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Research Article

Anti-Inflammatory Activity of A Full Spectrum CBD-Rich Hemp Formulation in Patients with COVID-19 Infection

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Abstract

Background: The coronavirus disease-19 (COVID-19) pandemic is attributable to the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The pathogenesis of SARS-CoV-2 is attributed to the activation of multiple inflammatory pathways secondary to the interaction of virus and host immune responses. 15% of patients over the age of 60 with COVID-19 require hospitalization. In addition, ICU admissions are as high as 5% of COVID-19 patients in this same age group. Most with one or more underlying conditions, undergo the pathophysiologic process of hyper-inflammation and its accompanying Cytokine Storm Syndrome (CSS) which results in significant morbidity and mortality. Therapeutics, which reduce the release of inflammatory cytokines, have been sought to slow disease progression. A growing body of literature attests to the anti-inflammatory effects of the naturally occurring cannabinoids found in both cannabis and hemp plants. The major cannabinoid, cannabidiol (CBD), results in decreased cytokine production via Cannabinoid receptor 2 (CB2). In addition, recent evidence indicates: (1) CBD may protect against infection by inducing anti-viral cellular activity; and (2) two specific cannabinoids exhibit binding to the spike protein thereby preventing infection in vitro. Therefore, examination of the activity of a CBD-rich oil on cellular inflammatory markers, as a potential natural intervention and as an adjuvant to recognized therapeutic interventions, is considered here.

Materials and methods: COVID-19 has influenced all sectors of the world's economic, scientific and commercial communities. This is true also of the investigative work within this report which adapted to the COVID-19 outbreak during the execution of the study. Part 1 of this report focuses on the initial study designed to evaluate the reported anti-inflammatory effects of a hemp-based full-spectrum CBD and cannabinoid-rich microcellular formulation (i.e. Hempzorb81™) on healthy volunteers comparing a treatment group of 100 with a placebo group of 50. Part 2 extends the report to the effects of the Hempzorb81™ formulation on a subset of 44 study subjects who tested positive for COVID-19 infection compared to a 39 subject COVID-19 negative test control group.

Results: In Part 1, the treatment cohort found two cytokines associated with the development of SARS-CoV-2. Both TNFα and IL-6 showed statistically significant reductions compared to placebo in healthy patients. Two inflammatory markers, ESR and CRP, showed reductions of 19.4% and 12.5%, respectively, but the results were not statistically significant. In Part 2, TNFα, CRP, IL-1,6 and White Blood Cell count (WBC) all showed statistically significant p-values in the COVID-19 positive cohort. In the course of the study, no COVID-19 positive patients were hospitalized or died. A 2-fold reduction in white blood cell count at the time of diagnosis over the treatment course was an additional significant indicator for improved outcome post-infection.

Conclusion: This study of a highly bioavailable cannabinoid-rich CBD formulation in both healthy volunteers and COVID-19 test positive patients resulted in the significant reduction of cytokines associated with development of the SARS-CoV-2 respiratory syndrome. As one of the first human subject studies evaluating CBD hemp-based formulations in COVID-19 test positive patients, substantial evidence was developed to consider highly bioavailable CBD cannabinoid-rich formulations as useful potential adjuvants to recognized palliative and therapeutic options for COVID-19 infections.

Keywords: Clinical study; COVID-19; SARS-CoV-2; Cytokine; Cannabinoid; Cannabidiol; Inflammatory markers; Cytokine Storm Syndrome; Hemp oil

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Abbreviations

COVID-19: Coronavirus Disease-19; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; ICU: Intensive Care Unit; CBD: Cannabidiol; CB2: Cannabinoid receptor 2; TNFα: Tumor Necrosis Factor - alpha; CRP: C-Reactive Protein; IL-1: Interleukin-1; IL-6: Interleukin-6; CSS: Cytokine Storm Syndrome; ECS: Endocannabinoid System; CBDV: Cannabidivarin; THCV: Tetrahydrocannabivarin; TRPV1: Transient Receptor Potential Cation Channel Subfamily V Member 1; NO: Nitric Oxide; ESR: Erythrocyte Sedimentation Rate; MCT: Medium Chain Triglyceride; GVHD: Graft Versus Host Disease; THC: Tetrahydrocannabinol; ml: milliliter; mg: milligrams; pg: picogram

