Human Clinical Trial Evaluating the Safety and Efficacy of Hempzorb81™ Full Spectrum Hemp Oil

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Background: Cannabidiol (CBD) is one of the naturally occurring cannabinoids found in cannabis plants. It is a 21-carbon terpenophenolic compound which is formed following decarboxylation from a cannabidiolic acid precursor. In contrast to Δ9-THC, CBD is non-intoxicating, but exerts a number of beneficial pharmacological effects. At lower doses, effects that promote and maintain health, including antioxidative, anti-inflammatory, and neuroprotection effects have been evaluated. The cannabis plant is also composed of a chemical mixture that includes phytocannabinoids, terpenoids, flavonoids, steroids and enzymes. While the exact mechanism of action are not fully known, all of these other components have a synergistic effect combined with cannabinoids. This has become known as the entourage effect. The comprehensive review of 132 original studies by Bergamaschi et al. suggest chronic use and high doses of CBD up to 1500 mg per day have been repeatedly shown to be well tolerated by humans.

Purzorb® is a proprietary micellization process which micellizes a decarboxylated full spectrum hemp oil (including CBD and trace amounts of THC) mixture suitable for oral ingestion. Hempzorb81™ is a patent pending 81% cannabinoid full spectrum hemp oil micellized using the Purzorb® technology. The oil is extracted from industrial hemp *Cannabis sativa* plants using supercritical CO_2 with column chromatography to remove THCΔ9. According to the manufacturer each particle size is approximately 22 nm making it highly permeable in water. Animal models with Hempzorb81™ have demonstrated a rapid and almost complete absorption (85%) in the intestinal lining using Franz diffusion apparatus.

Human pharmacokinetic studies have also demonstrated that the onset of Hempzorb81™ is rapid and it has a lasting duration of CBD availability in the blood stream. Patients in these pharmacokinetic studies were measured to have over 50% of the available CBD in their blood stream by the first measurement of 15 minutes. This exceeds what has been shown with CBD or THC that has been inhaled or vaped. The blood levels then measured significantly higher than what has been seen with standard CBD oil and other solubilizing methods.

Study Purpose: This was a one hundred and fifty subject, sixty-day, clinical study for the purpose of establishing safety and effectiveness of Hempzorb81™ Full Spectrum Hemp Oil (Med7). The serving size was 2 ml of the Med7 cinnamon flavor (the dose used for this study). The amount of Hempzorb81™ in each 2 ml serving was 150 mg. The CBD content in 150 mg of Hempzorb81™ was 10 mg. Placebo Product: 1.0 mg per 2 mL. Subjects were instructed to take 2ml dose once daily. No other change to diet, fluid intake, or exercise was recommended.

Study Type: This was a double-blind, placebo-controlled, multisite, and randomized effectiveness study performed on human subjects. Mean Age= 55 ± 5 yrs Male:Female= 58: 92
P values = 0.02 and 0.03

STUDY OVERVIEW:
Screening and Testing Procedures: Initial screening of subjects completed before the baseline data was taken for this test included: AST, ALT, to assess liver function, creatinine and BUN, TSH for the evaluation of the thyroid and to help evaluate kidney function, a standard RBC, CBC, and platelets were drawn and

evaluated for Wellness. Each of these tests was run on arterial blood drawn following standardized protocol for the procedures and completed by healthcare professionals.

Subjects were randomly assigned to either the live product group or the control group. Each subject signed a study consent form. Subjects were given instruction to consume this study product Hempzorb81™ Full Spectrum Hemp Oil. All subjects were instructed not to change their eating, drinking, or exercise habits for the duration of this study. All subjects were provided a 24-hour emergency number. Subjects were informed if there were any concerns to contact their healthcare professional at once or go directly to their local emergency room for evaluation.

Inclusion Criteria:

- Subjects who signed a written informed consent consistent with required guidelines and met prior to participation in the trial.
- Subjects 18 years of age or older, either sex.
- Subjects who are not on any medication or dietary supplement.
- Subjects who have normal kidney, liver, and thyroid functions, and normal CBC prior to the start date of this study.
- Subjects who are able to follow the protocol as designed.
- Subjects in generally good health.

