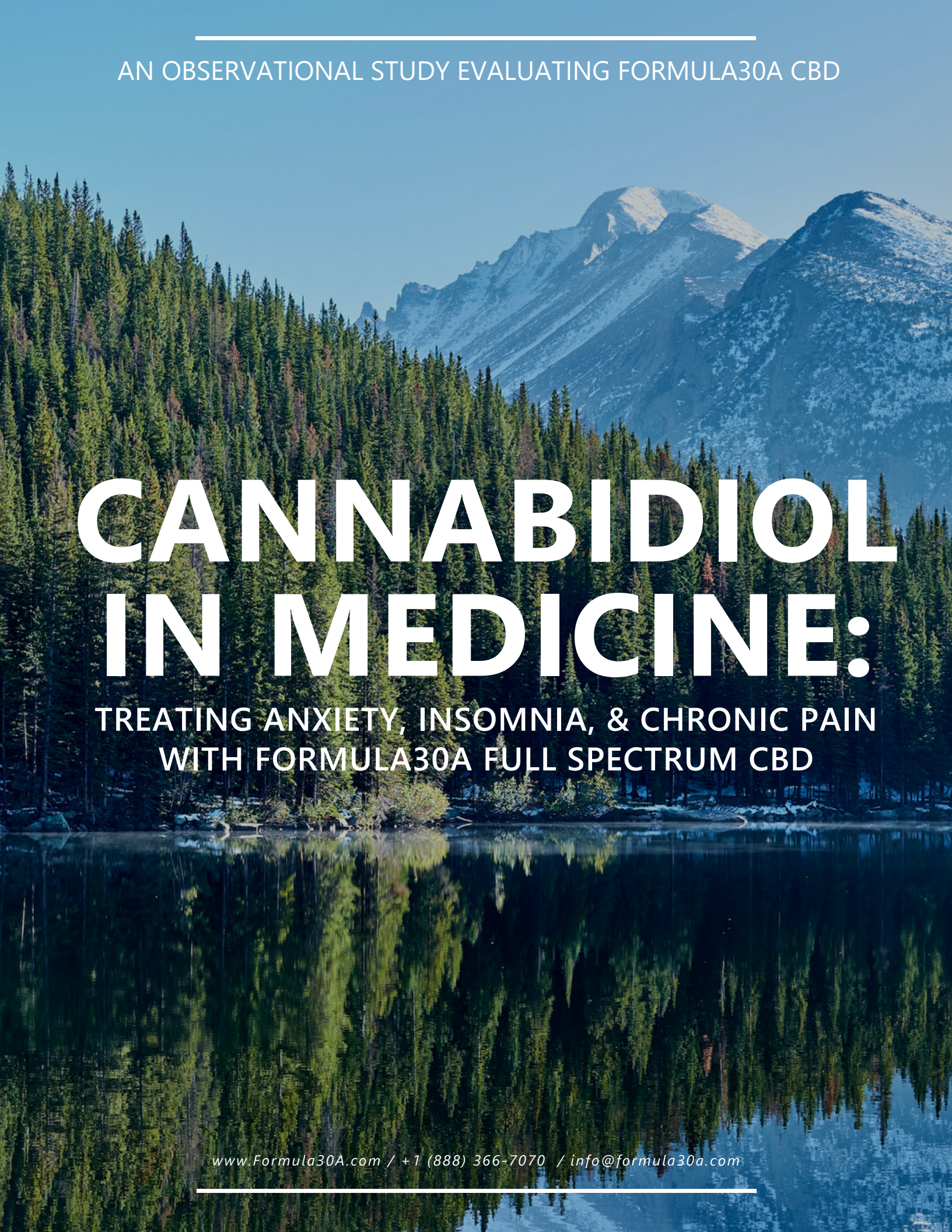
AN OBSERVATIONAL STUDY EVALUATING FORMULA30A CBD



CANNABIDIOL IN MEDICINE:

TREATING ANXIETY, INSOMNIA, & CHRONIC PAIN WITH FORMULA30A FULL SPECTRUM CBD

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ABOUT FORMULA30A

Formula30A is a producer of premium, all-natural hemp products to support daily health, wellness, healing, and recovery. We offer the highest quality cannabidiol (CBD) oils and full-spectrum extracts for healthcare providers and their patients. Industry experts with decades of experience ensure Formula30A products contain the purest ingredients, sourced through the safest methods, to support the pursuit of health and well-being. Our patent-protected manufacturing processes focus on principles of care and quality, delivering practitioners with premium cannabinoid products that meet the medical community's uncompromising standards of safety and efficacy. From seed to plant to the final product, we repeatedly verify the quality and potency of our products with independent 3rd-party lab testing, developing our formulas with the highest quality ingredients to address patients' needs.

Numerous clinical studies now show the beneficial effects cannabinoids have on a variety of illnesses, including anxiety, PTSD, depression, seizures, insomnia, chronic pain, arthritis, and many more. However, the unregulated CBD industry is creating chaos and confusion for the patient population. Patients are asking loved ones for advice or turning to internet searches for answers about cannabinoid products. In this volatile market, medical professionals need to be the trusted source of information and products so that patients can benefit from CBD without getting harmed.

Formula30A seeks to help medical professionals in three areas: educating their staff and their patients on CBD, providing access to CBD to those who need it most, and generating a cash-based revenue stream for our practitioner partners. Our founders have worked together for nearly thirty years in the medical industry helping practitioners source, market, and distribute premium wellness products to their patients. Formula30A provides medical practices with marketing materials and patient seminars to educate patients on the benefits of CBD. Additionally, we train and support medical providers and their staff to help grow their practice revenue stream.

Formula30A is produced with all-natural ingredients using a solvent-free, water-based extraction process. Experienced Colorado growers third-party test each batch at multiple points during the manufacturing process to ensure premium quality. Our products are only available for purchase through our medical practitioner network - you will not find Formula30A on ecommerce retailers! With industry growth projected to surpass $5.3 billion by 2025, CBD presents an immense opportunity for medical practices to thrive while providing significant and often life-changing outcomes for their patients.

Formula30A Full-Spectrum Hemp CBD Extract

Built on an all-natural formula with organic ingredients containing a full-spectrum of cannabidiol, phytocannabinoids, terpenes, and flavonoids that work together to magnify their combined therapeutic benefits.

FULL-SPECTRUM HEMP CBD EXTRACT

Formula30A Full Spectrum Hemp Extract from State Approved Organic Colorado Hemp farmers, using our patented water-based extraction process. What sets us apart from other companies: our Hemp Oil Capsules are made from specially bred industrial hemp plants. These plants are grown using organic farming practices and contain high-potency cannabinoids, essential oils, and terpenes that make for a pure, clean bio-available extract.

ORGANIC COCONUT MCT OIL

Organic Coconut Oil, used as a carrier oil, is the only ingredient added to our high-quality Full Spectrum Hemp Extract. CBD is a fat-soluble compound, so it requires a carrier oil to increase absorption in the bloodstream. The most effective carrier oils are those containing the highest percentage of saturated fats. Organic coconut oil contains approximately 90% saturated fat, thus optimizing bio-availability. It also protects the product from breaking down and becoming rancid, extending the shelf life of our CBD capsules.

VEGAN HEAT-SEALED CAPSULES

CBD Capsules come with a variety of benefits and, unlike tinctures, they are tasteless, easy to dose, and convenient to carry. Formula30A's commitment to pure, clean, and simple products extends through all of our ingredients, including the capsules our natural, organic formulation is delivered in. Not all capsules are created equal. That is why Formula30A CBD is encapsulated in plant-based, vegan caps that are heat-sealed to avoid potentially contaminating chemicals traditionally used to seal other capsules.

Pure. Clean. Simple.

ECO FRIENDLY · NO PESTICIDES · SOLVENT FREE · ORGANICALLY GROWN · MADE WITH NON-GMO INGREDIENTS · K · GOOD MANUFACTURING PRACTICE GMP CERTIFIED · USA GROWN

This product has not been evaluated by the Food and Drug Administration and is not intended to diagnose, treat, cure, or prevent any disease.

A LETTER FROM OUR MEDICAL ADVISORY BOARD

The therapeutic knowledge of cannabinoids is growing rapidly, and exponentially. As a company that produces products with the highest purity and standards, Formula30A has become a leader in physician-directed, premium quality cannabinoid supplementation. In addition to these profound product benefits, Formula30A as an organization believes that continuously seeking new horizons in knowledge surrounding cannabinoids is essential for wellness. These three studies are proof of that quest.

Cannabinoid science is one of the youngest fields in biology. The discovery of the endocannabinoid system (ECS) in the early 1990s, and the subsequent realization that the ECS encompasses the largest regulatory system thus far discovered, is incredibly significant for future therapies. This system is responsible for, among other things, homeostasis in mammalian physiology; it pushes the systems from the red to the green, if you will. The ramifications for therapy cannot be understated.

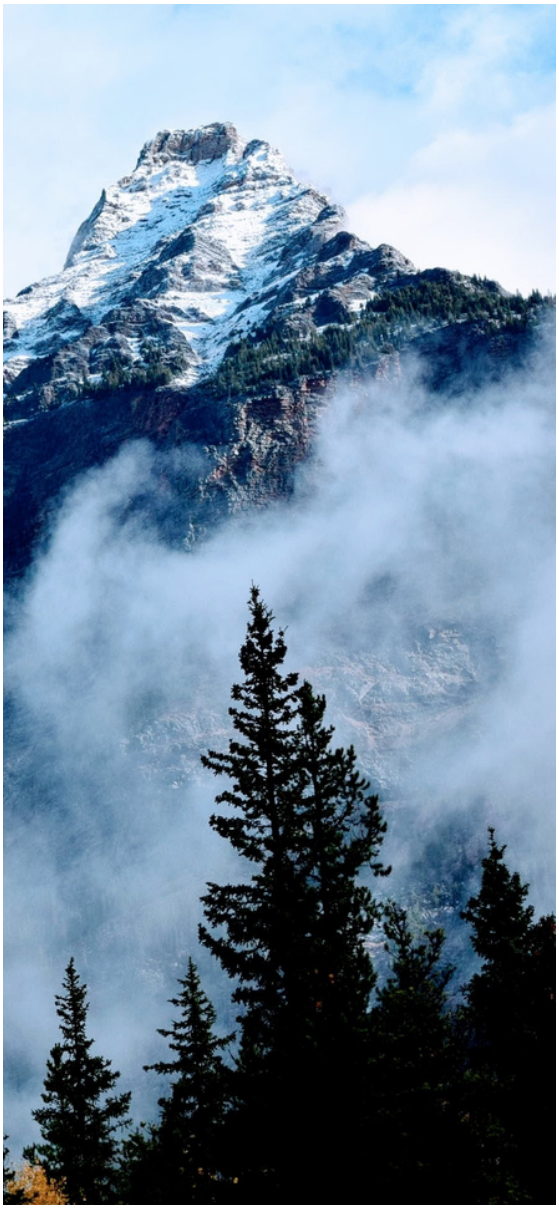
These three early studies suggest the need for continued concentration on the therapeutic benefits of phytocannabinoids to the ECS. Clearly, this work could not be done without the recognition that the non-THC cannabinoids are neither addicting nor intoxicating. The international trend towards relaxing the cannabis laws has continued, and this science is the result.

Our board is composed of many like-minded clinicians and "outside-the-box" thinkers. We learn from one another, and our practices have evolved to help improve wellness with fewer medications used and a focus on lifestyle modifications. In collaboration with these healthcare providers, we pooled our patients in an observational study that yielded results that supported the hypotheses that Formula30A CBD was a safe and effective adjunct to other health strategies for so many health conditions, particularly with regard to insomnia, anxiety, and chronic pain improvements.

Even though these three studies each focused on a specific symptom to investigate, patients under observation reported additional benefits when taking cannabinoids. This can tend to give the cannabidiol molecule the illusion of a "magic bean" of sorts, seeking out what is off axis in the ECS. It's not magic though, it's just biology - the ECS helps to regulate homeostasis in the human body. These observations have brought us to the conclusion that high quality cannabinoid products, such as Formula30A, should be seen and used as a support function for the ECS, as nutrition to the system.

Health and wellness clearly still require attention to improved dietary habits, compliance with exercise routines, and practices to decrease stress. However, balancing the ECS with a full spectrum CBD capsule that is easy to dose and implement has been a game changer for the health of our patients.

- Formula30A 2021 Medical Advisory Board



ABSTRACT

Cannabidiol (CBD) shows promise in clinical trials as an effective treatment for anxiety-related symptoms, insomnia, and chronic pain symptoms lacking the severity of adverse effects seen with other medications. However, CBD products available to the public vary immensely in formulation and resulting efficacy. Our objective was to examine the effects of a specific product, Formula30A Full Spectrum Hemp CBD Extract (25mg capsules), on self-reported anxiety, insomnia, and chronic pain symptoms over the course of eight weeks. We recruited participants from six clinic sites in the United States and Puerto Rico diagnosed with generalized anxiety disorder (GAD), insomnia, and/or experiencing chronic noncancer pain. In order to measure treatment effectiveness throughout the study, we used the Generalized Anxiety Disorder – 7 Item Scale (GAD7), the Insomnia Severity Index (ISI), and the Pain Assessment and Documentation Tool (PADT). Completion of the study required direct clinical observation and medical chart review during Baseline, Midpoint, and Final clinical visits, as well as the completion of weekly survey responses. Our results demonstrate that Formula30A Full Spectrum Hemp CBD Extract capsules exert significant beneficial effects on patient-reported symptom relief in subjects with health conditions associated with anxiety, insomnia, and chronic pain, supporting existing scientific evidence. Data analysis indicates that functional symptoms of anxiety, insomnia, and chronic pain were reduced within the first three weeks of treatment and total GAD7, ISI, and PADT scores were significantly reduced at two weeks compared with Baseline responses.

INTRODUCTION

Fear, alertness, and pain each developed as a part of human nature's greater survival instinct. They serve to keep us aware of potential dangers in the natural world, allow us to respond quickly when threatened, and know when our bodies have been injured and need care. When maladies override or antagonize these mechanisms, however, the results can be harmful both to individuals and the whole of society. Generalized anxiety disorder encompasses a wide array of often debilitating neurological and physical symptoms, such as persistent worrying, inability to relax, difficulty concentrating, and fatigue, and affects approximately 5% of adults in the United States alone at some point in their lives.[1] Often, this leaves patients with decreased quality of life, distress, poorer perceived physical health, and functional impairment, even in patients experiencing symptoms below the clinical diagnosis threshold.[2] Insomnia is a disorder characterized by difficulty falling or staying asleep, or nonrestorative sleep, that is chronic and associated with daytime impairment or distress. Nearly 30% of adults experience symptoms of insomnia, with 10% of the population meeting the daytime impairment or distress diagnostic requirement.[3] The consequences of chronic insomnia can be debilitating, with lower

quality of life reported in nearly every aspect, even when compared against those with congestive heart failure or depression.[3] The term "chronic pain" refers to a range of symptoms and conditions affecting between 50 to 116 million adults in the United States alone. In addition to the individual toll these three disease states impose on patients, they also have immensely detrimental impacts on our society and economy, costing the United States nearly $1 trillion annually in added medical costs and indirect expenses.[4–7] Clinical treatments currently exist to address these symptoms, such as benzodiazepines and selective serotonin reuptake inhibitors for anxiety, nonbenzodiazepine hypnotics and over-the-counter medications for insomnia, or opiates and nonsteroidal anti-inflammatory medications for chronic pain. However, these treatments can be accompanied by adverse effects that limit their real-world efficacy.[8–10] Exploring novel anxiety, insomnia, and chronic pain treatments that are both safe and effective is therefore imperative to alleviating the personal and societal impacts of these symptoms. Cannabidiol (CBD), an intriguing phytocannabinoid derived from the Cannabis sativa plant, is one compound under investigation for its reported anxiolytic and anti-inflammatory effects, as well as its ability to reduce symptom severity with insomnia and chronic pain. Lacking the widely known and often controversial psychoactive effects of Δ9-tetrahydrocannabinol (THC), research on cannabidiol has demonstrated symptom relief for a wide range of disorders,[10–16] due in some part to its effects on activity in limbic and paralimbic areas of the brain.[17] Additionally, CBD has an excellent safety profile with limited adverse effects compared with other available treatments.[18] However, while popular belief holds that CBD is a relatively benign substance, clinical evidence shows that there is a potential for drug-drug interactions. Given the wide availability of products containing CBD on the market today, from tinctures to coffee additives, this underscores the necessity for medical supervision of CBD intake and formulation-specific clinical research. The objective of this study is to observe the effects of Formula30A Full Spectrum Hemp CBD Extract on overall well-being assessed by multiple questionnaires in a group of volunteers recruited from six clinic sites.