Introduction

Development of a two-part clinical study

A double-blind, placebo-controlled, multisite, and randomized effectiveness study was performed on 150 healthy human subjects looking at the effects of Hempzorb81™ (Med 7, LLC, Bluffdale, Utah, USA) on Type II Diabetics (data in preparation). Hempzorb81™ is a micellized whole plant extract high in cannabidiol (CBD), cannabidivarin (CBDV) and tetrahydrocannabivarin (THCV). This extract has previously been shown to have superior bioavailability and positive effects on metabolic parameters including glycosylated hemoglobin (A1c) and inflammatory markers. During the first two months of this six-month study (Part 1), the COVID-19 virus pandemic broke out and was significant in the area where the study was being conducted. To take advantage of this unfortunate COVID-19 outbreak (Part 2), we realized the opportunity to study the potential of Hempzorb81™ to moderate the inflammatory markers associated with disease onset in a subset of patients who develop the Cytokine Storm Syndrome (CSS).

Cytokine Storm Syndrome

Cytokine Storm Syndrome is a variation of Systemic Inflammatory Response Syndrome (SIRS) [1-3]. It occurs in a small fraction of COVID-19 infections when large numbers of leukocytes, including B cells, T cells, macrophages, monocytes and natural killer cells become activated in response to the viral infection and some other conditions. The cells release a variety of pro-inflammatory cytokines [1,2]. These released cytokines then result in more leukocytes migrating to the area and subsequently releasing even more inflammatory cytokines in a dysregulated positive feedback loop. Tumor Necrosis Factor Alpha (TNFα) and interleulin-1 (IL-1), are cytokines released early which readily induce other pro-inflammatory cytokines [4]. One particular cytokine, known as interleukin-6 (IL-6), plays an important role in CSS [2].

The first reference to Cytokine Storm was described in 1993 [5] when describing Graft-Versus-Host-Disease (GVHD). This occurs when the body has an excessive immune response to transplanted organs. CSS was subsequently found to occur in several viral infections including Ebola, Avian influenza, SARS, MERS and COVID-19 [6]. The life-threatening severe acute respiratory syndrome from COVID-19 infection is known as SARS-CoV-2. It is due to dysregulated hyperinflammatory lymphocytic and monocytic infiltration of the heart and lung, causing an acute respiratory distress syndrome [2] and cardiac failure [7]. There are established risk factors for the development of SARS-CoV-2 in patients, [8] however, it is not clear exactly how this fulminant CSS condition is triggered. It is important to note, that in the vast majority of patients with COVID-19 infection, there is no excessive cytokine-driven inflammatory response [2].

The most recent study reviewing the utilization of white blood cell count as a predictor of outcome found a direct correlation between white blood cell count at admission and mortality in COVID-19 patients [9]. In a Chinese study of 1311 patients diagnosed with SARS-CoV2 [10], there were statistically significant elevations of the inflammatory markers Erythrocyte Sedimentation Rate (ESR) ($p<0.001$) and C-Reactive Protein (CRP) ($p<0.001$) in the 'severe' group compared to the 'non-severe' group. Although inflammatory cytokine storm is thought to be the mechanism for COVID-19 progression, the study did not find significantly increased levels of IL-2, IL-4, IL-6, IL-10, TNFα, or Interferon (IFN). The authors felt that these findings might be due to the "limited size of the study and the large heterogeneity at the time-points of the first detection."