Exclusion Criteria:

- History of head trauma.
- History of serious diseases or illness diagnosed at this time.
- Known moderate to severe renal insufficiency.
- Recent history (<6 months prior to Visit 1) of myocardial infarction.
- Subjects who regularly use oxygen therapy.
- Subjects with known active tuberculosis.
- Subjects with a history of cancer within the last 5 years.
- Subjects who have undergone thoracotomy with pulmonary resection within 1 year prior to the trial.

Exclusion Criteria (con't)

- Subjects who are currently in a pulmonary rehabilitation program or who have completed a pulmonary rehabilitation program in the 6 weeks prior to the screening visit (Visit 1).
- Subjects currently prescribed diuretic medications, cardiac stimulants, or any other prescribed or non-prescribed medication that may, in the opinion of the Clinical Studies USA staff, alter testing results.
- Use of opiate analgesics prescribed or otherwise obtained for any treatment reason including migraine treatment or for recreational purposes.
- History of drug or alcohol addiction.
- Females who are pregnant, lactating, or nursing or who may become pregnant during the course of the study.
- Patients diagnosed as HIV-positive, diagnosed with AIDS, or with any neuromuscular condition including CP, MS, ALS, or Huntington's Chorea.
- Patients with uncontrolled hypertension (e.g. BP>150/100).
- Subjects who have used steroid therapy within the last 6 months.
- Patients with any condition not previously named that, in the opinion of the investigators or intake staff, would jeopardize the safety of the patient or affect the validity of the data collected in this study.

DATA COLLECTION

Anxiety

This study evaluated anxiety using an online testing system of evaluation questions. Patients used computers to report their baseline and results. The Mood Rating Scale (MRS) was used to assess anxiety and current mood. CBD has shown a trend toward some reduction of anxiety as well as encouraged sleep.

Mood Rating Scale
1- Happy
2- Mostly Happy
3- Intermittently Happy
4- Sometimes Happy
5- Some Anxiety
6- Mild Anxiety
7- Some Periods of High Anxiety
8- Half the Time Anxiety is Dominate
9- Manageable Anxiety
10- Mostly Feeling Anxiety

<u>Med7 Study Product Group</u>
Day 0 average- 5 some anxiety
Day 60 average- 2 mostly happy
91% of the subjects in the live product group reported longer sleep with more periods of dreaming

<u>Placebo Product Group</u>
Day 0 average- 5 some anxiety
Day 60 average- 5 some anxiety
No changes in sleep were reported

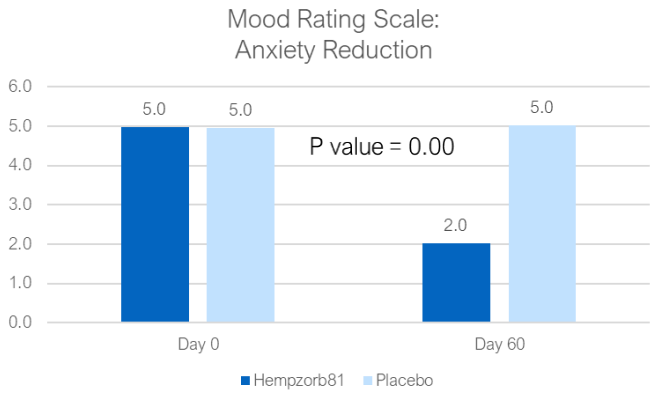

Figure 1. Mood Rating Scale

Joint Pain

Joint pain can be discomfort, pain or inflammation arising from any part of a joint — including cartilage, bone, ligaments, tendons, or muscles. Most commonly, however, joint pain refers to arthritis or arthralgia, which is inflammation or pain from within the joint itself.

Joint pain can be mild, causing soreness only after certain activities, or it can be severe, making even limited movement, particularly bearing weight, extremely painful.

We did not try to identify a disorder for the joint pain in this study.

Joints that were reported as being sore or in pain by fifty-six of the subjects in this study were evaluated for pain by measuring of the joint, evaluation of localized heat, evaluation of swelling, and range of motion. Initial evaluation was completed on Day 0 and final evaluation was completed on Day 60.

Fifty-one subjects reporting joint pain were in the live product group. Subjects on average reported a drop in pain levels of at least two levels.