METHODS

Procedure

Participants

This open-label, case observation study was conducted at six clinic sites in the United States and Puerto Rico from June 2020 through October 2020. A total of 50 patients with a varying range of anxiety, insomnia, and chronic pain symptoms were recruited to participate in the study. Selection inclusion and exclusion criteria can be found in the Appendix section. The six physicians recruited to participate in the study were each actively prescribing CBD in their practices and were actively caring for patients with anxiety, insomnia, and/or chronic pain symptoms. Clinician Credentials can be found in the Appendix section. They were selected for their collective diversity of expertise in family medicine, internal medicine, gynecology, emergency medicine, infectious disease, and functional medicine, their ready access to patients experiencing symptoms relevant to the study focus, and their experience prescribing CBD as a treatment for their patients. While this may present opportunities for bias, it was felt that having physicians with subject-matter expertise was beneficial in controlling for misinformation surrounding the public image of CBD and cannabinoids in general. The study was carried out in compliance with the Helsinki Declaration of 1975. Informed written consent was obtained from all participants prior to enrollment.

Study Design

Physicians were asked to identify a subset of their patient population that met study inclusion and exclusion parameters. After eligible patients registered to participate in the study, physicians were then instructed to collect initial Baseline data (GAD7, ISI, and/or PADT from a clinical interview, standard medical data, and direct clinical observation). After participants completed their initial clinical visit, they were provided with additional study instructions and a four-week supply of Formula30A CBD. Patients returned at the Midpoint (Week 4) for direct clinical observation and to receive the final four-week supply of Formula30A CBD to complete the study. A summary of the Clinical Visit Protocol can be found in the Appendix. A secure online survey tool was used to administer weekly GAD7/ISI/PADT surveys and collect responses from participants. With prior consent, email and text message reminders were employed to notify participants of upcoming and past due responses to increase survey tool compliance. Responses were collected once a week for eight weeks, starting on the eighth day after their initial Baseline clinic visit. Data collected from all six sites were randomized to obscure identifying information and then sent to the lead investigator for analysis as one cohort. Those who completed all eight weeks, and did not otherwise meet exclusion criteria, were included in the final analyses.

Treatment

Each participant was supplied with one daily 25mg capsule of Formula30A Full Spectrum Hemp CBD Extract, consisting of solvent-free hemp extract and coconut (MCT) oil as a carrier inside hydroxypropyl methylcellulose capsules, for the duration of the eight week study. The formulation under investigation is tested before, during, and after encapsulation for purity, consistency, and contaminants. Capsules used for the study were produced in the same batch, and Certificate of Analysis information can be found in the Appendix. Physicians instructed participants at the Baseline clinical visit to take the treatment at approximately the same time each day and to report any adverse events directly to the clinic. Participants were not instructed to cease any medications during the course of the study, including those used to manage symptoms under investigation, but were instructed to report any changes in their medications or treatment plans to their physician.

METHODS

Study Instruments

The Generalized Anxiety Disorder - 7 Item (GAD7) self-report scale was developed to address a lack of brief clinical measures for assessing GAD. The tool consists of seven questions and asks patients how often during the previous two weeks they were bothered by each symptom. Based on clinical evidence, the GAD-7 is a useful tool both in identifying likely GAD diagnoses due to its strong criterion validity, as well as providing an excellent severity measure, as increasing GAD7 scores are strongly associated with several areas of functional impairment. Cut points were identified, with a cut point of 10 optimizing sensitivity and specificity of the tool. Other benchmark cut points used include the means for those diagnosed with GAD (14.4) and those without GAD (4.9).[19]

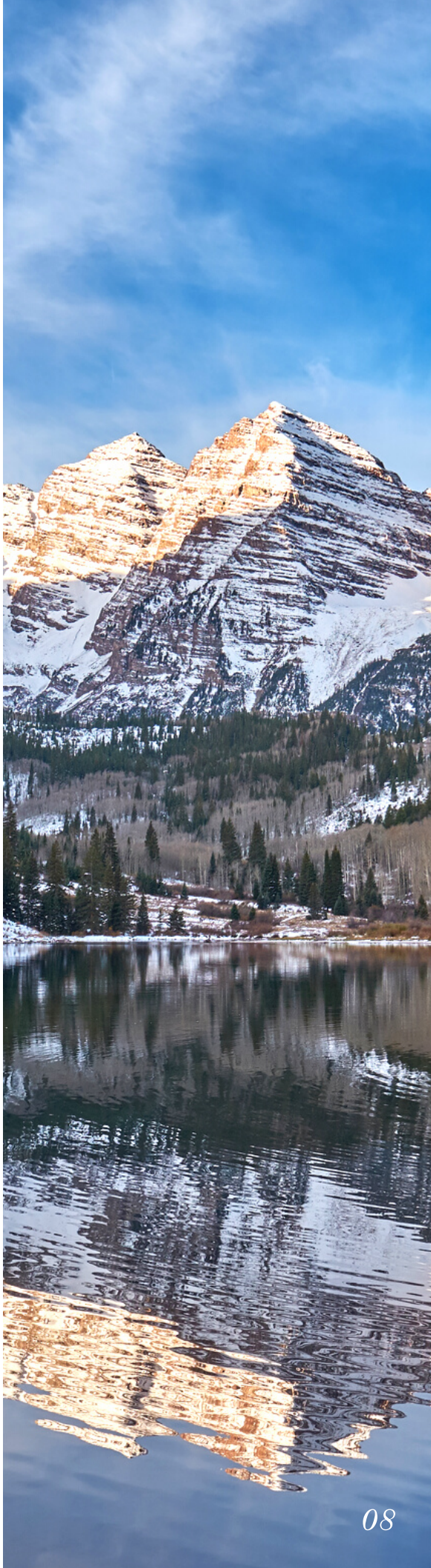
The Insomnia Severity Index (ISI) self-report scale was developed to address a lack of brief clinical measures for detecting insomnia in patient populations. The tool consists of seven questions and asks patients how often during the previous two weeks they were bothered by each symptom. Based on clinical evidence, the ISI is a useful both in identifying likely clinical insomnia diagnoses due to its strong criterion validity, as well as providing an excellent severity measure. Increasing ISI scores are strongly associated with several areas of fatigue, psychological symptoms, and decreased quality of life. Cut points were identified, with a cut point of 10 optimizing sensitivity and specificity of the tool. Other benchmarks used include the threshold for severe clinical insomnia (15) and the threshold for ISI score decrease indicating effective insomnia treatment (-8.4).[20]

The Pain Assessment and Documentation Tool (PADT) assessment scale was developed to address a lack of brief clinical measures for assessing chronic pain. The tool consists of four domains, commonly known as the "Fours As": analgesia, activities of daily living, adverse side effects, and aberrant drug-taking behaviors. Based on clinical evidence, the PADT provides an excellent severity measure, as decreasing analgesia and activities of daily living scores are associated with several areas of impairment.[21] Due to restrictions related to the SARS-CoV-2 (COVID-19) pandemic during the study period, questions related to analgesia and the activities of daily living sections of the PADT were converted to self-report questionnaires, rather than physician-recorded responses from clinical visits. The remaining sections of the PADT, adverse side effects and aberrant drug-related behaviors, were assessed at each of the participants' clinical visits, and individually as reported by participants. For PADT Average Pain (PAP) & PADT Max Pain (PMP) scores, cut points of 5.4 and 7.9, respectively were identified as benchmarks compared to patients with chronic pain being treated with opioids. In order to analyze the seven questions measured on the Same-Better-Worse (SBW) scale, a composite measure was formed by converting each response into an integer (Same = 0, Better = 1, Worse = -1) and combining them for a total SBW score on a -7 to 7 scale. A comparison point of zero was selected for SBW scores, representing no self-perceived change in a respondents pain status. Finally, a benchmark of 30% was selected for Percent Pain Relief (%PR) as compared to patients treated with opioids.[21]

METHODS

Analysis Plan

The goal of this observational study was to determine the effects of Formula30A Full Spectrum Hemp CBD Extract on patients experiencing anxiety, insomnia, and chronic pain symptoms. A secondary objective was to determine the point at which participants experience significant relief of symptoms, if any. To that regard, the data analysis plan was to gather participant responses, relevant demographics, and limited medical information. Descriptive analyses and tests for normalcy were performed to confirm the validity of the data collected. A series of one sample and paired samples z-tests were conducted to examine whether weekly GAD7, ISI, or PADT Scores could have been produced by distributions with means at the aforementioned cut points. Linear regressions were also used to see if number of weeks of treatment accurately predicts GAD7, ISI, or PADT Scores. Additional Friedman rank sum tests were used to explore the differences between Baseline, Midpoint, and Final responses for both PADT scores. Binary logistic regression was used to determine if number of weeks of treatment had a significant effect of observing a "Yes" in response to whether or not a participant's current treatment is working to alleviate pain symptoms. We were also interested to explore whether confounding variables were affecting GAD7, ISI, or PADT results. Path analysis was performed to determine whether SBW scores were mediated by Maximum Pain scores, which may indicate a need to control for overall pain severity when determining treatment efficacy. Finally, hierarchical linear regressions were used to explore the potential confounding effects of Relative Dose (measured as a ratio of milligrams of CBD to the participants average body weight), Age, and Gender.



Participant Data

Participant Characteristics

A total of 30 participants experiencing chronic anxiety symptoms, 33 participants experiencing chronic insomnia symptoms, and 32 participants experiencing chronic pain symptoms were enrolled in the study. From the six clinics, 21 women and 9 men completed the anxiety study, 24 women and 9 men completed the insomnia study, and 23 women and 9 men completed the chronic pain study. The three studies had mean ages of 43.9 years, 49.6 years, and 48.0 years, respectively. The frequency table for physician's participant distribution and gender is presented in Table 1, and bar charts of the samples' age distributions are presented in Figures 1-3.

Protocol Deviations & Violations

Infrequent protocol deviations were encountered during the study, most commonly of which was the need to adjust the treatment time of day due to optimize treatment effects. However, adjustments from day to night and vice versa were reported in relatively equal measure and causes for adjustment varied on a case-by-case basis. Protocol violations include incomplete survey responses and dropout. Reasons for dropout included requirements to start the study, prohibited medications, loss to follow-up, and symptom severity requiring external clinical intervention.

Table 1 - Participant Frequency Table

	ANXIETY	INSOMNIA	PAIN
CLINICIAN			
CLINIC A	7 (23.33%)	9 (27.27%)	10 (31.25%)
CLINIC B	5 (16.67%)	6 (18.18%)	3 (9.38%)
CLINIC C	2 (6.67%)	3 (9.09%)	4 (12.5%)
CLINIC D	9 (30.00%)	9 (27.27%)	7 (21.88%)
CLINIC E	6 (20.00%)	5 (15.15%)	7 (21.88%)
CLINIC F	1 (3.33%)	1 (3.03%)	1 (3.12%)
GENDER			
Male	9 (30.00%)	9 (27.27%)	9 (28.13%)
Female	21 (70.00%)	24 (72.73%)	23 (71.88%)

Note. Due to rounding errors, percentages may not equal 100%.

Fig. 1 - Age Distribution (Anxiety)

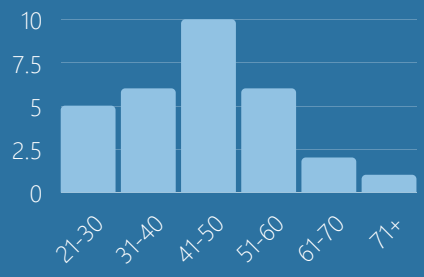


Fig. 2 - Age Distribution (Insomnia)

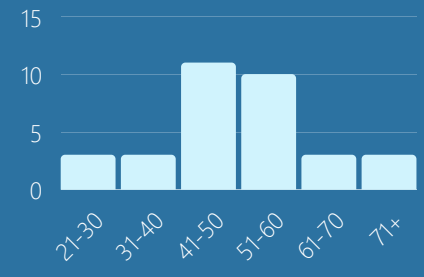
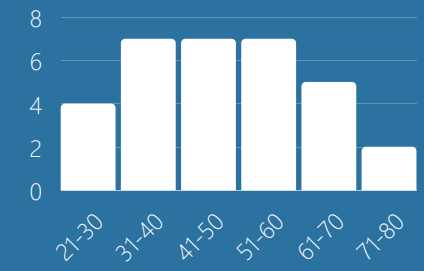


Fig. 3 - Age Distribution (Pain)



RESULTS

Reliability

The GAD7, ISI, and PADT as diagnostic tools each have a high degree of reliability and validity. In order to confirm the reliability of the study observations, Cronbach alpha coefficients were calculated for the scale of GAD7, ISI, and PADT questions. The sample of GAD7 responses had a Cronbach's alpha coefficient of 0.91, indicating excellent reliability. The ISI responses generated a Cronbach's alpha coefficient of 0.80, indicating good reliability. The items for PADT responses generated a Cronbach's alpha coefficient of 0.74, indicating acceptable reliability. Relevant summary statistics for Baseline and Final responses for each question, as well as the total scores, are presented in the Table 2.

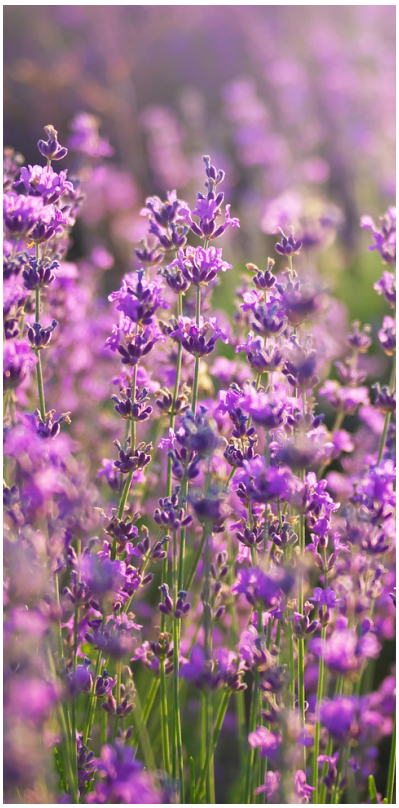


Table 2 - Summary Statistic for GAD7, ISI, & PADT Responses

ANXIETY		**M**	**SD**	**n**	**SEM**	**Min**	**Max**	**Skew**
Feeling nervous, anxious, or on edge?	*Base*	2.50	0.68	30	0.12	1.00	3.00	-0.99
	Final	0.73	0.64	30	0.12	0.00	2.00	0.28
Not being able to stop or control worrying?	*Base*	2.03	0.93	30	0.17	0.00	3.00	-0.33
	Final	0.53	0.51	30	0.09	0.00	1.00	-0.13
Worrying too much about different things?	*Base*	2.23	0.73	30	0.13	1.00	3.00	-0.38
	Final	0.57	0.50	30	0.09	0.00	1.00	-0.27
Trouble relaxing?	*Base*	2.13	0.90	30	0.16	0.00	3.00	-0.55
	Final	0.57	0.68	30	0.12	0.00	2.00	0.76
Being so restless that it is hard to sit still?	*Base*	1.90	0.84	30	0.15	0.00	3.00	-0.51
	Final	0.60	0.67	30	0.12	0.00	2.00	0.66
Becoming easily annoyed or irritable?	*Base*	2.07	0.87	30	0.16	0.00	3.00	-0.45
	Final	0.60	0.56	30	0.10	0.00	2.00	0.19
Feeling afraid as if something awful might happen?	*Base*	1.40	1.10	30	0.20	0.00	3.00	0.10
	Final	0.33	0.48	30	0.09	0.00	1.00	0.71
Total GAD7 Score	*Base*	14.27	4.43	30	0.81	6.00	21.00	-0.23
	Final	3.93	3.17	30	0.58	0.00	10.00	0.21
INSOMNIA		**M**	**SD**	**n**	**SEM**	**Min**	**Max**	**Skew**
Difficulty falling asleep:	*Base*	2.64	1.14	33	0.20	0.00	4.00	-0.66
	Final	0.97	0.88	33	0.15	0.00	3.00	0.61
Difficulty staying asleep:	*Base*	2.67	0.96	33	0.17	1.00	4.00	-0.16
	Final	0.94	0.75	33	0.13	0.00	2.00	0.10
Problems waking up too early:	*Base*	2.27	1.15	33	0.20	0.00	4.00	-0.18
	Final	0.82	0.81	33	0.14	0.00	2.00	0.34
How SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?	*Base*	3.24	0.75	33	0.13	1.00	4.00	-0.87
	Final	1.39	0.90	33	0.16	0.00	3.00	0.19
How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?	*Base*	2.42	1.03	33	0.18	0.00	4.00	-0.23
	Final	0.97	0.77	33	0.13	0.00	3.00	0.47
How WORRIED/DISTRESSED are you about your current sleep problem?	*Base*	2.64	0.99	33	0.17	0.00	4.00	-0.58
	Final	0.76	0.83	33	0.14	0.00	3.00	0.80
To what extent do you consider your sleep problem to INTERFERE with your daily functioning CURRENTLY?	*Base*	2.88	0.96	33	0.17	0.00	4.00	-1.05
	Final	0.85	0.87	33	0.15	0.00	3.00	0.58
Total ISI Score	*Base*	18.76	4.39	33	0.76	5.00	27.00	-0.68
	Final	6.70	4.76	33	0.83	0.00	17.00	0.56
CHRONIC PAIN		**M**	**SD**	**n**	**SEM**	**Min**	**Max**	**Skew**
What was your pain level on average during the past week?	*Base*	6.00	2.16	32	0.38	2.00	10.00	0.02
	Final	3.64	1.87	64	0.23	1.00	9.00	0.81
What was your pain level at its worst during the past week?	*Base*	7.91	1.55	32	0.27	5.00	10.00	-0.53
	Final	5.03	2.32	64	0.29	1.00	10.00	0.21
Same-Better-Worse Composite	*Base*	-0.72	1.53	32	0.27	-4.00	1.00	-1.36
	Final	2.38	3.44	64	0.43	-6.00	6.00	-0.68

Foreword from the Medical Advisory Board

Irritability, racing thoughts, fatigue, excessive worry and fear, insomnia, increased pain, palpitations, panic attacks... Do these symptoms sound familiar? If you have not personally experienced the challenges of anxiety, your patients definitely have. Generalized anxiety disorder, as well as other anxiety disorders such as OCD, social anxiety, and panic attacks, affects millions of people and has increased greatly since the start of the COVID-19 pandemic.