Cannabinoids and cannabidiol (CBD)

Cannabinoids have been shown to exert anti-inflammatory activities in various *in vivo* and *in vitro* models and have demonstrated the ability to ameliorate various inflammatory degenerative diseases [11,12]. However, the mechanisms of these effects are not completely understood but may be the result of interaction with the cannabinoid receptor 2 (CB2) resulting in decreased adenosine signaling [13-15]. The COVID-19 infection results in Severe Acute Respiratory Syndrome (SARS-CoV-2) in a small percentage of cases. This fulminant and life-threatening condition is due to Cytokine Storm Syndrome (CSS). In animal models mimicking CSS [16], CBD, administered as a single dose prior to the induced acute lung injury, resulted in decreased inflammation [17]. CSS has been identified, in several other viral infections in the past (Avian influenza, SARS, MERS) and in graft-versus-host disease when the body's immune system rejects a transplanted organ.

Cannabidiol (CBD) is a non-psychoactive cannabis derivative with a well-established safety record and wide therapeutic window [18]. CBD is an FDA-approved drug for intractable infantile seizures [19]. Successful Phase II trials for using CBD for the prevention and treatment of Graft-Versus-Host Disease (GVHD) are currently underway [5]. Full Spectrum Hemp including CBD and other cannabinoids (CBDV, THCV and CBC), have been shown in animal and human studies to reduce inflammatory response and decrease the release of the pro-inflammatory cytokines that are purported to cause CSS.

Varin cannabinoids (CBDV and THCV)

Cannabidivarin (CBDV) is a homologue of CBD, only differing slightly in the chemical composition: the 5-carbon (pentyl) side chain is substituted for a 3-carbon (propyl) sidechain. CBDV, similar to CBD, does not use the CB1 receptors like THC, and therefore does not interfere with psychomotor and psychological functions. CBDV actually prioritizes its action at TRPV1 (Transient Receptor Potential cation channel subfamily V member 1) receptors through modulation of gene expression.

THCV (Tetrahydrocannabivarin) structurally is a similar cannabinoid to THC, but instead of a pentyl (5-carbon) side chain, it contains a propyl (3-carbon) side chain and is non-psychoactive. THCV has been shown to be a CB1 antagonist and a CB2 agonist. Agonism of CB2 receptors on microglia has been shown to limit the ability of microglia to release proinflammatory agents including tumor necrosis factor (TNFα) and nitric oxide (NO) [20,21].

The cannabis plant is also composed of a chemical mixture that includes phytocannabinoids, terpenoids, flavonoids, steroids and enzymes. While the exact mechanism of action is 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. [22] suggests chronic use and high doses of CBD, up to 1500 mg per day, have been repeatedly shown to be well tolerated by humans.

Materials and Methods

Study part 1. healthy subjects

In Part 1, 150 subjects were included in the study from a subject database of 10,000 volunteers, mostly healthcare workers. Clinical Studies USA (Las Vegas, Nevada and Scottsdale, Arizona) conducted two double blinded, placebo controlled human studies to assess the effect of Hempzorb81™, a cannabinoid-rich CBD oil. Subjects of 100 were randomly assigned to the CBD treatment group and 50 subjects assigned to the placebo group. Each group was advised to dose orally with 3 milliliters (mls) a day of the oral extract. The subjects were recommended not to change diet, fluid intake, or exercise.

Initial screening of subjects included: AST, ALT, to assess liver function, creatinine and blood urea nitrogen [23], thyroid stimulating hormone [24] for the evaluation of thyroid activity and to help evaluate kidney function, a complete blood count (CBC), and platelets (manuscript in preparation). Each of these tests was run on arterial blood drawn following standardized protocol for the procedures and completed using standard techniques. Additionally, a number of inflammatory markers were also analyzed: enzyme-linked immunosorbent assays were used to measure TNFα and IL-6 levels; an immunochemiluminometric assay was used to measure CRP levels; and standard testing methods were used to measure the ESR. Inflammatory marker data is reported here (Table 1).

Each ml of CBD extract contained approximately 3.11 mg of CBD for a total of 9.3 mg a day. As part of this study, arterial blood was drawn at the end of the 60-day study and evaluated for serum concentration of CBD. No other cannabinoids were measured although it can be estimated that other cannabinoids such as THCV, CBG and CBN had similar pharmacokinetics [25].