Pain Levels

1. No pain
2. Mild pain - completely normal movement, no limits
3. Moderate pain -20% decrease in normal movement, some limits of daily use
4. Intermittent severe pain - up to 50% decrease in normal movement, some limits of daily use
5. Severe pain - up to 80% decrease in normal movement, more limits of daily use
6. Constant severe pain - up to 100% pain in normal movement or no movement

<u>On Day 0 of this study</u>
36 Subjects in the live product group on Day 0 were #3
7 Subjects in the live product group on Day 0 were #2
8 Subjects in the placebo group on Day 0 were #3

<u>On the final Day 60 of this study</u>
31 subjects in the live product group were at level #2
12 subjects in the live product group were at level #1
8 subjects in the placebo group were at #3

The positive effects this CBD product seems to be mainly mediated via CBD anti-inflammatory effects.

C-Reactive Protein

C-reactive protein (CRP) is produced by the liver. Its level rises when there is inflammation in your body. LDL cholesterol not only coats the walls of your arteries, but it also damages them. This damage causes inflammation that the body tries to heal by sending in response proteins, CRP is one of these proteins. Studies have found that testing for CRP levels may be a better gage of cardiovascular disease than the LDL test levels are. CRP test is not a test for heart disease, it is a test for inflammation in the body.
The testing method in this study was with the Immunochemiluminometric Assay.

CRP level of lower than 1.0 mg/L -- low risk of heart disease
CRP level of 1.0 mg/L and 3.0 mg/L -- moderate risk of CVD
CRP level of more than 3.0 mg/L -- high risk of CVD

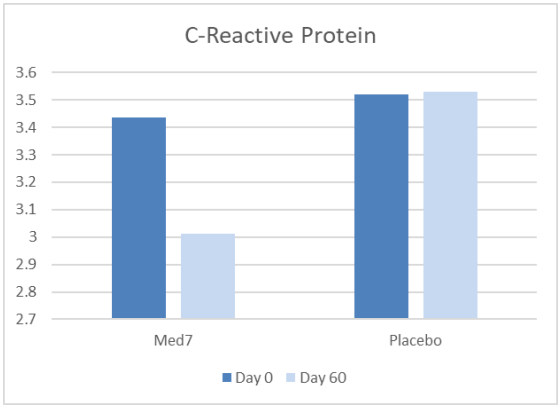

Figure 2. C-Reactive Protein

<u>Med7 Study Product Group</u>
Day 0 average- 3.436
Day 60 average- 3.012

<u>Placebo Product Group</u>
Day 0 average- 3.52
Day 60 average- 3.53

Tumor Necrosis Factor

Tumor necrosis factor (TNFα) is a multifunctional cytokine that plays important roles in diverse cellular events such as cell survival, proliferation, differentiation, and death. As a pro-inflammatory cytokine, TNF is secreted by inflammatory cells, which may be involved in inflammation-associated carcinogenesis.

TNF exerts its biological functions through activating distinct signaling pathways such as nuclear factor κB (NF-κB) and c-Jun N-terminal kinase (JNK). NF-κB is a major cell survival signal that is anti-apoptotic while sustained JNK activation contributes to cell death. The crosstalk between the NF-κB and JNK is involved in determining cellular outcomes in response to TNF. TNF could be an endogenous tumor promoter, because TNF stimulates cancer cells' growth, proliferation, invasion and metastasis, and tumor angiogenesis. The property of TNF in inducing cancer cell death affords it a potential cancer therapeutic.

Testing Used: Enzyme-Linked Immunosorbent Assay
TNF normal 0-5ng/mL

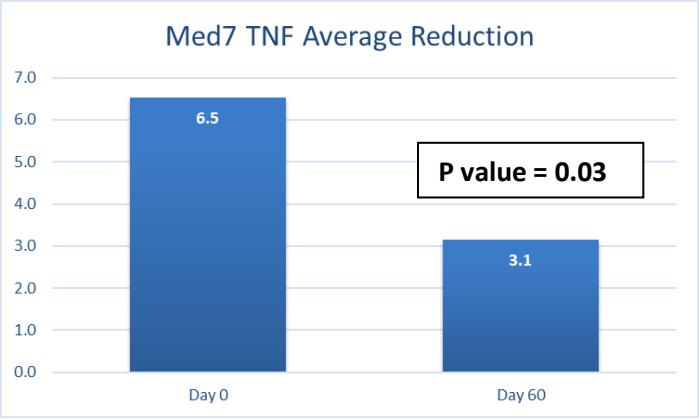

Figure 3. Tumor Necrosis Factor (TNFα)