The problem of anxiety is only growing, with prevalence at an all-time high. It is no surprise that prescription anxiolytics and anti-depressants represent a significant expenditure of the global health care dollar. We need practical, accessible, and immediate solutions to help patients balance health and well-being, particularly by decreasing anxiety.

Studies have demonstrated that targeting the Endocannabinoid System (ECS) can help regulate and improve anxiety. The body produces endocannabinoids, which are neurotransmitters that bind to cannabinoid receptors in your nervous system. Given that there is a large concentration of cannabinoid receptors in the central nervous system, it is not surprising that prevailing research shows significant changes in qualitative scoring of anxiety, as well as subjective improvement. We believe that we are at a frontier of knowledge on the endocannabinoid system, and the supplementation of this very important homeostatic regulatory system with exogenous phytocannabinoids such as Formula 30A.

The Medical Advisory Board of Formula 30A utilized the GAD 7 item test (GAD-7) to determine whether there was a significant decrease in anxiety in patients taking Formula 30A. In this study, extensive statistical analysis showed that the data were reliable, and showed significant improvement from baseline to final scores. The mean baseline GAD-7 score for all patients in the study was 14.27 (10-14 moderate anxiety, 15 or greater is severe). The mean after eight weeks of Formula 30A use was 3.93 (0-4 minimal anxiety). This was shown to be significant statistically, with a p value of $< .001$. The objective data alone suggests that exogenous supplementation with Formula 30A is an important adjunct to the health of the ECS, and can be used in therapeutic approaches to these conditions, such as anxiety.

Efficacy

A two-tailed paired samples z-test was conducted to examine whether the mean difference of Baseline and Final GAD7 Scores was significantly different from zero. The observations for Baseline GAD7 Scores had an average of 14.27 (SD = 4.43, SEM = 0.81, Min = 6.00, Max = 21.00, Skewness = -0.23, Mdn = 14.50), while observations for Final GAD7 Scores had an average of 3.93 (SD = 3.17, SEM = 0.58, Min = 0.00, Max = 10.00, Skewness = 0.21, Mdn = 3.50). The results were significant based on an alpha value of 0.05, z = 10.96, p < .001, indicating the null hypothesis can be rejected. This suggests that the difference in means was significantly different from zero and that the Baseline mean was significantly higher than the Final mean. A bar plot of the means is presented in Figure 4. The preceding statistical analysis suggests that participants experienced statistically significant decreases in GAD7 Scores over the course of the study, indicating that treatment with Formula30A CBD may decrease the severity of GAD symptoms.

Two-tailed one sample z-tests were conducted to examine whether GAD7 Scores could have been produced by a probability distribution with a mean at various cut points, split by Week. The comparison metrics used to investigate the efficacy of the product were total GAD7 scores of 14.4, 10, and 4.9. The comparison metric of 14.4 represents the mean GAD7 scores of patients diagnosed with GAD.[19] The result of the two-tailed one sample z-test for Week 0 (Baseline) was not significant based on an alpha value of 0.05, z = -0.17, p = .869, indicating the null hypothesis cannot be rejected. This finding suggests Baseline GAD7 Scores could have been produced by a distribution with a mean (14.27) equal to 14.4. Results for Weeks 1 through 8 were all significant, indicating that the null hypotheses can be rejected and suggesting distributions with means below 14.4.

The comparison metric of 10 represents the diagnosis cut point identified that optimizes sensitivity (89%) and specificity (82%) of GAD7 as a diagnostic tool in a clinical setting.[19] The result of the two-tailed one sample z-test for Week 0 (Baseline) was significant based on an alpha value of 0.05, z = 5.28, p < .001, indicating the null hypothesis can be rejected. This finding suggests Baseline GAD7 Scores were produced by a distribution with a mean (14.27) that is greater than

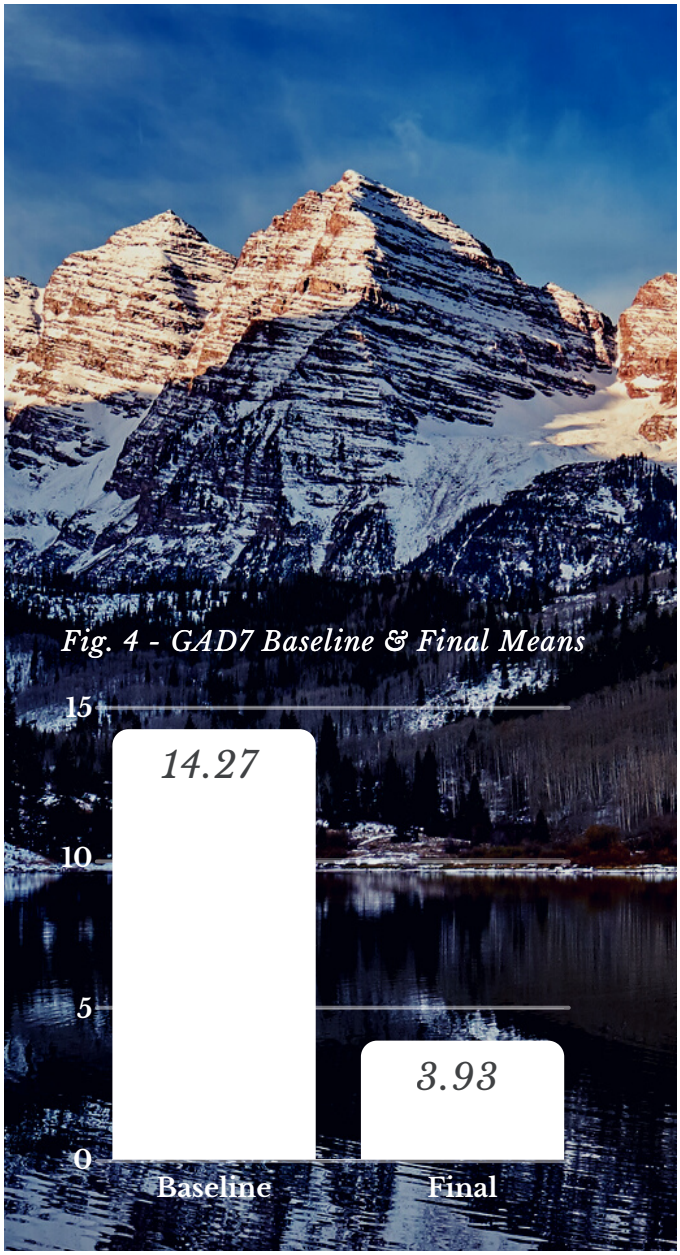


Fig. 4 - GAD7 Baseline & Final Means

10. The results for Week 1 and Week 2 were not significant (z = -0.25, p = .806; z = -1.58, p = .113, respectively) indicating the null hypotheses cannot be rejected. This suggests Week 1 and Week 2 GAD7 Scores could have been produced by distributions with means equal to 10 (9.8 and 8.77, respectively). Results for Week 3 were significant (z = -4.76, p < .001), indicating the null hypothesis can be rejected. This finding suggests GAD7 Scores were produced by a distribution with a mean (6.73) that is less than 10. Week 4 (Midpoint) results were also significant (z = -5.92, p < .001), rejecting the null hypothesis and suggesting Midpoint GAD7 Scores were produced by a distribution with a mean (5.60) that is less than 10. Further analyses of Weeks 5 through 7 were also significant, rejecting

the null hypothesis. This suggests that GAD7 Scores for Weeks 5 through 7 were produced by distributions with means less than 10. Lastly, Week 8 (Final) results were significant ($z = -10.47$, $p < .001$). Thus, we can reject the null hypothesis and infer that Final GAD7 Scores were produced by a distribution with a mean (3.93) that is less than 10.

The comparison metric of 4.9 represents the mean GAD7 scores of patients who did not have GAD.[19] The result of the two-tailed one sample z-test for Week 0 (Baseline) was significant based on an alpha value of 0.05, $z = 11.59$, $p < .001$, indicating the null hypothesis can be rejected. This finding suggests Baseline GAD7 Scores were produced by a distribution with a mean (14.27) that is greater than 4.9. Results for Week 1 ($z = 6.01$, $p < .001$), Week 2 ($z = 4.97$, $p < .001$), and Week 3 ($z = 2.67$, $p = .008$) were also significant, rejecting the null hypothesis and suggesting Midpoint GAD7 Scores were produced by distributions with means greater than 4.9. The results for Week 4 (Midpoint) were not significant ($z = 0.94$, $p = .347$) indicating the null hypotheses cannot be rejected. This suggests Midpoint GAD7 Scores could have been produced by a distribution with a mean (5.60) equal to 4.9. Further analyses of Weeks 5 through 7 were also not significant, indicating the null hypothesis cannot be rejected. This suggests that GAD7 Scores for Weeks 5 through 7 could have been produced by distributions with means equal to 4.9. Lastly, Week 8 (Final) results were not significant ($z = -1.67$, $p = .095$), indicating the null hypothesis cannot be rejected. This finding suggests Final GAD7 Scores could have been produced by a distribution with a mean that is equal to 4.9. Complete weekly results for the selected comparison metrics are presented in Table 3.

Table 3 - z-Test for the Difference between GAD7 Scores and Analysis Points (14.4, 10, & 4.9)

				Test Value: 14.4		Test Value: 10		Test Value: 4.9	
GAD7 SCORES	**M**	**SD**	**μ**	**z**	**p**	**z**	**p**	**z**	**p**
Week 0 (Baseline)	14.27	4.43	10	-0.17	0.869	5.28	< .001	11.59	< .001
Week 1	9.8	4.47	10	-5.64	< .001	-0.25	0.806	6.01	< .001
Week 2	8.77	4.26	10	-7.24	< .001	-1.58	0.113	4.97	< .001
Week 3	6.73	3.76	10	-11.17	< .001	-4.76	< .001	2.67	0.008
Week 4 (Midpoint)	5.6	4.07	10	-11.83	< .001	-5.92	< .001	0.94	0.347
Week 5	5.57	3.16	10	-15.32	< .001	-7.69	< .001	1.16	0.248
Week 6	5.27	4.09	10	-12.22	< .001	-6.33	< .001	0.49	0.624
Week 7	4.33	3.57	10	-15.46	< .001	-8.71	< .001	-0.87	0.384
Week 8 (Final)	3.93	3.17	10	-18.07	< .001	-10.47	< .001	-1.67	0.095

Further linear regression analysis was conducted to assess whether Week significantly predicted GAD7 Score. The results of the linear regression model were significant, $F(8,261) = 21.33$, $p < .001$, $R^2 = 0.40$, indicating that approximately 40% of the variance in GAD7 Score is explainable by Week. Additionally, each individual Week category significantly predicted GAD7 Scores according to the regression model. Based on this sample, this suggests that moving from Week 0 to Week 2 will decrease the mean value of GAD7 Score by 5.50 units on average [$B = -5.50$, $t(261) = -5.44$, $p < .001$]. From Week 0 to the Midpoint of the study at Week 4, the mean value of GAD7 Scores will decrease by 8.67 units on average [$B = -8.67$, $t(261) = -8.57$, $p < .001$]. Finally, by Week 8 this sample suggest that the mean value of GAD7 Scores will decrease by 10.33 units on average ($B = -10.33$, $t(261) = -10.22$, $p < .001$). Table 4 summarizes the results of the regression model. Additionally, a line graph displaying the linear regression model is presented in Figure 5.

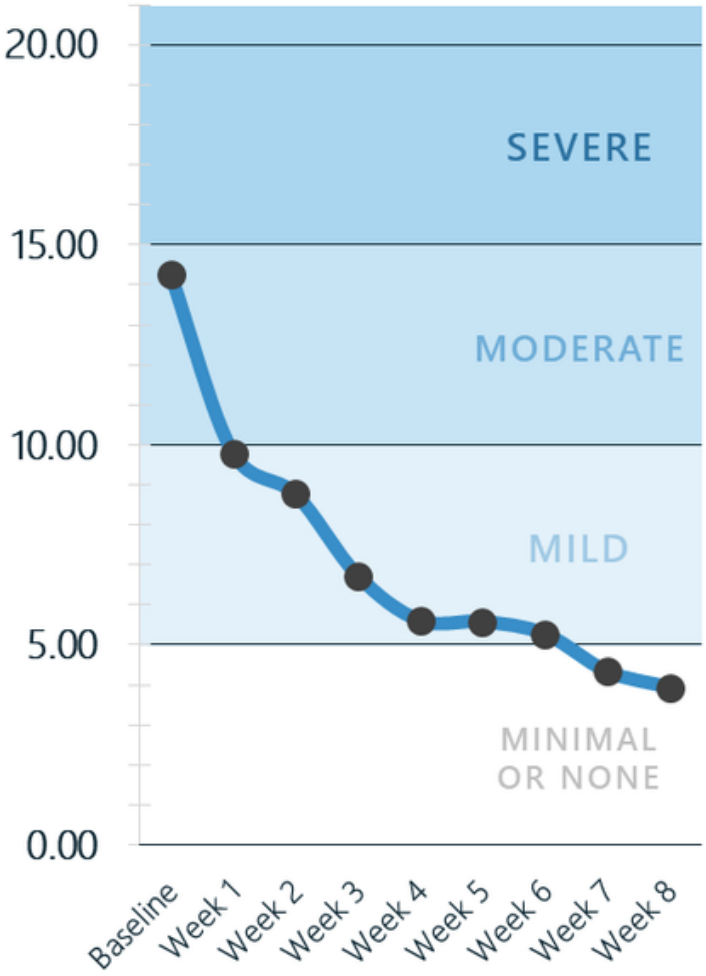
Table 4 - Results for Linear Regression with Week predicting GAD7 Score

GAD7 SCORES	B	SE	95% CI	β	t	p
Week 0 (Baseline)	14.27	0.71	[12.86, 15.67]	0.00	19.96	< .001
Week 1	-4.47	1.01	[-6.46, -2.48]	-0.28	-4.42	< .001
Week 2	-5.50	1.01	[-7.49, -3.51]	-0.35	-5.44	< .001
Week 3	-7.53	1.01	[-9.52, -5.54]	-0.48	-7.45	< .001
Week 4 (Midpoint)	-8.67	1.01	[-10.66, -6.68]	-0.55	-8.57	< .001
Week 5	-8.70	1.01	[-10.69, -6.71]	-0.55	-8.61	< .001
Week 6	-9.00	1.01	[-10.99, -7.01]	-0.57	-8.90	< .001
Week 7	-9.93	1.01	[-11.92, -7.94]	-0.63	-9.83	< .001
Week 8 (Final)	-10.33	1.01	[-12.32, -8.34]	-0.65	-10.22	< .001

72.5%

average decrease in GAD7 Scores after 8 weeks of treatment with Formula30A

Fig. 5 - Linear Regression Line for GAD7 Scores



Note. F(8,288) = 21.13, p < .001, R2 = 0.37
*Unstandardized Regression Equation: Total ISI Score = 18.76 - 4.64*Week1 - 7.94*Week2 - 10.00*Week3 - 9.82*Week4 - 11.12*Week5 - 11.48*Week6 - 11.12*Week7 - 12.06*Week8*

It was also of interest to explore if relative dose a patient received affected the results. A two-step hierarchical linear regression was conducted with GAD7 Score as the dependent variable. For Step 1, Week was entered as a predictor variable into the null model. Relative Dose (µg/kg) was added as a predictor variable into the model at Step 2. Each step in the hierarchical regression was compared to the previous step using F-tests based on an alpha of 0.05. The F-test for Step 1 was significant, F (1, 58) = 108.05, p < .001, ΔR^2 = 0.65, indicating that adding Week explained an additional 65.07% of the variation in GAD7 Score. The F-test for Step 2 was not significant, F (1, 57) = 0.20, p = .656, ΔR^2 = 0.00. This model indicates that adding Relative Dose (µg/kg) did not account for a significant amount of additional variation in GAD7 Score. Week 8 significantly predicted GAD7 Score, B = -10.40, t(57) = -10.29, p < .001. Based on this sample, this suggests that moving from Baseline to Week 8 will decrease the mean value of GAD7 Score by 10.40 units on average. However, Relative Dose did not significantly predict GAD7 Score, B = 0.00, t(57) = 0.45, p = .656, suggesting differences in Relative Dose did not have a significant effect on GAD7 Scores. The results for the model comparisons and for each regression are presented in the Appendix.