Subjects were randomly assigned to either the CBD treatment product group or the control group. Each subject signed a study consent form. Subjects were given instruction to orally ingest this study product once daily. 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.

Study inclusion criteria

- Subjects 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

Study 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
- 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 their safety

Full spectrum hemp oil

Purzorb® is a proprietary micellization process that micellizes a decarboxylated full-spectrum hemp oil including cannabidiol (CBD), cannabidivarin (CBDV) and tetrahydrocannabivarin (THCV) in a mixture suitable for oral ingestion. This patent-pending 81% cannabinoid full-spectrum micellized hemp oil utilizes the Purzorb® technology trademarked as Hempzorb81™. The oil is extracted from industrial hemp *Cannabis sativa* plants using supercritical CO_2 with column chromatography to remove THCΔ9. Substantial amounts of CBDV and THCV are present in the oil. According to the manufacturer, (Med7), each particle size is approximately 22 nm, making it highly soluble 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 with 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.

Hempzorb81™ has previously been evaluated in unpublished studies using an animal intestinal model (Bioactive Research - Bioavailability of Test Samples Project INT-THAT-3515) and a trial on 14 human subjects. Human Clinical Trial Evaluating the Safety and Efficacy of Full Spectrum Hemp Oil (2019) unpublished manuscript). It was shown to have much more rapid absorption and four times the bioavailability of standard CBD extract in medium-chain triglyceride (MCT) oil.

Results

Part 1. healthy subjects

The end-point determinants of CRP, ESR, TNFα and IL-6 levels were measured at day 0 and day 60 in both the CBD Oil and placebo study groups. Statistical analysis was done using two-tailed. paired t-tests where statistical significance was set to p- values < 0.05.

Statistically significant reductions were measured in tumor necrosis factor alpha (TNFα) and interleukin-6. C-Reactive Protein, and ESR determinations showed reductions though not statistically significant.

Discussion

Part 1. healthy subjects

CBD has been shown in animal and human studies to have beneficial effects on inflammation, inflammatory markers, cytokine production and in animal models of acute lung injury and inflammatory asthma. CBD has had initial positive results in Phase 2 human trials of the treatment of GVHD, a condition that is pathophysiologically similar to SARS-CoV-2.

This study revealed that 9.3 mg of CBD sublingually (3.8% micellized nano-particle whole-plantextract) with bioavailability previously shown to be 85% when used for 60 days resulted in several positive therapeutic effects related to pro-inflammatory cytokine production.

Two cytokines associated with development of SARS-CoV-2, TNFα and IL-6, showed statistically significant reductions compared to placebo (Table 1). Two inflammatory markers, ESR and CRP, showed reductions of 19.4% and 12.5%, respectively, but the results were not statistically significant.

No side effects were reported or stated during this 60-day trial. No drug-drug interactions were noted for the period of this study. No statistically significant changes were measured in the Control Group for any of the tested blood levels.

Introduction

Part 2. COVID-19 test positive subjects

During the first two months of this six-month study, the COVID-19 virus pandemic broke out and was significant in the area where the study was being conducted. The opportunity, therefore, arose to enroll study patients who subsequently tested positive for SARS-Cov-2. As in Part 1, a selected panel of inflammatory proteins, i.e.,TNFα, CRP, IL-1,6 with the addition of the WBC, were similarly selected to evaluate patients with a positive test result. Part 2 extends the report to the effects of the Hempzorb81™ formulation on a subset of 44 study subjects within the original 150 patients who tested positive for COVID infection compared to a 44 subject COVID-19 negative tested control group made up of original study subjects as well as from the clinical practices of the authors. All enrolled subjects conformed to the inclusion and exclusion criteria set out in Study 1.

Results

Part 2. COVID-19 test positive subjects

This section utilizes statistical mean comparison (paired sampled and independent samples t-test) to evaluate the impact that the Hempzorb81™ product has on study participant immune response among patients diagnosed with SARS-Cov2 when compared to placebo. Outcomes analyzed include TNFα, CRP, IL-1, IL-6, and WBC.