<u>Med7 Study Product Group</u>
Day 0 average- 6.52ng/mL
Day 60 average- 3.14ng/mL

<u>Placebo Product Group</u>
Day 0 average- 2.6ng/mL
Day 60 average- 2.3ng/mL

Interleukin 6

Interleukin 6 (IL-6) is a multifunctional cytokine produced by various cells. The molecular cloning of the cDNAs encoding B cell stimulatory factor 2 (BSF-2), interferon β2, and 26 kDa protein showed that all these molecules are identical. Furthermore, hybridoma/plasmacytoma growth factor (HPGF) and hepatocyte-stimulating factor (HSF) were also found to be identical to this molecule and, therefore, this molecule has been called IL-6. Subsequent studies demonstrated that IL-6 acts not only on B cells but also on hematopoietic stem cells and hepatocytes and induces hematopoiesis as well as acute phase reactions. It was also shown to act on T cells, nerve cells, keratinocytes, renal mesangial cells, megakaryocytes and myeloma/plasmacytoma cells. Since antibody production, hematopoiesis, and acute phase reactions are three major responses against infection, inflammation and tissue injury, IL-6 may have a central role in host defense mechanisms.

On the other hand, the deregulation of IL-6 gene expression was shown to be involved in the pathogenesis of polyclonal and monoclonal B cell abnormalities, such as rheumatoid arthritis and multiple myeloma.
Testing Method: Enzyme-Linked Immunosorbent Assay

<u>Med7 Study Product Group</u>
Normal 1.8pg/mL
Day 0 average- 2.67
Day 60 average- 1.68pg/mL

<u>Placebo Product Group</u>
Day 0 average- 3.47
Day 60 average- 3.29pg/mL

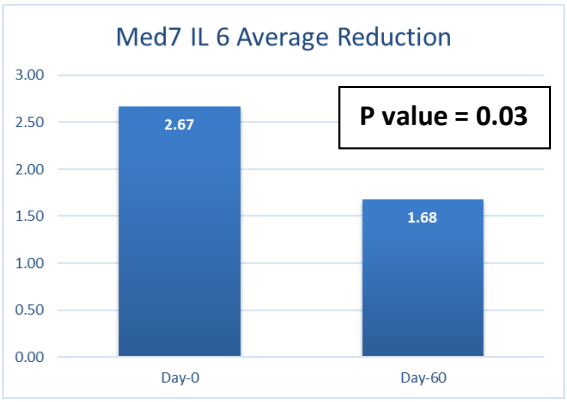

Figure 4. Il-6 Reduction

Erythrocyte Sedimentation Rate

Erythrocyte sedimentation rate (ESR) test may also be called a sedimentation rate test or sed rate test. This blood test facilitates in determining whether the body is experiencing inflammation. The ESR test may be used to monitor inflammatory diseases. This test can identify and measure inflammation, in general, in the body. However, it doesn't help pinpoint the cause of inflammation. That's why the ESR test is rarely performed alone. Instead, practitioners will likely combine it with other tests to determine the cause of inflammatory symptoms. Inflammation can cause abnormal proteins to appear in blood. These proteins cause RBCs to clump together. This makes them fall more quickly.

ESR test results that are higher than normal are also associated with autoimmune diseases, including:

- lupus
- certain types of arthritis, including RA

- Waldenstrom's macroglobulinemia, a rare cancer
- temporal arteritis, a condition in which your temporal artery becomes inflamed or damaged
- polymyalgia rheumatica, which causes muscle and joint pain
- hyperfibrinogenemia, which is too much of the protein fibrinogen in your blood
- allergic or necrotizing vasculitis

Some types of infection that cause ESR test results to become higher than normal are:

- bone infection
- heart infections causing myocarditis (affects heart muscle), pericarditis (affects tissue around the heart, or the pericardium) and endocarditis (affects the lining of the heart, which can include the heart valves)
- rheumatic fever
- skin infection
- systemic infections
- tuberculosis (TB)

The higher the number, the higher the likelihood of inflammation
Testing Method: The result of the ESR is the amount of plasma remaining at the top of the test tube after 1 hour.