Foreword from the Medical Advisory Board

We're not getting enough sleep. That is a fact. Recent research by Mathew Walker, Ph.D. of Berkeley shows that sleep is far more important a factor in life and health span than we previously realized. Not only does it decrease our inflammation and risk of metabolic disorders, it also is the time for healing of the brain. Increasing one's deep and REM sleep is a great strategy to reduce the risk of Alzheimer's disease. Conversely, losing sleep can affect your critical thinking, reaction time, energy, and emotional stability. Lack of quality sleep correlates with increased mental health symptoms and pain. Improving sleep improves overall health and well-being.

Sleep is paramount to our overall wellness. Optimal sleep can improve immune systems, can reduce risks of weight gain, can be great for cardiovascular health, can result in improved mood stability, can improve exercise performance, and is essential for reducing risk for chronic disease and even dementia. The long term negative side effects of therapeutic hypnotics, however, make the class a subpar solution for extended treatment. Additionally, the decrease in effectiveness over time in this class of medications is another difficult issue for patients with chronic insomnia.

The endocannabinoid system (ECS) plays a critical role in circadian components of sleep-wake cycling. By targeting the ECS, studies have demonstrated improvements in decreased sleep onset latency, decreased waking after sleep onset, and increased slow-wave sleep. Long-term studies of sleep quality assessed CBD effects using a common self-report instrument and found a modest improvement in sleep, and more patients with improved sleep compared to poorer sleep.

A small observational trial was organized amongst a group of clinicians comprising the Formula 30A Advisory Board, which impressively validated that Formula30A CBD helped with insomnia improvements. In our study of 33 patients with baseline insomnia, our data showed significant improvement on their Insomnia Severity Index (ISI) after eight weeks on Formula 30A. In fact, after only 3 weeks there was an average decrease of 10 points on their ISI. The mean baseline score was 18.76, which is considered Clinical Insomnia (15-21; moderate severity). Below a score of 8 is considered No Significant Insomnia. This same study group observed many additional potential health impacts of targeting the ECS, including, but not limited to, improvements in chronic pain and anxiety.

Efficacy

A two-tailed paired samples z-test was conducted to examine whether the mean difference of Baseline and Final ISI Scores was significantly different from zero. The observations for Baseline ISI Scores had an average of 18.76 (SD = 4.39, SEM = 0.76, Min = 5.00, Max = 27.00, Skewness = -0.68), while observations for Final ISI Scores had an average of 6.70 (SD = 4.76, SEM = 0.83, Min = 0.00, Max = 17.00, Skewness = 0.56). The results were significant based on an alpha value of 0.05, z = 15.47, p < .001, indicating the null hypothesis can be rejected. This suggests that the difference in means was significantly different from zero and that the Baseline mean was significantly higher than the Final mean. A bar plot of the means is presented in Figure 6. The preceding statistical analysis suggests that participants experienced statistically significant decreases in ISI Scores over the course of the study, indicating that treatment with Formula30A CBD may decrease the severity of insomnia symptoms.

Two-tailed one sample z-tests were conducted to examine whether ISI Scores could have been produced by a probability distribution with a mean at various cut points, split by Week. The comparison metrics used to investigate the efficacy of the product were total ISI scores of 15 and 10. The comparison metric of 15 represents the ISI diagnosis threshold for severe clinical insomnia. The result of the two-tailed one sample z-test for Week 0 (Baseline) was significant based on an alpha value of 0.05, z = 4.92, p < .001, indicating the null hypothesis can be rejected. This finding suggests Baseline ISI Scores were produced by a distribution with a mean (18.76) that is greater than 15. The results for Week 1 were not significant (z = -1.14, p = .254) indicating the null hypotheses cannot be rejected. This suggests Week 1 ISI Scores could have been produced by a distribution with a mean (14.12) equal to 15. Results for Week 2 were significant (z = -5.25, p < .001), indicating the null hypothesis can be rejected. This finding suggests ISI Scores were produced by a distribution with a mean (10.82) that is less than 15. Week 3 results were also significant (z = -7.23, p < .001), rejecting the null hypothesis and suggesting Week 3 ISI Scores were produced by a distribution with a mean (8.76) that is less than 15. Further analyses of Weeks 4 through 7 were also significant, rejecting the null hypothesis. This suggests that ISI Scores for Weeks 4 through 7 were produced by distributions

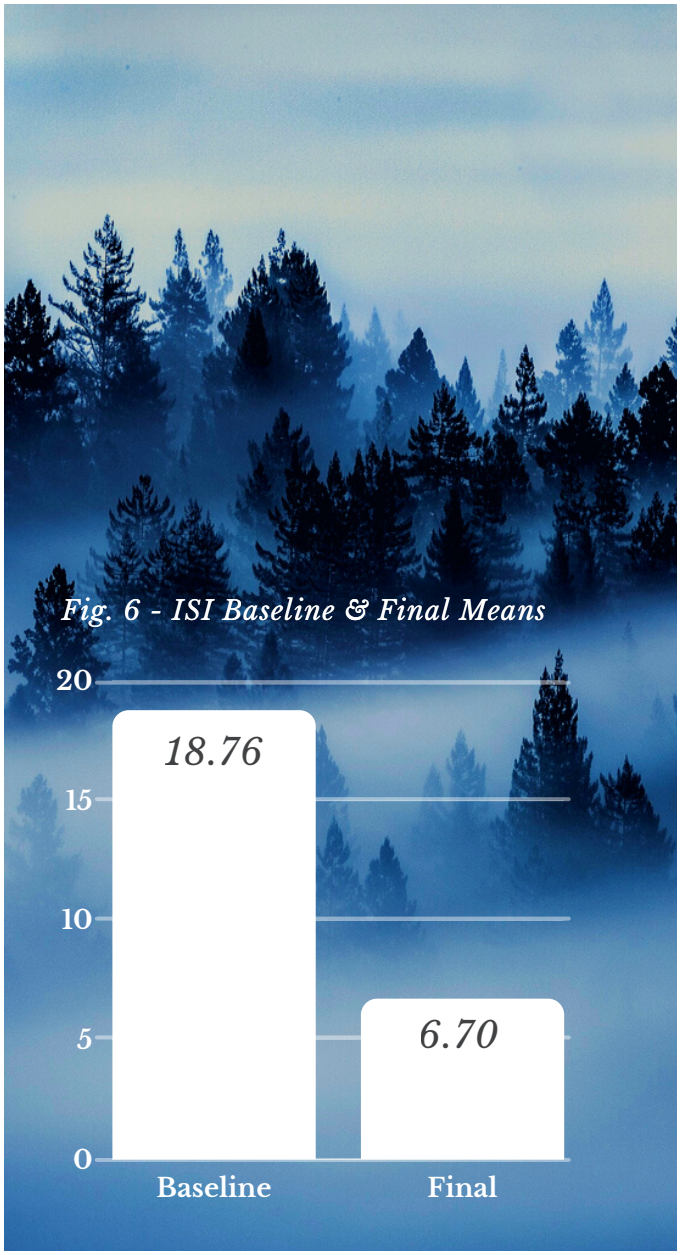


Fig. 6 - ISI Baseline & Final Means

with means less than 15. Lastly, Week 8 (Final) results were significant (z = -10.02, p < .001). Thus, we can reject the null hypothesis and infer that Final ISI Scores were produced by a distribution with a mean (6.70) that is less than 15.

The comparison metric of 10 represents the diagnosis cut point identified that optimizes sensitivity (89%) and specificity (82%) of ISI as a diagnostic tool in a clinical setting.[20] The result of the two-tailed one sample z-test for Week 0 (Baseline) was significant based on an alpha value of 0.05, z = 11.47, p < .001, indicating the null hypothesis can be rejected. This finding suggests Baseline ISI Scores were produced by a distribution with a mean (18.76) that is greater than 10. Week 1

results were also significant (z = 5.35, p < .001), rejecting the null hypothesis and suggesting Week 1 ISI Scores were produced by a distribution with a mean (14.12) that is greater than 10. Results for Week 2 (z = 1.03, p = .304), Week 3 (z = -1.44, p = .150), and Week 4 (z = -1.07, p = .284) were not significant, indicating the null hypothesis cannot be rejected and suggesting ISI Scores could have been produced by distributions with means (10.82, 8.76, and 8.94, respectively) equal to 10. Results for Week 5 were significant (z = -2.58, p < .001), indicating the null hypothesis can be rejected. This finding suggests ISI Scores were produced by a distribution with a mean (7.64) that is less than 10. Further analyses of Weeks 6 and 7 were also significant, rejecting the null hypothesis. This suggests that ISI Scores for Weeks 6 and 7 were produced by distributions with means less than 10. Lastly, Week 8 (Final) results were significant z = -10.02, p < .001). Thus, we can reject the null hypothesis and infer that Final ISI Scores were produced by a distribution with a mean (6.70) that is less than 10. Complete weekly results for each of the selected comparison metrics are presented in Table 5.

Table 5 - z-Test for the Difference between ISI Scores and Analysis Points (15 & 10)

				Test Value: 15		Test Value: 10	
ISI SCORES	**M**	**SD**	**μ**	**z**	**p**	**z**	**p**
Week 0 (Baseline)	18.76	4.39	15	4.92	< .001	11.47	< .001
Week 1	14.12	4.42	15	-1.14	0.254	5.35	< .001
Week 2	10.82	4.57	15	-5.25	< .001	1.03	0.304
Week 3	8.76	4.96	15	-7.23	< .001	-1.44	0.150
Week 4 (Midpoint)	8.94	5.69	15	-6.12	< .001	-1.07	0.284
Week 5	7.64	5.27	15	-8.03	< .001	-2.58	0.010
Week 6	7.27	5.16	15	-8.60	< .001	-3.04	0.002
Week 7	7.64	5.34	15	-7.92	< .001	-2.54	0.011
Week 8 (Final)	6.70	4.76	15	-10.02	< .001	-3.99	< .001

Further linear regression analysis was conducted to assess whether Week significantly predicted ISI Score. The results of the linear regression model were significant F(8,288) = 21.13, p < .001, R^2 = 0.37, indicating that approximately 37% of the variance in ISI Score is explainable by Week. Additionally, each individual Week category significantly predicted ISI Scores according to the regression model. Based on this sample, this suggests that moving from Week 0 to Week 2 will decrease the mean value of ISI Score by 7.94 units on average [B = -7.94, t(288) = -6.49, p < .001]. From Week 0 to the Midpoint of the study at Week 4, the mean value of ISI Scores will decrease by 9.82 units on average [-9.82, t(288) = -8.02, p < .001. Finally, by Week 8 this sample suggests that the mean value of ISI Scores will decrease by 12.06 units on average [B = -12.06, t(288) = -9.86, p < .001]. Additionally, analysis of the linear regression in comparison to the clinical reduction threshold for effective insomnia treatment, a decrease of 8.4 units, is exceeded from Week 3 of the study on. This suggests that the studied treatment is effective at reducing insomnia symptoms after three weeks of treatment. Table 6 summarizes the results of the regression model. Additionally, a line graph displaying the linear regression model is presented in Figure 7.

It was also of interest to explore if a patient's age or the relative dose a patient received affected the results. A three-step hierarchical linear regression was conducted with ISI Score as the dependent variable. For Step 1, Week was entered as a

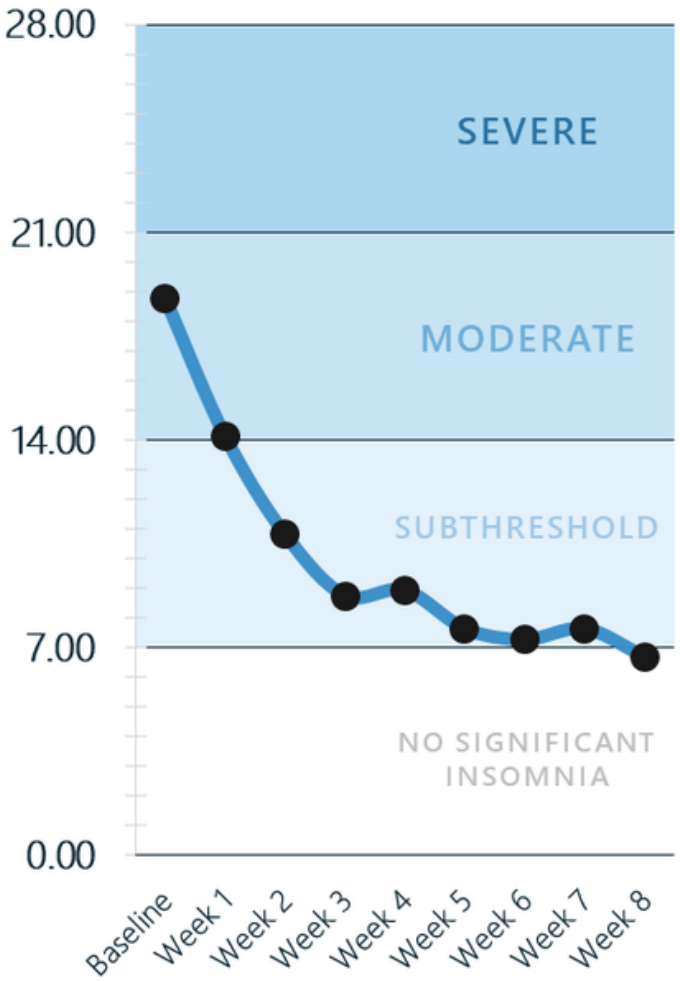
Table 6 - Results for Linear Regression with Week predicting ISI Score

ISI SCORES	B	SE	95% CI	β	t	p
Week 0 (Baseline)	18.76	0.87	[17.05, 20.46]	0.00	21.68	< .001
Week 1	-4.64	1.22	[-7.04, -2.23]	-0.24	-3.79	< .001
Week 2	-7.94	1.22	[-10.35, -5.53]	-0.40	-6.49	< .001
Week 3	-10.00	1.22	[-12.41, -7.59]	-0.51	-8.17	< .001
Week 4 (Midpoint)	-9.82	1.22	[-12.23, -7.41]	-0.50	-8.02	< .001
Week 5	-11.12	1.22	[-13.53, -8.71]	-0.57	-9.09	< .001
Week 6	-11.48	1.22	[-13.89, -9.08]	-0.58	-9.39	< .001
Week 7	-11.12	1.22	[-13.53, -8.71]	-0.57	-9.09	< .001
Week 8 (Final)	-12.06	1.22	[-14.47, -9.65]	-0.61	-9.86	< .001

64.3%

average decrease in ISI Scores after 8 weeks of treatment with Formula30A

Fig. 7 - Linear Regression Line for ISI Scores



Note. F(8,288) = 21.13, p < .001, R2 = 0.37
*Unstandardized Regression Equation: Total ISI Score = 18.76 - 4.64*Week1 - 7.94*Week2 - 10.00*Week3 - 9.82*Week4 - 11.12*Week5 - 11.48*Week6 - 11.12*Week7 - 12.06*Week8*

predictor variable into the null model. Age was added as a predictor variable into the model at Step 2. Relative Dose (µg/kg) was added as a predictor variable into the model at Step 3. Each step in the hierarchical regression was compared to the previous step using F-tests based on an alpha of 0.05. The F-test for Step 1 was significant, F (8, 288) = 21.13, p < .001, ΔR^2 = 0.37. This model indicates that adding Week explained an additional 36.98% of the variation in Total ISI Score. The F-test for Step 2 was significant, F (1, 287) = 26.99, p < .001, ΔR^2 = 0.05. This model indicates that adding Age explained an additional 5.42% of the variation in Total ISI Score. The F-test for Step 3 was significant, F (1, 286) = 32.23, p < .001, ΔR^2 = 0.06. This model indicates that adding Relative Dose explained an additional 5.83% of the variation in Total ISI Score. While this model indicates that age and relative dose each had effects total ISI Scores, further examination indicates the effect is mild and does not impact the overall conclusions of the study. The results for the model comparisons and for each regression are presented in the Appendix.