Markers evaluated

Tumor necrosis factor alpha (TNFα): Tumor necrosis factor alpha (TNFα) is an anti-inflammatory cytokine produced by microphages/monocytes during periods of acute inflammation. Higher levels of TNFα indicate disease, such as arthritis, diabetes, Crohn's and even cancer. The normal range for TNFα is 0 pg/ml to16 pg/ml. Table 2 shows the distribution of change in TNFα over the 4-week study period for each of the three dosage groups.

C-Reactive Protein (CRP): C-reactive protein is made by the liver increasing when there is inflammation somewhere in the body. It is often used to monitor the severity of disease in chronic conditions. The normal range for CRP is between less than 10 mg/ml. Table 2 shows the average change in C-Reactive Protein (CRP) over the 4-week study period for each of the dosage groups.

Interleukin-1 beta (IL-1 β)**:** Interleukin-1 β is a pro-inflammatory cytokine associated with insulin secretion, appetite regulation and fever reduction. It is known to be a better measure associated with severity of simple steatosis (fatty liver) than liver function tests in obese patients. Table 2 shows the blood levels of IL-1 among study participants. Normal range for IL-1 range from 0 pg/ml to 5 pg/mL.

Interleukin-6: Interleukin-6 is a cytokine that induces the synthesis of acute-phaseproteins, like CRP, and inhibits the production of albumin. High levels have been shown to predict the need for mechanical ventilation and extensive lung damage among SARS Cov-2 patients. Normal range for IL-6 is less 5 pg/ml to 15 pg/ml.

White Blood Count (WBC): White blood count measures the number of white blood cells or leukocytes in the blood. If the volume is too low, it can indicate that an individual may have a hard time fighting off an infection. The normal white blood cell count in a healthy adult is between 4,000 and 11,000 WBCs per microliter.

Statistically significant reductions were measured in tumor necrosis factor alpha (TNFα), Interleukin-1, Interleukin-6, C-Reactive Protein and WBC in patients given Hempzorb81™ per protocol in Part 1. No patients withdrew from the study or were hospitalized as a result of their infection.

Discussion

Part 2. COVID-19 test positive patients

In both Part 1, where healthy subjects were evaluated, and Part 2, where original study subjects tested COVID-19 positive, reductions in major cytokines known to play a part in Cytokine Storm Syndrome were found to be reduced for TNFα, CRP, and IL-1,6 over the study time. The current working hypothesis for SARS-CoV-2 is that decreasing the release of inflammatory cytokines should result in reduced morbidity and mortality. Additionally, in our study, the Full-

Table 1: Effect of Hempzorb81™ on inflammatory markers in normal subject controls.

Marker	TNFα		IL-6		CRP		ESR	
Study Group	Day 0	Day 60	Day 0	Day 60	Day 0	Day 60	Day 0	Day 60
CBD Hemp Oil	6.52	3.14	2.67	1.68	3.44	3.01	24.2	19.52
Placebo	2.6	2.3	3.47	3.29	3.52	3.53	24.16	23.88
P-Value =	p = 0.03		p = 0.03		Reduced 12.5% Not statistically significant		Reduced 19.4% Not statistically significant	

Table 2: Effect of Hempzorb81™ on COVID-19 activated inflammatory markers.

Marker		TNFα			CRP			IL1			IL-6			WBC Count		
Study Group		Week 1	Week 2	Week 4	Week 1	Week 2	Week 4	Week 1	Week 2	Week 4	Week 1	Week 2	Week 4	Week 1	Week 2	Week 4
CBD Hemp	3 ml	1.82	1.66	1.43	13.3	2.965	2.615	6.2	5.785	6.025	2.835	2.495	1.74	19,750	8,462	7,705
Oil	4 ml	1.16	1.21	1.23	12	3.831	2.975	5.343	5.3	5.281	1.844	1.669	1.569	27,618	18,003	7,868
Placebo		1.43	1.64	1.93	11.07	10.94	11.38	8.56	9.14	9.01	2.61	2.88	2.82	3,246	3,521	4,017
P-Value =		p= <0.001			p= <0.001			p=0.145			p=0.003			p=0.010		

Spectrum Hemp Oil Hempzorb81™ significantly reduced white blood cell counts in these patients over the course of treatment more than 2-fold. Previously a patient's WBC count on admission significantly correlated with death in COVID-19 patients.