Normal Testing Values 0-20 mm/hr

<u>Med7 Study Product Group</u>
Day 0 average-24.2
Day 60 average-19.52

<u>Placebo Product Group</u>
Day 0 average- 24.16
Day 60 average-23.88

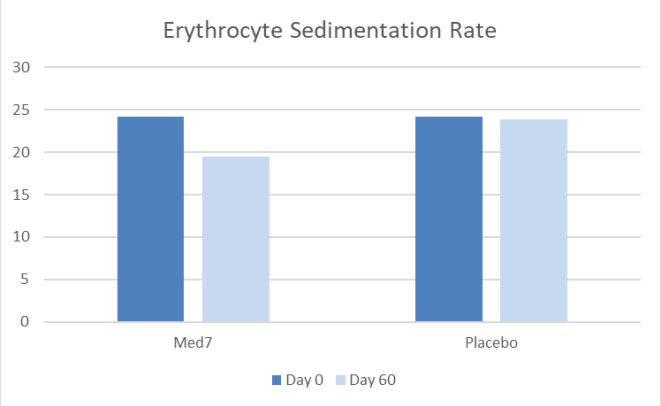

Figure 5. Erythrocyte Sedimentation Rate

The final data average for this group moved into the Wellness area. Eighty-two of the subjects in this group had their data move into the Wellness area. Eighteen subjects of this group had numbers slightly above twenty, but they have had a significant move into a better Wellness area.

High Density Lipoprotein

Each fragment of high-density lipoprotein (HDL) cholesterol is a microscopic blob that consists of a rim of lipoprotein surrounding a cholesterol center. The HDL cholesterol particle is dense compared to other types of cholesterol particles, hence the name high-density. Cholesterol is a lipid (fat) wax-like substance found in all body tissues, including the blood and nerves. Our bodies require it because it is an essential structural component of all membranes. Cholesterol is carried by lipoproteins (fat and protein bound together) in the blood to the cells in the body.

There are two types of lipoproteins, high-density lipoproteins HDL and low-density lipoproteins LDL. The protein component allows a lipid molecule to become more soluble in watery fluids. HLD and LDL cholesterol play a significant role in heart disease. To travel through the bloodstream, cholesterol has to be transported by helper molecules called lipoproteins. Each lipoprotein has its own preferences for cholesterol, and each act differently with the cholesterol it transports.

Experts believe HDL cholesterol may act in a variety of beneficial ways that tend to reduce the risk for heart disease:

- HDL cholesterol scavenges and removes LDL, bad cholesterol.
- HDL reduces, and recycles LDL cholesterol by transporting it to the liver where it is reprocessed.
- HDL cholesterol repairs the inner walls (endothelium) of blood vessels. Damage to the inner walls is the first step in the process of atherosclerosis, which causes heart attacks and strokes. HDL scrubs the wall clean and promotes healthy vessels.
- HDL cholesterol levels greater than 60 milligrams per deciliter (mg/dL) are high. That's good.
- HDL cholesterol levels less than 40 mg/dL are low. That's not so good.

Testing Method: Metered
<u>Med7 Study Product Group</u>
Day 0 average- 56.62
Day 60 average- 61.27

<u>Placebo Product Group</u>
Day 0 average-50.1
Day 60 average-49.9

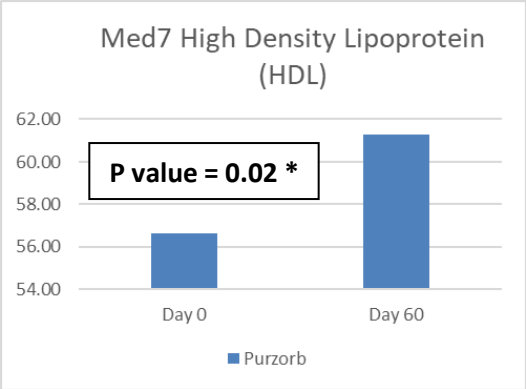

Figure 6. High Density Lipoprotein (HDL)

* The one hundred subjects in the Med7 Product Group showed a significant change in their HDL numbers into more Wellness numbers

Low Density Lipoprotein

Low density lipoprotein (LDL) is a microscopic layer made up of an outer rim of lipoprotein and a cholesterol center. LDL is "bad" because it becomes part of plaque, clogs your arteries, and increases the risk of heart attacks and strokes. If you have a high LDL level, this means that you have too much LDL cholesterol in your blood. This extra LDL, along with other substances, forms plaque. The plaque builds up in your arteries; this is a condition called atherosclerosis.