Foreword from the Medical Advisory Board

Regardless of the origin point, many strategies in medicine try to show the relational connections between emotional pain resulting in physical pain and/or physical pain causing emotional turmoil. As has long been understood and acknowledged, pain can be from an acute or chronic inflammatory process or injury. However, pain is often heightened, and at times originated from, imbalances in the perceptions and understanding of pain.

As we are all aware, there are a large number of people who are addicted to opioid pain medicines. The business of pain is a multi-billion dollar a year venture; from over-the-counter remedies, to prescription narcotics, we spend a great deal of time and money to help alleviate pain. In that quest we have created a crisis for which the medical community and lawmakers are trying to find a solution.

In medical publications, there is a growing acceptance that the development of medical interventions that work ubiquitously (or under most circumstances) for the majority of common chronic conditions is exceptionally difficult and all too often has proved to be fruitless. The endocannabinoid system (ECS), however, holds tremendous value and potential in almost every system of the human body. Sleep improvements, decreased anxiety, and more manageable pain are just a few of the many potential health implications that CBD can help improve.

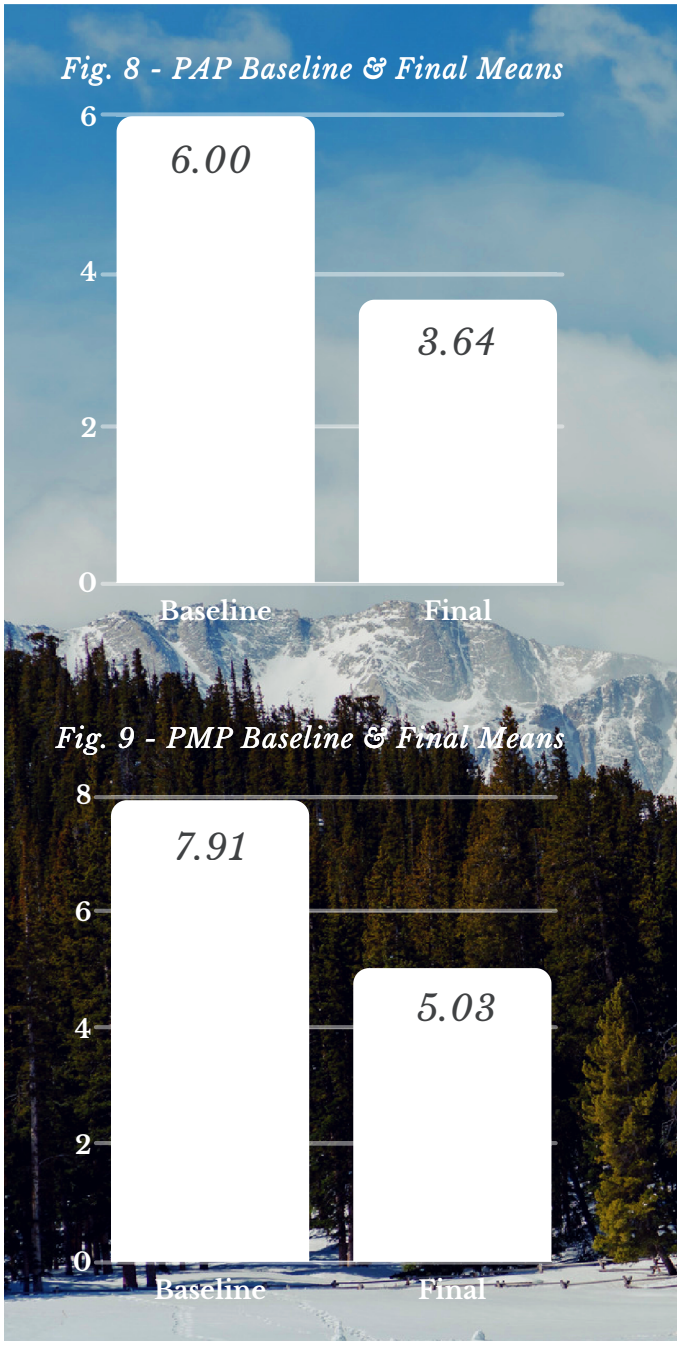
Understanding the ECS can be a critical component in managing basic and complex pain syndromes. Essentially, the body produces endocannabinoids, which are neurotransmitters that bind to cannabinoid receptors in your nervous system. Studies have demonstrated that CBD may help reduce chronic pain by impacting endocannabinoid receptor activity, reducing inflammation, and interacting with neurotransmitters.

With pain as the focus, a small observational study performed by practicing clinicians using 25mg of a Full Spectrum CBD oil resulted in subjectively improved and reduced pain. The Medical Advisory Board of Formula30A used the Pain Assessment and Documentation Tool (PADT) to see if there was a significant improvement in pain utilizing F30A. Extensive statistical analysis proved the data were reliable and that there were no significant differences in response due to gender or age. The data showed that after two weeks on the Formula 30A there was a 25% decrease in average and max pain. By week eight, that improvement was over 40% better than baseline. Statistical significance was proven. This same study group observed many additional potential health impacts of targeting the ECS, including, but not limited to, improvements in sleep and anxiety.

Efficacy

A two-tailed paired samples z-test was conducted to examine whether the mean differences of Baseline and Final Average Pain (PAP), Max Pain (PMP), and Same-Better-Worse Composite (SBW) scores were significantly different from zero. The observations for Baseline PAP Scores had an average of 6.00 (SD = 2.16, SEM = 0.38, Min = 2.00, Max = 10.00, Skewness = 0.02), while observations for Final PAP Scores had an average of 3.64 (SD = 1.87, SEM = 0.23, Min = 1.00, Max = 9.00, Skewness = 0.81). The results were significant based on an alpha value of 0.05, $z = 5.97$, $p < .001$, indicating the null hypothesis can be rejected. This suggests that the difference in means was significantly different from zero and that the Baseline PAP mean was significantly higher than the Final PAP mean. A bar plot of the means is presented in Figure 8. The observations for Baseline PMP Scores had an average of 7.91 (SD = 1.55, SEM = 0.27, Min = 5.00, Max = 10.00, Skewness = -0.53), while observations for Final PAP Scores had an average of 5.03 (SD = 2.32, SEM = 0.29, Min = 1.00, Max = 10.00, Skewness = 0.21). The results were significant based on an alpha value of 0.05, $z = 6.98$, $p < .001$, indicating the null hypothesis can be rejected. This suggests that the difference in means was significantly different from zero and that the Baseline PMP mean was significantly higher than the Final PMP mean. A bar plot of the means is presented in Figure 9.

Friedman rank sum tests were conducted on PAP and PMP scores to examine whether the medians of Baseline, Midpoint, and Final were equal. The Friedman test is a non-parametric alternative to the repeated measures one-way ANOVA and does not share the ANOVA's distributional assumptions.[22,23] The results of the Friedman test for PAP scores were significant based on an alpha value of 0.05, $\chi^2(2) = 25.80$, $p < .001$, indicating significant differences in the median Baseline, Midpoint, and Final PAP values. The results of the Friedman test for PMP scores were also significant based on an alpha value of 0.05, $\chi^2(2) = 35.91$, $p < .001$, indicating significant differences in the median Baseline, Midpoint, and Final PMP values. Table 7 presents the results of the Friedman rank sum test. Pairwise comparisons were examined between each combination of variables. The results of the multiple comparisons indicated significant differences, based on an alpha value of 0.05,



between the following variable pairs: PAP Baseline-Midpoint, PAP Baseline-Final, PMP Baseline-Midpoint, and PMP Baseline-Final. Table 8 presents the results of the pairwise comparisons.

A binary logistic regression was conducted to examine whether treatment weeks had a significant effect on the odds of observing the "Yes" response to the question "Is the amount of pain relief you are now obtaining from your current pain reliever(s) enough to make a real difference in your life?" The overall model was significant based on an alpha of 0.05, $\chi^2(1) = 13.70$, $p < .001$, suggesting that treatment weeks had a significant effect on the

Table 7 - Freidman Rank Sum Test for PADT

PADT SCORES		Mean Rank	χ2	df	p
Average Pain (PAP)	*Base*	2.64	25.80	2	< .001
	Mid	1.86			
	Final	1.50			
Max Pain (PMP)	*Base*	2.80	35.91	2	< .001
	Mid	1.78			
	Final	1.42			

Table 8 - Pairwise Comparisons of Mean Ranks

PADT SCORES	Group	Observed Diff.	Critical Diff.
Average Pain (PAP)	*Base-Mid*	25.00	19.15
	Base-Final	36.50	19.15
	Mid-Final	11.50	19.15
Max Pain (PMP)	*Base-Mid*	32.50	19.15
	Base-Final	44.00	19.15
	Mid-Final	11.50	19.15

Note. Observed Diff. > Critical Diff. indicate significance at the p < 0.05 level.

odds of observing a Yes response. The regression coefficient for Week was significant, B = 0.17,OR = 1.19, p < .001, indicating that for each additional week of treatment, the odds of observing a Yes response would increase by approximately 19%. Table 9 summarizes the results of the regression model. The preceding statistical analysis suggests that participants experienced statistically significant decreases in PADT Scores over the course of the study, indicating that treatment with Formula30A CBD may decrease the severity of chronic pain symptoms.

Table 9 - Binary Logistic Regression Results

	B	SE	χ2	p	OR	95% CI
Intercept	-0.93	0.23	16.00	< .001	-	-
Week	0.17	0.05	13.11	< .001	1.19	[1.08, 1.31]

Note. $\chi^2(1) = 13.70$, $p < .001$, McFadden $R^2 = 0.03$.

Two-tailed one sample z-tests were conducted to examine whether PADT Scores (PAP, PMP, SBW, and %PR) could have been produced by a probability distribution with a mean at various cut points, split by Week. The comparison metrics used to investigate the efficacy of the product were: PAP = 5.4, PMP = 7.9, SWB = 0, %PR = 30%. The PAP comparison metric of 5.4 represents the PAP mean score for patients prescribed opioids to alleviate chronic pain symptoms.[21] The result of the two-tailed one sample z-test for Week 0 (Baseline) was not significant (z = 1.57, p = .115) indicating the null hypotheses cannot be rejected. This suggests Baseline PAP Scores could have been produced by a distribution with a mean (6.00) equal to 5.4. The results for Week 1 were also not significant (z = -1.73, p = .084) indicating the null hypotheses cannot be rejected and Week 1 PAP Scores could have been produced by a distribution with a mean (4.81) equal to 5.4. Results for Week 2 were significant (z = -2.95, p = .003), indicating the null hypothesis can be rejected. This finding suggests PAP Scores were produced by a distribution with a mean (4.44) that is less than 5.4. Week 3 results were also significant (z = -2.09, p = .037), rejecting the null hypothesis and suggesting Week 3 PAP Scores were produced by a distribution with a mean (4.53) that is less than 5.4. Further analyses of Weeks 4 through 7 were also significant, rejecting the null hypothesis. This suggests that PAP Scores for Weeks 4 through 7 were produced by distributions with means less than 5.4. Lastly, Week 8 (Final) results were significant (z = -5.56, p < .001). Thus, we can reject the null hypothesis and infer that Final PAP Scores were produced by a distribution with a mean (3.50) that is less than 5.4.

The PMP comparison metric of 7.9 represents the PMP mean score for patients prescribed opioids to alleviate chronic pain symptoms.[21] The result of the two-tailed one sample z-test for Week 0 (Baseline) was not significant (z = 0.02, p = .982) indicating the null hypotheses cannot be rejected. This suggests Baseline PMP Scores could have been produced by a distribution with a mean (7.91) equal to 7.9. Results for Week 1 were significant (z = -4.06, p < .001), indicating the null hypothesis can be rejected. This finding suggests PMP Scores were produced by a distribution with a mean (6.50) that is less than 7.9. Week 2 results were also significant (z = -6.15, p < .001), rejecting the null hypothesis and suggesting Week 2 PMP Scores were produced

by a distribution with a mean (5.88) that is less than 7.9. Further analyses of Weeks 3 through 7 were also significant, rejecting the null hypothesis. This suggests that PAP Scores for Weeks 3 through 7 were produced by distributions with means less than 7.9. Lastly, Week 8 (Final) results were significant ($z = -7.19$, $p < .001$). Thus, we can reject the null hypothesis and infer that Final PAP Scores were produced by a distribution with a mean (4.81) that is less than 7.9.

The SBW comparison metric of 0 represents a score indicating no change to participants' self-perceived state and is consistent with validated methods of PADT scoring.[21] The result of the two-tailed one sample z-test for Week 0 (Baseline) was significant based on an alpha value of 0.05, $z = -2.66$, $p = .008$, indicating the null hypothesis can be rejected. This finding suggests Baseline SBW Scores were produced by a distribution with a mean (-0.72) that is less than 0. Week 1 results were also significant ($z = 3.96$, $p < .001$), albeit in the opposite direction, rejecting the null hypothesis and suggesting Week 1 SBW Scores were produced by a distribution with a mean (1.50) that is greater than 0. Further analyses of Weeks 2 through 7 were also significant, rejecting the null hypothesis. This suggests that SBW Scores for Weeks 2 through 7 were produced by distributions with means greater than 0. Lastly, Week 8 (Final) results were significant ($z = 2.98$, $p = .003$). Thus, we can reject the null hypothesis and infer that Final SBW Scores were produced by a distribution with a mean (1.91) that is greater than 0.

The PMP comparison metric of 7.9 represents the PMP mean score for patients prescribed opioids to alleviate chronic pain symptoms.[21] The result of the two-tailed one sample z-test for Week 0 (Baseline) was not significant ($z = 0.00$, $p = 1.000$) indicating the null hypotheses cannot be rejected. This suggests Baseline %PR Scores could have been produced by a distribution with a mean (30.00) equal to 30%. The results for Week 1 were also not significant ($z = 1.73$, $p = .084$) indicating the null hypotheses cannot be rejected and Week 1 %PR Scores could have been produced by a distribution with a mean (38.59) equal to 30%. Results for Week 2 were significant ($z = 3.19$, $p = .001$), indicating the null hypothesis can be rejected. This finding suggests %PR Scores were produced by a distribution with a mean (44.22) that is greater than

41.7%

average decrease in PADT Average Pain Scores after 8 weeks of treatment with Formula30A

39.2%

average decrease in PADT Maximum Pain Scores after 8 weeks of treatment with Formula30A

30%. Week 3 results were also significant ($z = 2.34$, $p = .019$), rejecting the null hypothesis and suggesting Week 3 %PR Scores were produced by a distribution with a mean (41.25) that is greater than 30%. Further analyses of Weeks 4 through 7 were also significant, rejecting the null hypothesis. This suggests that %PR Scores for Weeks 4 through 7 were produced by distributions with means greater than 30%. Lastly, Week 8 (Final) results were significant ($z = 2.02$, $p = .049$). Thus, we can reject the null hypothesis and infer that Final %PR Scores were produced by a distribution with a mean (41.09) that is greater than 30%. Complete weekly results for the selected comparison metrics are presented in Tables 10-13.