Recent publication of data indicating at least two cannabinoid acids, cannabigerolic acid (CBGA) and cannabidiolic acid (CBDA) from hemp varietals of cannabis, were found to bind the SARS-CoV-2 spike protein [26], thereby preventing the virus from entering cells. This report supports the utility of hemp extracts as therapeutic and/or protective agents against COVID-19. In response to this report [27], it was noted the research involved neither human subjects nor laboratory animals. These pre-clinical cell culture *in vitro* experiments documented two acidic cannabinoids attached to the spike protein with micromolar affinities. In clinical pharmacology, developing drugs exceeding nanomolar concentrations in tissues is extraordinarily challenging. Though an entertaining preliminary finding, many, many years of development await any significant advance from these findings to clinical application of either as singular pharmaceutical entities.

Another recent publication designed to determine whether CBD is capable of inhibiting infection of cells by SARS-CoV-2 has presented strong experimental evidence suggesting CBD and its metabolite 7-OH-CBD, but not other closely related CBD congeners, have the capability of blocking SARS-CoV-2 viral infection both at early and late stages [28]. The authors present: (i) CBD potently inhibited viral replication in three different human and monkey cell lines, including human lung carcinoma A549 cells expressing exogenous human ACE-2 receptor (A549-ACE2); (ii) in a pre-clinical animal model, CBD treatment at non-toxic levels of SARS-CoV-2 infected mice reduced viral titers in the lungs and nasal turbinates; and (iii) analysis of patients with documented CBD consumption of 100 mg/ml CBD at time of testing revealed fewer positive test results. Results of RNA-seq data from various cell lines, including knockout cell lines, indicated CBD induction of IRE1α is critical to its anti-viral activity against SARS-CoV-2.

The data presented in our human clinical study indicates a preliminary understanding of how micellular delivery of the Hempzorb81™ formulation affects a number of recognized inflammatory markers associated with SARS-CoV2. Administration of this hemp full-spectrum formulation should not be seen as attempting a therapeutic cure. However, with the evidence presented above, utilization of the protocol described may at some future day, following larger regulatory track trials, offer a useful adjuvant to modifying the effects of a patient-facing the Cytokine storm scenario. We advise caution in utilizing formulations that have not been thoroughly vetted and conforming to U.S. FDA standards.

Summary

Growing evidence from multiple investigators, utilizing a broad array of hemp-based compounds spanning individual isolates to full-spectrum formulations, is developing an ongoing dictum of a role to be played by CBD and/or other cannabinoids or cannabinoid metabolites as a potential source of new treatments to control the COVID-19 pandemic spread. In our study, an early and one of the first human subject studies, substantial evidence has been developed to consider highly bioavailable CBD formulations, i.e. Hempzorb81™ as a potential adjuvant to agents available as preventative and therapeutic options for COVID-19 infections. We report analysis on a number of inflammatory molecules or markers associated with inflammatory pathways, including TNFα, CRP, IL-1, IL-6 and WBCs, whose expression are characteristic of the Cytokine Storm Syndrome, are significantly reduced in COVID-19 positive patients following institution of a Hempzorb81™ regimen. Together with the reduction in these anti-inflammatory markers, additional strong evidence for such a consideration include: (i) there were no reported side effects over the course of the studies; (ii) there were no drug-drug interactions identified; and (iii) the important fact that no patients withdrew from the study or were hospitalized as a result of the infection acquired during the study strongly indicates utilization of highly bioavailable CBD formulations and are gaining consideration as potential natural adjuvants in SARS-CoV2 treatment and prevention strategies. Finally, until widespread vaccination and therapeutics are available worldwide, a careful institution of hemp-based formulations are a consideration to potentially limit the spread and clinical course of the SARS-Co-V2 COVID-19 pandemic in areas lacking access to such resources.

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