Coronary artery disease happens when plaque builds up in the arteries of your heart. It causes the arteries to become hardened and narrowed, which slows down or blocks the blood flow to your heart. Since your blood carries oxygen to your heart, this means that your heart may not be able to get enough oxygen. This can cause angina (chest pain), or if the blood flow is completely blocked, a heart attack.

Testing Method: Metered
Normal test results 150-199 mg/dL

<u>Med7 Study Product Group</u>
Day 0 average- 201.6 mg/dL
Day 60 average- 198.1 mg/dL

<u>Placebo Product Group</u>
Day 0 average-191.86 mg/dL
Day 60 average-191.0 mg/dL

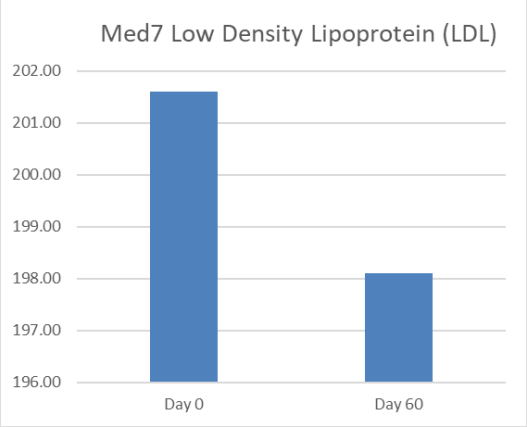

Figure 7. Low Density Lipoprotein (LDL)

Homocysteine

Homocysteine is an amino acid. Amino acids are the building blocks of proteins. When proteins break down, elevated levels of amino acids like homocysteine may be found in the bloodstream. Homocysteine levels increase in the body when the metabolism to cysteine of methionine is compromised.

Having elevated levels of homocysteine in the blood (hyperhomocysteinemia) is associated with atherosclerosis and blood clots. Cysteine is an important protein in the body that has many roles. It is involved in the way proteins within cells are folded, maintain their shape, and link to each other. Cysteine is a source of sulfide and is part of the metabolism of different metals in the body, including iron, zinc and copper. Cysteine also acts as an antioxidant.

If homocysteine cannot be converted into cysteine or returned to the methionine form, levels of homocysteine in the body increase. Elevated homocysteine levels have been associated with heart attack, stroke, clot formation, and possibly the development of Alzheimer's disease. Elevated homocysteine levels in the body do not cause any symptoms.

Elevated homocysteine levels affect the interior lining of blood vessels in the body, increasing the risk of atherosclerosis or narrowing of blood vessels. This can result in early heart attack and stroke. There is also a relationship between the levels of homocysteine in the body and the size of the carotid arteries that supply the brain with blood; the higher homocysteine level, the narrower (stenosed) the carotid artery becomes.

The risk of deep vein thrombosis (DVT) and pulmonary embolism may be linked to elevated homocysteine levels. There also may be a relationship between elevated homocysteine levels and broken bones, especially in the elderly. Alzheimer's disease and other types of dementia may be more frequently seen in patients with increased or elevated levels of the amino acid in the blood.

Testing Method: Automated Fluorescence Polarization Immunoassay
Normal Homocysteine 4-15umol/L

Med7 Study Product Group
Day 0- average was 24.2/umol/L
Day 60- average was 19.52 umol/L

Placebo Product Group
Day 0 average-19.42
Day 60 average-19.86

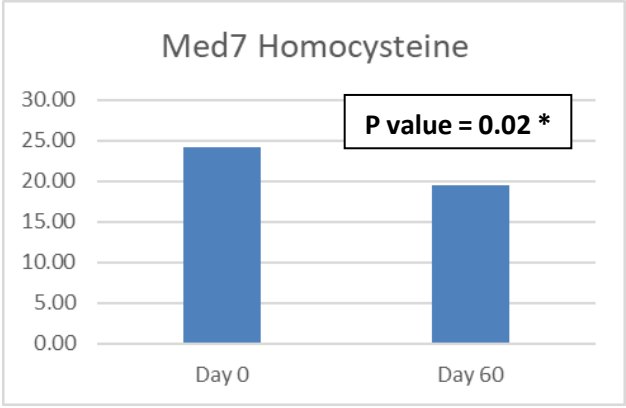

Figure 8. Homocysteine

*A significant decrease in homocysteine was measured in the Med7 group into a more Wellness set of numbers.