Further linear regression analysis was conducted to assess whether Week significantly predicted PAP, PMP, and SBW Scores. The results of the linear regression model for Average Pain Score were significant, $F(8,279) = 3.83$, $p < .001$, $R^2 = 0.10$, indicating that approximately 10% of the variance in PAP Score is explainable by Week. Additionally, each individual Week category significantly predicted PAP Scores according to the regression model. Based on this sample, this suggests that moving from Week 0 to Week 2 will decrease the mean value of PAP Score by 1.56 units on average [$B = -1.56$, $t(279) = -3.07$, $p = .002$]. From Week 0 to the Midpoint of the study at Week 4, the mean

Table 10- z-Test for Difference between PADT Avg. Pain Scores and Analysis Point (5.4)

PAP SCORES	M	SD	μ	z	p
Week 0 (Baseline)	6.00	2.16	5.4	1.57	0.115
Week 1	4.81	1.93	5.4	-1.73	0.084
Week 2	4.44	1.85	5.4	-2.95	0.003
Week 3	4.53	2.36	5.4	-2.09	0.037
Week 4 (Midpoint)	4.31	2.04	5.4	-3.02	0.003
Week 5	4.50	2.20	5.4	-2.31	0.021
Week 6	4.22	1.98	5.4	-3.38	< .001
Week 7	3.78	1.83	5.4	-5.01	< .001
Week 8 (Final)	3.50	1.93	5.4	-5.56	< .001

Table 11 - z-Test for Difference between PADT Max Pain Scores and Analysis Point (7.9)

PMP SCORES	M	SD	μ	z	p
Week 0 (Baseline)	7.91	1.55	7.9	0.02	0.982
Week 1	6.50	1.95	7.9	-4.06	< .001
Week 2	5.88	1.86	7.9	-6.15	< .001
Week 3	5.81	2.40	7.9	-4.92	< .001
Week 4 (Midpoint)	5.53	2.24	7.9	-5.97	< .001
Week 5	5.88	2.23	7.9	-5.15	< .001
Week 6	5.50	2.17	7.9	-6.26	< .001
Week 7	5.25	2.23	7.9	-6.73	< .001
Week 8 (Final)	4.81	2.43	7.9	-7.19	< .001

Table 12 - z-Test for Difference between Same-Better-Worse Scores and Analysis Point (0.0)

SBW SCORES	M	SD	μ	z	p
Week 0 (Baseline)	-0.72	1.53	0	-2.66	0.008
Week 1	1.50	2.14	0	3.96	< .001
Week 2	2.75	2.40	0	6.49	< .001
Week 3	2.19	3.00	0	4.13	< .001
Week 4 (Midpoint)	1.53	3.24	0	2.67	0.008
Week 5	1.81	2.75	0	3.72	< .001
Week 6	2.19	3.13	0	3.96	< .001
Week 7	2.84	3.24	0	4.96	< .001
Week 8 (Final)	1.91	3.61	0	2.98	0.003

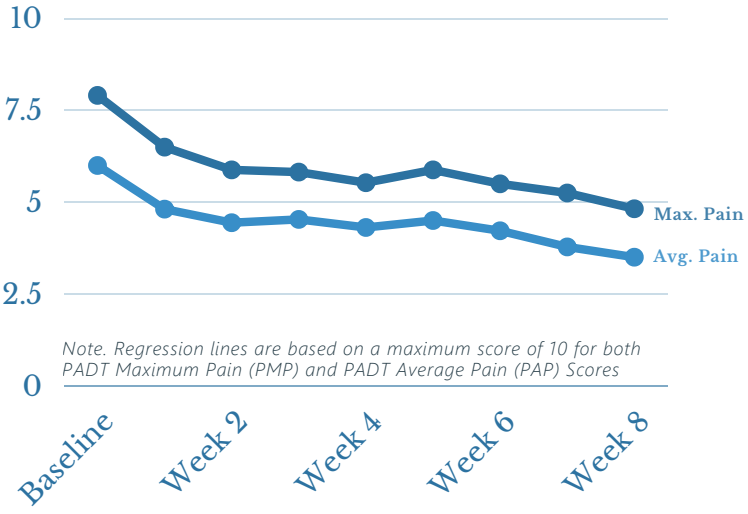
Table 13 - z-Test for Difference between % Pain Relief Scores and Analysis Point (30%)

%PR SCORES	M	SD	μ	z	p
Week 0 (Baseline)	30.00	26.94	30	0.00	1.000
Week 1	38.59	28.12	30	1.73	0.084
Week 2	44.22	25.18	30	3.19	0.001
Week 3	41.25	27.21	30	2.34	0.019
Week 4 (Midpoint)	43.75	30.90	30	2.52	0.012
Week 5	45.78	27.42	30	3.26	0.001
Week 6	41.09	29.53	30	2.12	0.034
Week 7	45.78	31.68	30	2.82	0.005
Week 8 (Final)	41.09	30.77	30	2.02	0.049

value of PAP Scores will decrease by 1.69 units on average [B = -1.69, t(279) = -3.32, p = .001]. Finally, by Week 8 this sample suggest that the mean value of PAP Scores will decrease by 2.50 units on average [B = -2.50, t(279) = -4.91, p < .001]. The results of the linear regression model for Max Pain Score were significant, F(8,279) = 5.53, p < .001, R^2 = 0.14, indicating that approximately 14% of the variance in PMP Score is explainable by Week. Additionally, each individual Week category significantly predicted PMP Scores according to the regression model. Based on this sample, this suggests that moving from Week 0 to Week 2 will decrease the mean value of PMP Score by 2.03 units on average [B = -2.03, t(279) = -3.81, p < .001]. From Week 0 to the Midpoint of the study at Week 4, the mean value of PMP Scores will decrease by 2.38 units on average [B = -2.38, t(279) = -4.45, p < .001]. Finally, by Week 8 this sample suggest that the mean value of PMP Scores will decrease by 3.09 units on average [B = -3.09, t(279) = -5.80, p < .001]. The results of the linear regression model for Same-Better-Worse Composite Score were significant, F(8,279) = 4.34, p < .001, R^2 = 0.11, indicating that approximately 11% of the variance in SBW Score is explainable by Week. Additionally, each individual Week category significantly predicted SBW Scores according to the regression model. Based on this sample, this suggests that moving from Week 0 to Week 2 will increase the mean value of SBW Score by 3.47 units on average [B = 3.47, t(279) = 4.87, p < .001]. From Week 0 to the Midpoint of the study at Week 4, the mean value of SBW Scores will increase by 2.25 units on average [B = 2.25, t(279) = 3.16, p = .002]. Finally, by Week 8 this sample suggest that the mean value of SBW Scores will increase by 2.63 units on average [B = 2.63, t(279) = 3.68, p < .001]. Table 14 summarizes the results of the regression model. Additionally, visualizations the linear regression models are presented in Figures 10 & 11.

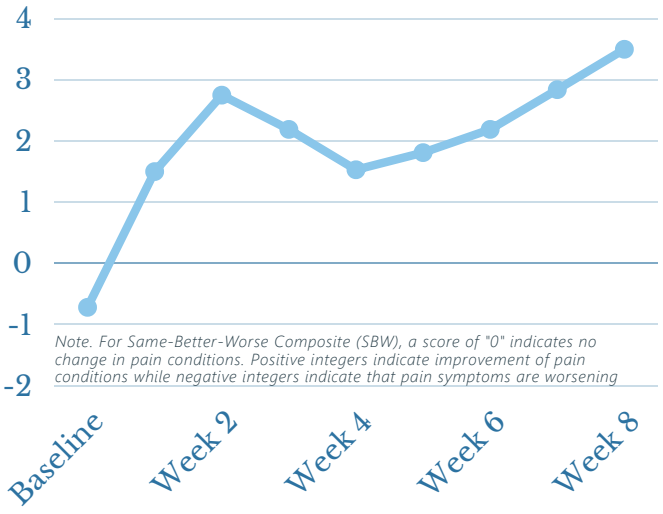
We were additionally interested in examining the results of perceived pain status (SBW Score) when

Fig. 10 - Linear Regression Lines for PAP & PMP Scores



Note. Regression lines are based on a maximum score of 10 for both PADT Maximum Pain (PMP) and PADT Average Pain (PAP) Scores

Fig. 11 - Linear Regression Lines for SBW Scores



Note. For Same-Better-Worse Composite (SBW), a score of "0" indicates no change in pain conditions. Positive integers indicate improvement of pain conditions while negative integers indicate that pain symptoms are worsening

Table 14 - Results for Linear Regression with Week predicting PAP, PMP, & SBW Scores

PADT SCORES		B	SE	95% CI	β	t	p
Average Pain *(PAP)*	*Intercept*	6.00	0.36	[5.29, 6.71]	0.00	16.67	< .001
	Week 1	-1.19	0.51	[-2.19, -0.19]	-0.18	-2.33	0.020
	Week 2	-1.56	0.51	[-2.56, -0.56]	-0.23	-3.07	0.002
	Week 3	-1.47	0.51	[-2.47, -0.47]	-0.22	-2.89	0.004
	Week 4	-1.69	0.51	[-2.69, -0.69]	-0.25	-3.32	0.001
	Week 5	-1.50	0.51	[-2.50, -0.50]	-0.22	-2.95	0.003
	Week 6	-1.78	0.51	[-2.78, -0.78]	-0.26	-3.50	< .001
	Week 7	-2.22	0.51	[-3.22, -1.22]	-0.33	-4.36	< .001
	Week 8	-2.50	0.51	[-3.50, -1.50]	-0.37	-4.91	< .001
Maximum Pain *(PMP)*	*Intercept*	7.91	0.38	[7.16, 8.65]	0.00	20.95	< .001
	Week 1	-1.41	0.53	[-2.46, -0.36]	-0.20	-2.63	0.009
	Week 2	-2.03	0.53	[-3.08, -0.98]	-0.28	-3.81	< .001
	Week 3	-2.09	0.53	[-3.14, -1.04]	-0.29	-3.92	< .001
	Week 4	-2.38	0.53	[-3.43, -1.32]	-0.33	-4.45	< .001
	Week 5	-2.03	0.53	[-3.08, -0.98]	-0.28	-3.81	< .001
	Week 6	-2.41	0.53	[-3.46, -1.36]	-0.33	-4.51	< .001
	Week 7	-2.66	0.53	[-3.71, -1.61]	-0.37	-4.98	< .001
	Week 8	-3.09	0.53	[-4.14, -2.04]	-0.43	-5.80	< .001
Same-Better-Worse Composite *(SBW)*	*Intercept*	-0.72	0.50	[-1.71, 0.27]	0.00	-1.43	0.155
	Week 1	2.22	0.71	[0.82, 3.62]	0.23	3.11	0.002
	Week 2	3.47	0.71	[2.07, 4.87]	0.37	4.87	< .001
	Week 3	2.91	0.71	[1.50, 4.31]	0.31	4.08	< .001
	Week 4	2.25	0.71	[0.85, 3.65]	0.24	3.16	0.002
	Week 5	2.53	0.71	[1.13, 3.93]	0.27	3.55	< .001
	Week 6	2.91	0.71	[1.50, 4.31]	0.31	4.08	< .001
	Week 7	3.56	0.71	[2.16, 4.97]	0.38	5.00	< .001
	Week 8	2.63	0.71	[1.22, 4.03]	0.28	3.68	< .001

controlling for participants' pain severity as measured by their Max Pain Score. A path analysis model was conducted to determine whether the model of regressions accurately describe the data. Maximum likelihood estimation was performed to determine the standard errors for the parameter estimates. Influential points were identified in the data by calculating Mahalanobis distances and comparing them with the quantiles of a χ^2 distribution. There was 1 observation detected as an outlier, defined as any Mahalanobis distance that exceeds the .999 quantile of a χ^2 distribution (16.27) with 3 degrees of freedom. To assess multicollinearity, the squared multiple correlations were inspected, and the determinant of the correlation matrix was calculated. There were no variables that had an $R^2 > .90$ and the value of the determinant for the correlation matrix was 0.7375, indicating that there was no multicollinearity in the data. First, the reliability of the analysis was tested based on the sample size used to construct the model. Next, the results were evaluated using the Chi-square goodness of fit test and fit indices. Lastly, the squared multiple correlations (R^2) for each endogenous variable were examined. The results of the path analysis model are presented in Table 8. The participant to item ratio for this analysis was approximately 57 to 1, where sample size was 288 and the number of variables included was 5. According to the N:q ratio rule-of-thumb, the given sample size is sufficient to produce reliable results. The regressions were examined based on an alpha value of 0.05. Week did not significantly predict SBW, B = 0.07, z = 1.08, p = .280, suggesting there is no relationship between Week and SBW Score. Week significantly predicted PMP Score, B = -0.28, z = -5.73, p < .001, indicating a one-unit increase in Week will decrease the expected value of PMP Score by 0.28 units. PMP Score significantly predicted SBW Score, B = -0.52, z = -7.08, p < .001, indicating a one-unit increase in PMP Score will decrease the expected value of SBW Score by 0.52 units. A test of mediation was conducted based on an alpha of 0.05 to determine whether PMP Scores mediated the relationship between Week and SBW Score. The direct effect between Week and SBW Score was not significant, suggesting that full mediation by PMP Score may have occurred. Full mediation was examined using the indirect and total effects of PMP Score on the relationship between Week and SBW Score. The indirect effect of PMP Score on the relationship of SBW Score regressed on Week was significant, B = 0.15, z = 4.45, p < .001, indicating a one-unit increase in Week, based on its effect on PMP Score, will increase the expected value of SBW Score by 0.15 units. The total effect of Week on SBW Score was significant, B = 0.22, z = 3.26, p = .001, indicating a one-unit increase in Week will increase the expected value of SBW by 0.22 units. Since the indirect and total effects were significant, full mediation was supported by PMP Score.[24–26]

Table 15 - Path Analysis Model Results

Parameter Estimate	Unstandardized	Standardized	p
SBW ← Week	0.07(0.06)	0.06	.280
PMP ← Week	-0.28(0.05)	-0.32	< .001
SBW ← PMP	-0.52(0.07)	-0.40	< .001
Indir. Effect of SBW On Week by PMP	0.15(0.03)	0.13	< .001
Total Effect of SBW on Week	0.22(0.07)	0.19	.001
Error in SBW	7.27(0.61)	0.82	< .001
Error in PMP	4.59(0.38)	0.90	< .001
Error in Week	6.67(0.00)	1.00	--

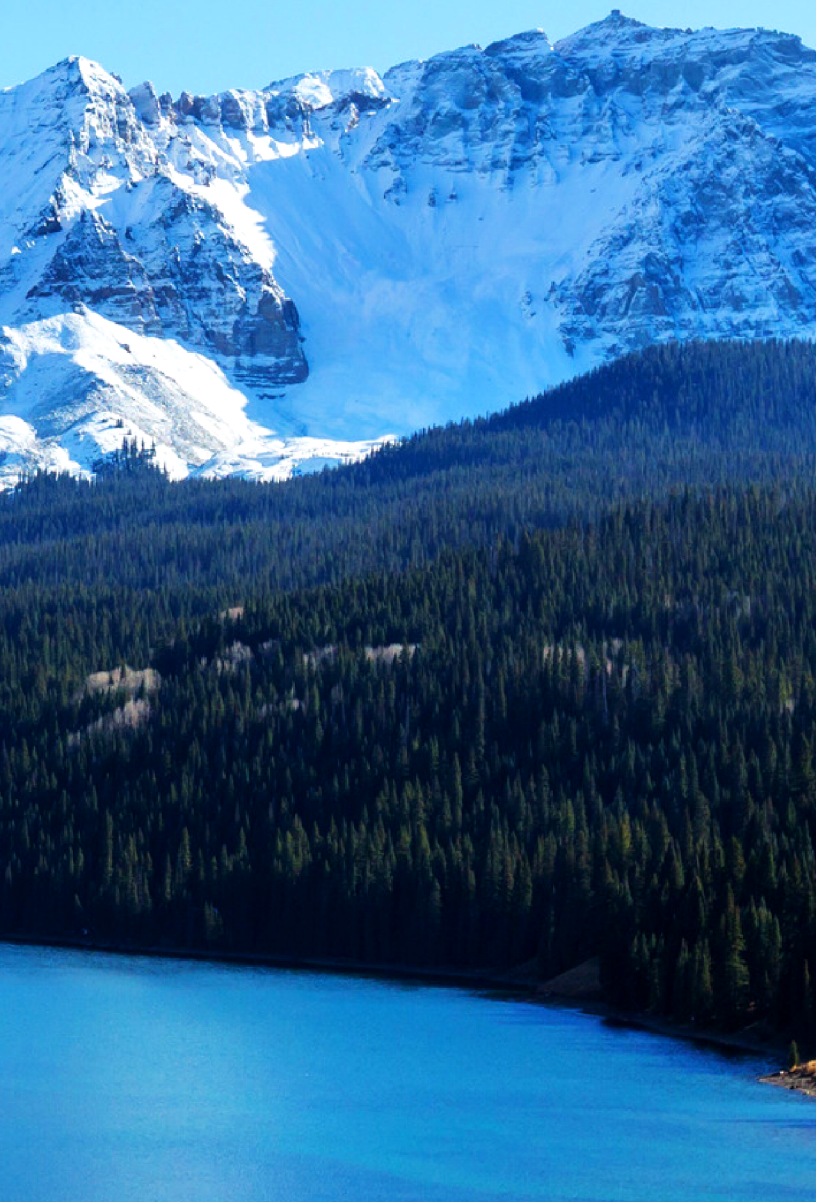
Lastly, it was also of interest to explore if other factors affected the results, such as age, gender, and relative pain severity. Three-step hierarchical linear regressions were conducted with PAP, PMP, and SBW Scores as the dependent variables. For Step 1, Gender was entered as a predictor variable into the null model. Age was added as a predictor variable into the model at Step 2. Week was added as a predictor variable into the model at Step 3. Each step in the hierarchical regression was compared to the previous step using F-tests based on an alpha of 0.05. For all three measure, the F-tests for Step 1 and Step 2 were not significant, indicating that adding Age and Gender did not account for a significant amount of variation in PAP, PMP, or SWB Scores. The PAP F-test for Step 3 was significant, F (1, 284) = 23.68, p < .001, $\Delta R^2 = 0.08$, indicating that adding Week explained an additional 7.64% of the variation in PAP Score. The PMP F-test for Step 3 was significant, F (1, 284) = 32.90, p < .001, $\Delta R^2 = 0.10$, indicating that adding Week explained an additional 10.24% of the variation in PAP Score. The SBW F-test for Step 3 was significant, F (1, 284) = 10.51, p = .001, $\Delta R^2 = 0.04$, indicating that adding Week explained an additional 3.55% of the variation in PAP Score. The results for the model comparisons and for each regression are presented in the Appendix.