HbA1c

The HbA1c test also called the hemoglobin A1c, HbA1c, glycated hemoglobin, or glycohemoglobin test. Hemoglobin is the part of a red blood cell that carries oxygen to the cells. Glucose attaches to or binds with hemoglobin in the blood cells, and the A1c test is based on this attachment of glucose to hemoglobin. The A1c test is a common and the standard blood test used to diagnose type 1 and type 2 diabetes and to monitoring diabetes. The A1c test goes by many other names, including glycated hemoglobin, glycosylated hemoglobin, hemoglobin A1c and HbA1c.

The A1c test result reflects the average blood sugar level for the past two to three months. Specifically, the A1c test measures what percentage of hemoglobin — a protein in red blood cells that carries

oxygen — is coated with sugar (glycated). The higher A1c levels are, the poorer the blood sugar control is and the higher risk there is of diabetes complications.

Normal A1c level is below 5.7 percent. Levels between 5.7 and 6.4 percent are considered prediabetes (also called impaired fasting glucose), indicating a high risk of developing diabetes in the future.

An A1c level of 6.5 percent or higher on two separate occasions shows that you have diabetes. An A1c level above 8 percent indicates diabetes is not well-controlled and there is a higher risk of developing the complications of diabetes.

A1c level	**Estimated average blood sugar (glucose) level**
6 percent	126 mg/dL (7 mmol/L)
7 percent	154 mg/dL (8.6 mmol/L)
8 percent	183 mg/dL (10.2 mmol/L)
9 percent	212 mg/dL (11.8 mmol/L)
10 percent	240 mg/dL (13.4 mmol/L)
11 percent	269 mg/dL (14.9 mmol/L)
12 percent	298 mg/dL (16.5 mmol/L)

Testing Method
TS Diagnostics A1CNow®

Normal A1c 4-5.6mmol/L

<u>Med7 Study Product Group</u>
Day 0- average was 6.0mmol/L
Day 60- average was 5.075 mmol/L

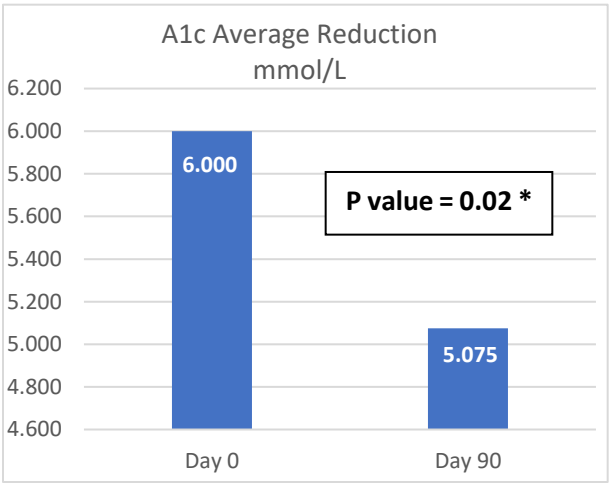

Figure 9. Hemoglobin A1c (A1c)

*A significant decrease in A1c was measured in the Med7 group into a more Wellness set of numbers.

CONCLUSION

Hempzorb81™ Full Spectrum Hemp Oil (Med7) was shown in this study to be a safe way to use CBD. No side effects were reported or stated. No interactions were noted for the period of this study. Nine significant areas of Wellness showed a marked improvement. No statistically significant changes were measured in the Control Group for any of the tested areas. No subjects reported any reactions of interactions for the duration of this study.

The study patients on Med7 reported positive effects on Anxiety, joint pain and sleep. Inflammatory markers including TNF and IL-6 showed statistically significant reductions further demonstrating a propensity of the Med7 to have a positive effect on key inflammatory markers. Other cardiovascular markers such as HDL and LDL also showed positive effects in the Med7 study group. Perhaps the most surprising and significant results were of that on the HbA1c and Homocysteine. A significant decrease of the A1c on the average of near 1.0 mmol was seen in this study. Further studies are needed to verify and assess the extent and potential of Med7 to affect A1c and Homocysteine and the relationship of the endocannabinoid receptors effect on the endocrine system. Further study into each of these areas is recommended as to expand understanding and study data to support claims.