RESULTS

Safety

Adverse events are presented below:

COVID-19 Quarantine: one participant withdrew
Leaving the Country: one participant withdrew
Non-Compliance: two participants removed
Insomnia Severity: one participant withdrew
Unrelated Surgery: two participants withdrew
Unelated Medical Reason: one participant withdrew



Individual Case Management

Of the participant sample that completed the study, the following six cases are described in detail.

ANXIETY CASES

Case One (30 y/o Male)
BACKGROUND: This patient is a 30 y/o male with chronic co-morbidities of metabolic syndrome, obesity, hormone imbalance, Obstructive Sleep Apnea, and anxiety. Anxiety levels affect work and home life.
BASELINE: Patient had varied levels of compliance in the past with treatment strategies for all health concerns. He became more serious about health after experiencing higher levels of stress after COVID affected home and work environments.
NUTRITION MANAGEMENT: The patient was as encouraged to eat a low inflammatory diet and was given recommendations regarding multivitamins and methylated B vitamins.
PROGRESS: Over the course of the study we had three follow-ups, each with reported improvements in anxiety and improvements in lower back pain.
CLINICIAN PERSPECTIVE: Adding Formula30A has had a tremendous impact on his anxiety, helping him re-focus on other health concerns. He has remained on 25mg of Formula30A after the study end and reported sleep improvements as well.

Case Two (61 y/o Female)
BACKGROUND: Patient is a 61 y/o, 162lb. female that has been a patient since 2019. She has history of anxiety, depression and more recently insomnia.
BASELINE: Patient has diagnoses of anxiety, depression, insomnia. These conditions have been treated in the past with SSRIs, SNRIs, and supplements (Melatonin).
NUTRITION MANAGEMENT: Discussion of healthy eating habits and exercise to help with symptoms.
PROGRESS: Enrolled in anxiety, patient's anxiety drastically went down, had less overall anxiety and fewer spikes in anxiety
CLINICIAN PERSPECTIVE: Anxiety dropped quickly and drastically, and her sleep improved. Since stopping Formula30A at study end, she has had increased anxiety, started grinding her teeth, and started other medication. She is considering going back on Formula30A because it is less expensive than the medications used to manage her conditions.

INSOMNIA CASES

Case Three - (67 y/o Male)

BACKGROUND: 67 y/o male patient with chronic pain disorder, Hashimoto's hypothyroidism, and severe insomnia. He agreed to participate in this study to determine if Formula30A might be of benefit for his intractable insomnia.

BASELINE: He was only getting 3 to 4 hours of restful sleep prior to starting Formula30A. He needed to take prescription medication to even get those few short hours of rest.

NUTRITION MANAGEMENT: One nightly 25mg capsule of Formula30A was started and after 2 weeks of improvement increased to 2 capsules.

PROGRESS: Patient reported he was able to get restful sleep of 7 hours by the end of the study.

CLINICIAN PERSPECTIVE: Formula30A is a natural product that can improve sleep quality and duration in many patients. With my patients suffering from insomnia, I currently recommend Formula30A CBD to aid in treatment.

Case Four - (23 y/o Female)

BACKGROUND: Patient is a young female in a post graduate program with significant past medical history of mild, intermittent asthma, depression, and anxiety.

BASELINE: The patient has had fluctuating anxiety and depression since adolescence. After COVID restrictions altered her graduate program, she felt her anxiety increase to the point it limited her ability to perform day-to-day activities without fear or panic. Ruminating thoughts and fear affected her ability to initiate and maintain quality sleep.

NUTRITION MANAGEMENT: She was encouraged to eat a healthy, rotation style meal plan, reminded to lightly exercise, and continue previously advised balanced multivitamins and methylated B vitamins. She was advised to begin taking Formula30A 25mg capsule nightly.

PROGRESS: The patient consistently reported improvements in sleep efficiency and quality, as well as improvements in anxiety.

CLINICIAN PERSPECTIVE: The patient has remained on Formula30A since completion of the study. She continues to report improved sleep characteristics and markedly improved anxiety with no reported depressive symptoms.

CHRONIC PAIN CASES

Case Five - (68 y/o Female)

BACKGROUND: Patient is a 68 y/o female with a history of L shoulder pain for the past few months. Additionally, she had significant reduced range of motion (ROM) of this shoulder joint to the point that it was difficult to put her clothes on by herself.

BASELINE: For the pain, she takes a few OTC Tylenol for relief. She states that this did not relieve the pain on most occasions and also did not improve the ROM. She has not had any manipulation, physical therapy, or massage to the shoulder joint.

NUTRITION MANAGEMENT: Patient was placed on one capsule/day of Formula30A CBD.

PROGRESS: Within 1-2 weeks she reported significant improvement in discomfort levels and also her ROM of the shoulder joint. By the end of the 2 months she was completely pain free and had full ROM of her L shoulder. She also reports having less anxiety since starting Formula30A CBD.

CLINICIAN PERSPECTIVE: No adverse or side effects reported. She continued taking 1 Formula30A CBD capsule per day and has no shoulder issues.

Case Six - (55 y/o Male)

BACKGROUND: Patient with history of HTN, hypothyroidism, anxiety, depression, insomnia, chronic pain and muscle spasms due to multilevel degenerative disc disease of cervical spine with arthropathy and radiculopathy. The patient indicated pain was 9/10.

BASELINE: or those conditions, the patient was under Candesartan, Cymbalta, Lunesta, Celebrex, and Flexeril. As part of his treatment, he was also taking physical therapy and waiting for a neurosurgeon evaluation.

NUTRITION MANAGEMENT: As part of a complete wellness approach, patient was recommended to start an anti inflammatory diet.

PROGRESS: After initiating Formula30A, by week 4 the patient had notable improvement on the pain scale, now indicating pain at a 4/10. The patient also reported better sleep patterns and improvements in his anxiety and depression.

CLINICIAN PERSPECTIVE: In my opinion, the impressive results obtained with Formula30A were due probably to antinociception in inflammatory hyperalgesia and neuropathic pain.

DISCUSSION

Study Conclusions

Preclinical and clinical research currently provide ample research supporting CBD's efficacy in the treatment of symptoms related to generalized anxiety disorder, clinical insomnia, and chronic noncancer pain disorders. Human trials have also shown that CBD is generally well tolerated and lacks comparative adverse effects of currently available treatments. This 8-week multi-center open-label observational study demonstrated that Formula30A, containing Full Spectrum Hemp CBD Extract, exerted beneficial effects on patient-reported symptom relief in subjects with health conditions associated with anxiety, insomnia, and chronic pain, supporting existing scientific evidence. Functional symptoms associated with anxiety, as assessed by various health status questionnaires and quality-of-life questionnaires, were also improved after consumption of Formula30A.

Data analysis indicates statistically significant reductions in GAD symptoms at Week 1, with additional decreases as weeks on Formula30A CBD increase. When compared with means for GAD-diagnosed respondents (14.4), statistically significant decreases were found in Week 1. When compared with the GAD7 diagnosis threshold (10), statistically significant decreases were found in Week 3. When compared with means for respondents without GAD (4.9), no statistically significant difference could be found after Week 5.

Analysis suggests statistically significant reductions in insomnia symptoms at Week 2, with additional decreases as weeks on Formula30A CBD increase. When compared with the ISI threshold for severe clinical insomnia, statistically significant decreases were found in Week 3. When compared with the ISI diagnosis threshold (10), statistically significant decreases were found in Week 5 and continued throughout the study.

Based on the preceding statistical analysis, we can conclude that participants did experience statistically significant decreases in chronic pain symptoms throughout the course of the study. When compared with the Average Pain Score benchmark for chronic pain patients receiving treatment with opioids (5.4), statistically significant decreases were found in Week 2 and continued throughout the remainder of the study. Additionally, when compared with the Maximum Pain Score benchmark for chronic pain patients receiving treatment with opioids (7.9), statistically significant decreases were found from Week 1 onward. Finally, when compared with the S/B/W Composite Score (0) and Percent Pain Relief Score patient baselines for chronic pain patients receiving treatment with opioids (0 and 30%, respectively), statistically significant increases were found from Week 2 onward. This means we can conclude that participants experience significant reduction in chronic pain symptoms by Week 2 of treatment, continuing through the end of the study period.

Functional symptoms of anxiety, insomnia, and chronic pain were reduced within the first three weeks of treatment and total GAD7, ISI, and PADT scores were significantly reduced at two weeks compared with Baseline responses. While the results of this open-label, nonrandomized study should be interpreted with appropriate scientific skepticism, it is clear that Formula30A CBD is a promising tool for decreasing chronic pain symptoms in patient populations.

Acknowledgement

This project was supported with educational grants from Formula30A, LLC.

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To supply the Medical Community and their patients with the finest, high-quality cannabinoid products and lead the industry in clinical research & education. -Formula30A's Mission

APPENDIX

Inclusion & Exclusion Criteria

Study Inclusion Criteria

- Age between 21 and 85 years old.
- Research participants of both sexes.
- Good health conditions and without conditions that characterize them as belonging to the risk groups associated with adverse reactions to the product ingredients.
- Research participants with the potential to become pregnant may be included in the study as long as they are sexually abstinent or using a contraceptive method considered effective.
- Signature of the Free and Informed Consent Term.

Study Exclusion Criteria

- Initiation of or changes in use of medication or therapies in the past 2 weeks of start of study.
- Pregnancy or breastfeeding.
- History of hepatic compromise with transaminases of 2 times the upper limit of normal or cirrhosis.
- Diagnosis of Bi-Polar disorder, Schizophrenia or Suicidal Ideation.
- Current use of recreational marijuana, medical marijuana, or other CBD formulations.
- History of any substance or alcohol abuse.
- Under the age of 18.
- Current use of High Dose or Extended-Release Narcotics.
- Patients diagnosed with sleep apnea.

Clinician Credentials

Dr. Cory Rice, D.O.

Dr. Rice received his undergraduate degree in Biochemistry and Forensic Science from Baylor University before completing medical school in Arizona. He then went on to complete his Residency and was named Chief Resident of the year in Internal Medicine at Methodist Hospital in Dallas. He then worked as a hospitalist and in critical care before devoting himself 100% to outpatient medicine. Today, he owns and operates 2 full-time cash based Functional and Lifestyle Medicine clinics in the Dallas area. His area of expertise is Functional Medicine and Nutrition based chronic disease management along with bioidentical hormone replacement therapy.

Dr. Robin Hall, D.O.

Robin A. Hall, D.O. is board-certified in Family Medicine and has been practicing in the Colleyville/Southlake area since 1991. She graduated magna cum laude from Texas Wesleyan University in Ft. Worth with a B.S. in Biology and a minor in Business. After completing medical school and her family practice residency from the University of North Texas Health Science Center (Texas College of Osteopathic Medicine), she founded Colleyville Family Medicine where she practiced from 1991-2005. In 2006, Dr. Hall opened Destination Health®, a unique concierge medical practice that was the first of its kind in the area. This model allows her to provide comprehensive, optimal and preventive care that patients want and need but are unable to obtain under the managed care reimbursement model. Dr. Hall's practice provides state-of-the art evidenced based heart attack, stroke and diabetes risk assessment and prevention program, in addition to other cutting-edge therapies.

Dr. Michael Jelinek, M.D.

Dr. Jelinek received his undergraduate degree in Psychology from Wayne State University, Detroit, Michigan, before completing medical school in the Dominican Republic. He then went on to complete his Residency in Internal Medicine at Mt. Carmel Mercy Hospital in Detroit, Michigan. He went on to complete his Fellowship in Infectious Disease at Wayne State University. Today, he owns and

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and operates an internal medicine practice in Edinburg, TX and offers his expertise in infectious disease, bio-identical hormone replacement therapy and other wellness-based protocols. Dr. Jelinek is board certified in internal medicine in 1985 and board certified in infectious diseases in 1988, both by the American Board of Internal Medicine.

Mary Becton-Crouse, N.P.

Mary Becton-Crouse has been a Family Nurse Practitioner for 12 years with a passion for taking care of the whole patient in the most holistic way possible. "I love taking care of entire families and helping them achieve the best health possible." Mary received her undergraduate degree and BSN in Nursing from the University of Texas at Arlington and has been doing bio-identical hormones for 13 years and hormone pellet therapy for 7 yrs. Mary opened her practice in October of 2009. NP Care Clinic is a walk-in clinic for the entire family, that provides holistic care for every patient. Specializing in Functional & Integrative Medicine, Adult & Children's Medicine, Primary Care, Sick and Well visits, Bio-identical Hormones, Weight Loss and Aesthetics.

Dr. Jenaro Vélez, M.D., ABAARM, FAAMM

Jenaro A. Vélez Arteaga, M.D. is a duly licensed physician to practice General Medicine in the Commonwealth of Puerto Rico, and among the first physicians to become a Medical Cannabis Certified Doctor in Puerto Rico. With over twelve years of experience in primary care medicine, Dr. Vélez emphasizes a more holistic approach, integrating conventional medicine with other non-conventional wellness and health alternatives. In addition, Dr. Vélez is a well-recognized professor of The Cannaworks Institute, one of the leading Medical Cannabis educational institutions in Puerto Rico, where he teaches the required certification courses to all Medical Cannabis professionals for their occupational license, as well as continuing education courses to all the medical doctors certified in the local Medical Cannabis industry. He collaborates and works closely with other speakers to improve the quality of the Medical Cannabis courses offered in the Island.

Dr. Daniel Melville, M.D., DABFM

Dr. Daniel Melville has enjoyed a diverse and successful medical career in academic and private sectors, concierge services to conventional medical practices, and emergency room settings to outpatient clinics. Dr. Melville is a "Distinguished Graduate" of the United States Air Force Academy and went on to earn his Medical Degree from Louisiana State University in 2004. He became Board Certified in the American Academy of Family Medicine, after completing his residency in Family Medicine with emphasis in "Rural Medicine" in 2007. He owns and is the Medical Director of Melville Medicine, as well as maintaining full time credentialing as an emergency medicine physician at Texas Health Resources Hospital in Southlake, TX. Melville Medicine represents a dream opportunity to build upon his experiences to serve patients with an unparalleled thoroughness and availability. Dr. Melville's work has been published in seven peer reviewed textbooks and journals.

Clinical Visit Overview

Baseline Visit (Week 0)

- Educate Participant on Study Protocol
- Obtain Participant Informed Consent
- Provide Participant with Formula30A Full Spectrum Hemp CBD Extract (30 count bottle)
- Collect Participant Vitals & Weight Data
- Participant Completes the Medical Symptom Questionnaire (MSQ)

Midpoint Visit (Week 4)

- Refresh Participant on Study Protocol
- Review Anecdotal Participant Experience
- Collect Adverse Event Information (if applicable)
- Provide Participant with Formula30A Full Spectrum Hemp CBD Extract (30 count bottle)

Final Visit (Week 8)

- Review Anecdotal Participant Experience
- Collect Participant Vitals & Weight Data
- Collect Adverse Event Information (if applicable)

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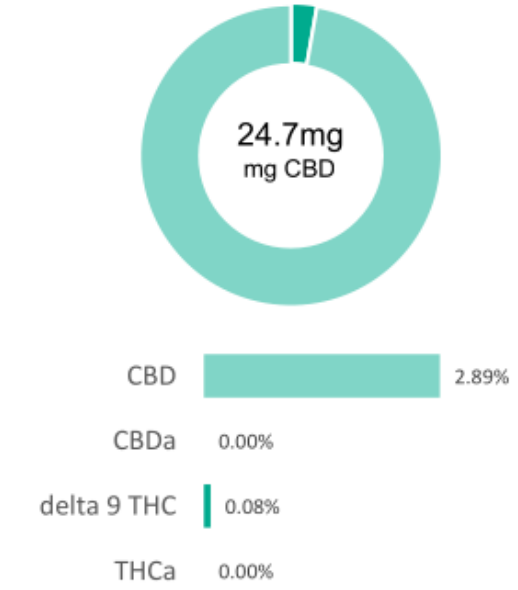
CERTIFICATE OF ANALYSIS

prepared for: Formula30A

25mg Capsule

Batch ID:	F30A-1361	**Test ID:**	8484815.005
Reported:	11-May-2020	**Method:**	TM14
Type:	Unit		
Test:	Potency		

CANNABINOID PROFILE



% = % (w/w) = Percent (Weight of Analyte / Weight of Product)

* Total Cannabinoids result reflects the absolute sum of all cannabinoids detected.

** Total Potential THC/CBD is calculated using the following formulas to take into account the loss of a carboxyl group during decarboxylation step.
Total THC = THC + (THCa *(0.877)) and Total CBD = CBD + (CBDa

ND = None Detected (Defined by Dynamic Range of the method)

Compound	LOQ (mg)	Result (mg)	Result (mg/g)
Delta 9-Tetrahydrocannabinolic acid (THCA-A)	0.29	ND	ND
Delta 9-Tetrahydrocannabinol (Delta 9THC)	0.15	0.70	0.8
Cannabidiolic acid (CBDA)	0.32	ND	ND
Cannabidiol (CBD)	0.18	24.70	28.9
Delta 8-Tetrahydrocannabinol (Delta 8THC)	0.16	ND	ND
Cannabinolic Acid (CBNA)	0.40	ND	ND
Cannabinol (CBN)	0.18	ND	ND
Cannabigerolic acid (CBGA)	0.26	ND	ND
Cannabigerol (CBG)	0.14	0.90	1.1
Tetrahydrocannabivarinic Acid (THCVA)	0.25	ND	ND
Tetrahydrocannabivarin (THCV)	0.13	ND	ND
Cannabidivarinic Acid (CBDVA)	0.29	ND	ND
Cannabidivarin (CBDV)	0.16	0.20	0.2
Cannabichromenic Acid (CBCA)	0.22	ND	ND
Cannabichromene (CBC)	0.27	1.30	1.5
Total Cannabinoids		**27.80**	**32.54**
Total Potential THC**		0.70	0.82
Total Potential CBD**		24.70	28.91

NOTES:

# of Servings = 1, Sample Weight=0.85436g

N/A

FINAL APPROVAL

Ryan Weems
11-May-2020
5:19 PM

PREPARED BY / DATE

Greg Zimpfer
11-May-2020
6:37 PM

APPROVED BY / DATE

Testing results are based solely upon the sample submitted to Botanacor Laboratories, LLC, in the condition it was received. Botanacor Laboratories, LLC warrants that all analytical work is conducted professionally in accordance with all applicable standard laboratory practices using validated methods. Data was generated using an unbroken chain of comparison to NIST traceable Reference Standards and Certified Reference Materials. This report may not be reproduced, except in full, without the written approval of Botanacor Laboratories, LLC. ISO/IEC 17025:2005 Accredited A2LA Certificate Number 4329.02

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APPENDIX

Additional Tables

Table 16 - Model Comparisons for Variables Predicting GAD7 Scores

GAD7 Model	R^2	dfmod	dfres	F	p	ΔR^2
Step 1	0.65	1	58	108.05	< .001	0.65
Step 2	0.65	1	57	0.20	0.656	0.00

Table 17 - Model Comparisons for Variables Predicting ISI Scores

ISI Model	R^2	dfmod	dfres	F	p	ΔR^2
Step 1	0.37	8	288	21.13	< .001	0.37
Step 2	0.42	1	287	26.99	< .001	0.05
Step 3	0.48	1	286	32.23	< .001	0.06

Table 18 - Model Comparisons for Variables Predicting PADT Scores

PADT Model		R^2	dfmod	dfres	F	p	ΔR^2
Average Pain (PAP)	*Step 1*	0.01	1	286	1.74	0.188	0.01
	Step 2	0.01	1	285	0.22	0.640	0.00
	Step 3	0.08	1	284	23.68	< .001	0.08
Maximum Pain (PMP)	*Step 1*	0.01	1	286	2.59	0.108	0.01
	Step 2	0.01	1	285	1.45	0.230	0.01
	Step 3	0.12	1	284	32.90	< .001	0.10
Same-Better-Worse Composite (SBW)	*Step 1*	0.00	1	286	1.23	0.268	0.00
	Step 2	0.00	1	285	0.00	0.998	0.00
	Step 3	0.04	1	284	10.51	0.001	0.04

Table 19 - Summary of Hierarchical Regression Analysis for Variables Predicting GAD7 Score

GAD7 SCORES	Variable	B	SE	95% CI	β	t	p
Step 1	*(Intercept)*	14.27	0.70	[12.86, 15.67]	0.00	20.30	< .001
	Week 8	-10.33	0.99	[-12.32, -8.34]	-0.81	-10.39	< .001
Step 2	*(Intercept)*	13.71	1.44	[10.82, 16.59]	0.00	9.52	< .001
	Week 8	-10.40	1.01	[-12.42, -8.37]	-0.81	-10.29	< .001
	Relative_Dose	0.00	0.00	[-0.01, 0.01]	0.04	0.45	0.656

Table 20 - Summary of Hierarchical Regression Analysis for Variables Predicting ISI Score

ISI SCORES	Variable	B	SE	95% CI	β	t	p
Step 1	*(Intercept)*	18.76	0.87	[17.05, 20.46]	0.00	21.68	< .001
	Week 1	-4.64	1.22	[-7.04, -2.23]	-0.24	-3.79	< .001
	Week 2	-7.94	1.22	[-10.35, -5.53]	-0.40	-6.49	< .001
	Week 3	-10.00	1.22	[-12.41, -7.59]	-0.51	-8.17	< .001
	Week 4	-9.82	1.22	[-12.23, -7.41]	-0.50	-8.02	< .001
	Week 5	-11.12	1.22	[-13.53, -8.71]	-0.57	-9.09	< .001
	Week 6	-11.48	1.22	[-13.89, -9.08]	-0.59	-9.39	< .001
	Week 7	-11.12	1.22	[-13.53, -8.71]	-0.57	-9.09	< .001
	Week 8	-12.06	1.22	[-14.47, -9.65]	-0.61	-9.86	< .001
Step 2	*(Intercept)*	13.79	1.27	[11.30, 16.28]	0.00	10.89	< .001
	Week 1	-4.64	1.17	[-6.94, -2.33]	-0.24	-3.96	< .001
	Week 2	-7.94	1.17	[-10.25, -5.63]	-0.40	-6.78	< .001
	Week 3	-10.00	1.17	[-12.31, -7.69]	-0.51	-8.53	< .001
	Week 4	-9.82	1.17	[-12.12, -7.51]	-0.50	-8.38	< .001
	Week 5	-11.12	1.17	[-13.43, -8.81]	-0.57	-9.49	< .001
	Week 6	-11.48	1.17	[-13.79, -9.18]	-0.59	-9.80	< .001
	Week 7	-11.12	1.17	[-13.43, -8.81]	-0.57	-9.49	< .001
	Week 8	-12.06	1.17	[-14.37, -9.75]	-0.61	-10.29	< .001
	Age	0.10	0.02	[0.06, 0.14]	0.23	5.19	< .001
Step 3	*(Intercept)*	8.91	1.48	[6.01, 11.82]	0.00	6.04	< .001
	Week 1	-4.64	1.11	[-6.83, -2.45]	-0.24	-4.17	< .001
	Week 2	-7.94	1.11	[-10.13, -5.75]	-0.40	-7.13	< .001
	Week 3	-10.11	1.11	[-12.30, -7.92]	-0.52	-9.08	< .001
	Week 4	-10.08	1.11	[-12.28, -7.89]	-0.51	-9.05	< .001
	Week 5	-11.76	1.12	[-13.97, -9.56]	-0.60	-10.52	< .001
	Week 6	-12.13	1.12	[-14.33, -9.93]	-0.62	-10.84	< .001
	Week 7	-11.87	1.12	[-14.08, -9.67]	-0.61	-10.59	< .001
	Week 8	-12.70	1.12	[-14.91, -10.50]	-0.65	-11.36	< .001
	Age	0.12	0.02	[0.08, 0.16]	0.28	6.37	< .001
	Relative_Dose	0.01	0.00	[0.01, 0.02]	0.25	5.68	< .001

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Additional Tables

Table 21 - Summary of Hierarchical Regression Analysis for Variables Predicting PADT Score

PADT SCORES		Variable	B	SE	95% CI	β	t	p
Average Pain (PAP)	Step 1	(Intercept)	4.21	0.22	[3.77, 4.65]	0.00	18.92	< .001
		Gender	0.35	0.27	[-0.17, 0.88]	0.08	1.32	0.188
	Step 2	(Intercept)	4.02	0.47	[3.09, 4.95]	0.00	8.51	< .001
		Gender	0.35	0.27	[-0.18, 0.88]	0.08	1.29	0.197
		Age	0.00	0.01	[-0.01, 0.02]	0.03	0.47	0.640
	Step 3	(Intercept)	4.92	0.49	[3.95, 5.89]	0.00	10.02	< .001
		Gender	0.35	0.26	[-0.16, 0.86]	0.08	1.34	0.180
		Age	0.00	0.01	[-0.01, 0.02]	0.03	0.49	0.627
		Week	-0.23	0.05	[-0.32, -0.13]	-0.28	-4.87	< .001
Maximum Pain (PMP)	Step 1	(Intercept)	5.58	0.24	[5.11, 6.05]	0.00	23.42	< .001
		Gender	0.46	0.29	[-0.10, 1.03]	0.09	1.61	0.108
	Step 2	(Intercept)	6.11	0.50	[5.12, 7.10]	0.00	12.13	< .001
		Gender	0.48	0.29	[-0.08, 1.05]	0.10	1.67	0.095
		Age	-0.01	0.01	[-0.03, 0.01]	-0.07	-1.20	0.230
	Step 3	(Intercept)	7.23	0.52	[6.22, 8.25]	0.00	14.01	< .001
		Gender	0.48	0.27	[-0.06, 1.02]	0.10	1.76	0.079
		Age	-0.01	0.01	[-0.03, 0.01]	-0.07	-1.27	0.205
		Week	-0.28	0.05	[-0.38, -0.18]	-0.32	-5.74	< .001
Same-Better-Worse Composite (SBW)	Step 1	(Intercept)	1.49	0.31	[0.87, 2.11]	0.00	4.74	< .001
		Gender	0.42	0.38	[-0.33, 1.17]	0.07	1.11	0.268
	Step 2	(Intercept)	1.49	0.67	[0.18, 2.80]	0.00	2.23	0.026
		Gender	0.42	0.38	[-0.33, 1.17]	0.07	1.11	0.270
		Age	0.00	0.01	[-0.02, 0.02]	0.00	0.00	0.998
	Step 3	(Intercept)	0.62	0.71	[-0.77, 2.01]	0.00	0.87	0.383
		Gender	0.42	0.37	[-0.32, 1.16]	0.07	1.12	0.262
		Age	0.00	0.01	[-0.02, 0.02]	0.00	0.00	0.998
		Week	0.22	0.07	[0.09, 0.35]	0.19	3.24	0.001

Glossary of Terms

95% Confidence Interval (95% CI)
An interval that is expected to contain the true value of a statistic in 95% of repeated samples from the same probability distribution.

Alpha Level for Subscales (α)
Ranges from 0.00 to 1.00; gives the reliability/consistency of the responses to the groups of questions or items that make up a subscale.

CBD (Cannabidiol)
A crystalline, nonintoxicating cannabinoid $C_{21}H_{30}O_2$ found in marijuana and hemp that is sometimes used medicinally.

Chi-Squared Statistic (χ^2)
A test statistic based on the χ^2 distribution. Used with the df to calculate a p-value.

Cohen's d
Effect size for the t-test; determines the strength of the differences between the matched scores. The larger the effect size, the greater the differences in the matched pairs.

Composite Score
A single overall score (usually an average or a sum) computed from multiple items or measurements.

Cronbach's Alpha
The purpose of this test is to determine if a group of questions all measure the same construct, concept, or idea. The Cronbach reliability test calculates the reliability coefficient alpha (α), which indicates the degree of consistency among the items.

Degrees of Freedom (df)
Determined by multiplying the (number of rows - 1) × (number of columns - 1).

Endocannabinoid System (ECS)
The endocannabinoid system (ECS) is a biological system composed of endocannabinoids, which are endogenous lipid-based retrograde neurotransmitters that bind to cannabinoid receptors, and cannabinoid receptor proteins that are expressed throughout the vertebrate central nervous system (including the brain) and peripheral nervous system.

Equality of Variance
Refers to the spread of data for all groups; the spread (i.e., variance) of the dependent variable should be equal for all groups. If the equality of variance assumption is violated, the results may not be reliable.

F-Ratio (F)
Used with the two df values to determine the p value, calculated by dividing the between subjects MS by the residuals MS.

Generalized Anxiety Disorder 7-Item Scale (GAD7)
The Generalized Anxiety Disorder - 7 Item (GAD7) self-report scale was developed to address a lack of brief clinical measures for assessing GAD. The tool consists of seven questions and asks patients how often during the previous two weeks they were bothered by each symptom.

Hierarchical Linear Regression
Hierarchical linear regression is used to analyze and compare sequential regression models in steps. Each successive step is a new regression with additional predictor variables entered into the previous regression model. Each step is then compared by using the F-test to determine if the change in explained variance is significant.

Independent Samples z-Test
The independent samples z-test is used to determine if there is a significant difference between two groups on a scale-level dependent variable. This test uses the difference between the average scores of the two groups to compute the z statistic, which is used to compute the p-value (i.e., significance level).

Insomnia Severity Index (ISI)
The Insomnia Severity Index (IS) self-report scale was developed to address a lack of brief clinical measures for detecting insomnia in patient populations. The tool consists of seven questions and asks patients how often during the previous two weeks they were bothered by each symptom.

Mahalanobis Distance
The Mahalanobis distance (MD) is the distance between two points in multivariate space. The most common use for the Mahalanobis distance is to find multivariate outliers, which indicates unusual combinations of two or more variables.

McFadden R^2
Measures the goodness-of-fit of the model. McFadden R^2 values of .2 or greater indicate an excellent model fit.

Mean (M)
The average value of a scale variable.

Normality
Refers to the distribution of the residuals; the assumption is that the residuals follow a bell-shaped curve; the assumption is met when the q-q plot has the points distributed approximately on the normality line.

PADT Average Pain (PAP)
The PADT Average Pain score represents a participant's average pain level experienced during the observation window.

PADT Maximum Pain (PMP)
The PADT Maximum Pain score represents a participant's maximum pain level experienced during the observation window.

PADT Percent Pain Relief (%PR)
The PADT Percent Pain Relief score represents a participant's perceived level of symptom relief due to current treatments regimens during the observation period.

Pain Analysis and Diagnosis Tool (PADT)
The Pain Assessment and Documentation Tool (PADT) assessment scale was developed to address a lack of brief clinical measures for assessing chronic pain. The tool consists of four domains, commonly known as the "Fours As": analgesia, activities of daily living, adverse side effects, and aberrant drug-taking behaviors.

Path Analysis
Path analysis is a multivariate statistical technique to assess how well the regression paths of the observed scale variables represent the data. The path analysis model is commonly used to determine mediating or indirect effects for relationships between observed variables. Path analysis is a special type of SEM model without any latent constructs.

p-Value (p)
The probability of obtaining the observed results if the null hypothesis is true. A result is usually considered statistically significant if the p-value is ≤ .05.

Residuals
Refers to the difference between the predicted value for the dependent variable and the actual value of the dependent variable.

R-Squared Statistic (R2)
Tells how much variance in the dependent variable is explained by only the predictor variables.

Same-Better-Worse Composite (SBW)
The PADT Same-Better-Worse Composite score represents a participant's average responses to seven questions related to their pain symptoms during the observation window. Individual responses are scored as Worse = -1, Same = 0, and Better = 1, for a total SBW scale of -7 to 7.

Shapiro-Wilk Test
A test to assess if the assumption of normality is met. If statistical significance is found in this test, the data is not normally distributed.

Standard Deviation (SD)
The spread of the data around the mean of a scale variable.

Standard Error (SE)
How much the B is expected to vary.

Standard Error of the Mean (SEM)
The estimate of how far the sample mean is likely to differ from the actual population mean.

Standardized Beta (β)
Ranges from -1 to 1; gives the strength of the relationship between the predictor and dependent variable.

THC (Δ9-tetrahydrocannabinol)
Either of two physiologically active isomers $C_{21}H_{30}O_2$ from hemp plant resin, especially : one that is the chief intoxicant in marijuana

Unstandardized Beta (B)
The slope of the predictor with the dependent variable.

z-Test Statistic (z)
Used with the df to determine the p value.

For more information on the contents of this report, as well as additional educational materials regarding cannabidiol and the endocannabinoid system, please visit our website at www.Formula30A.com.