



FUNDAMENTAL RESEARCH

A	TITLE OF FUNDAMENTAL RESEARCH PROJECT:
i	CBD oil potential to aid anxiety disorders with antidepressant-like effect
B	DETAILS OF AUTHORS & RESEARCH OFFICER
	Author 1: Muhammad Za'im Ruba'ie Author 2: Syafiqah Shikh Abdul Rahman Author 3: Muhammad Hazim Zakaria Research Officer: Dr. Hj. Mohd. Khafidz Hj. Mohd Ishak
C	DETAILS OF FUNDAMENTAL RESEARCH
	Abstract <p>Cannabidiol (CBD), a component of Cannabis sativa, is a pharmacologically broad-spectrum medication that has attracted growing interest as a treatment for a variety of neuropsychiatric illnesses in recent years. The current review aims to study the efficacy of CBD to identify CBD's potential to aid anxiety disorders with antidepressant-like effect. We discovered that preclinical evidence strongly supports CBD as a treatment for generalised anxiety disorder, panic disorder, social anxiety disorder, obsessive-compulsive disorder, and post-traumatic stress disorder when administered acutely. The evidence for anxiolytic effects of CBD in humans is also supported by studies, however it is currently restricted to acute doses and there are few investigations in clinical populations.</p> <p>Concurrently, the therapeutic response to currently available antidepressants takes a long time to manifest, and they are only moderately effective. The creation of medications that address these restrictions is essential for enhancing public health. Accordingly, the objectives of this investigation were to determine in 7 respondents if CBD could cause quick and lasting antidepressant-like effects.</p> <p>The test was performed on 7 volunteered adult respondents aged 25-58 in 7 days time frame and the results showed that a single dosage of CBD generated an antidepressant-like response either 20-30 min (acute) or 7 days (sustained) after treatment.</p> <p>These findings suggest that CBD generates an immediate and long-lasting antidepressant-like effect. The information supports CBD's therapeutic potential as a brand-new, rapidly acting antidepressant medication.</p>

Keywords: Cannabidiol, Symptoms, Medical cannabis, Effectiveness, Depression, Pain, Anxiety, Antidepressant

1 Introduction

Anxiety and fear are adaptive reactions that are necessary for overcoming survival risks. But severe or ongoing dread may be detrimental and cause impairment. Numerous neuropsychiatric disorders, such as generalised anxiety disorder (GAD), panic disorder (PD), post-traumatic stress disorder (PTSD), social anxiety disorder (SAD), and obsessive-compulsive disorder (OCD), present with symptoms of excessive dread and worry (OCD). Notably, in the most recent revision of the Diagnostic and Statistical Manual of Mental Disorders-5, PTSD and OCD are no longer categorised as anxiety diseases; yet, excessive anxiety is key to the symptomatology of both disorders. These anxiety-related disorders have been linked to lower levels of wellbeing, higher rates of unemployment and relationship dissolution, and higher risks of suicide [1-3].

According to a 2015 Health ministry report, 29% of Malaysians, or one in three people, experienced mental health problems. For the time being in 2022, the numbers have not changed. The second major health problem impacting Malaysians is mental illness. Most of those afflicted are between the ages of 16 and 19 and come from low-income families. The ailment affects over 2.3 million people in the nation at some time in their life [72].

A study conducted in Serdang Hospital based on 11-year data from January 2008 to December 2018 using defined daily doses per 1000 populations per year metric (DDDs / 1000 / year) to compare the popularity of psychotropic classes and individual drugs showed total utilization of psychotropic drugs increased markedly by 859.2 % (from 75.9 to 727.8 DDDs / 1000 / year). Antidepressants were the most frequently dispensed class, with a significant increase by 1828.6 % (from 20 to 385.9 DDDs / 1000 / year) [4].

Serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, benzodiazepines, monoamine oxidase inhibitors, tricyclic antidepressants, and partial 5-hydroxytryptamine (5-HT)_{1A} receptor agonists are some of the pharmacological treatments now on the market. Atypical antipsychotics and anticonvulsants are also used to treat PTSD. Particularly in PTSD, these drugs are linked to low response rates and lingering symptoms, and side effects may make them harder to tolerate and keep taking [5–8]. The need for new pharmaceutical treatments is urgent due to the significant burden of anxiety-related diseases and the shortcomings of existing therapies.

Cannabis sativa has a phytocannabinoid called cannabidiol (CBD), which doesn't have the same intoxicating effects as 9-tetrahydrocannabinol (THC). Due to its various central nervous system activities, CBD offers extensive therapeutic benefits for a variety of neuropsychiatric illnesses [9, 10].

	<p>As a potential anxiolytic medication, CBD has gained growing interest in recent years [11–13]. This review's objective is to evaluate the evidence from recent preclinical, clinical, and epidemiological studies in relation to the possible drawbacks and advantages of CBD as an anxiety disorder treatment by giving CBD oil treatment to adult respondents and recording their response.</p>
<p>2</p>	<p>Materials and Method</p> <p>Using the search terms "cannabidiol" and "anxiety" or "fear" or "stress" or "anxiety disorder" or "generalised anxiety disorder" or "social anxiety disorder" or "social phobia" or "post-traumatic stress disorder" or "panic disorder" or "obsessive compulsive disorder," a search of the databases MEDLINE (PubMed), PsycINFO, Web of Science Scopus, and the Cochran, there were a total of 49 initial preclinical, clinical, or epidemiological research. Included were neuroimaging studies that presented outcomes from anxiety-related tasks or resting brain activity. Studies that examined the epidemiological or clinical effects of CBD on anxiety symptoms or the possible preventative effects of CBD on anxiety symptoms brought on by cannabis use were included.</p> <p>In this Fundamental Research, we conducted an experiment on volunteered adult respondents in Thailand as CBD oil is widely used and easily obtained. Test was done based on observation and feedback from respondents unbiased as no reward was given to any respondent.</p>
<p>2.1</p>	<p>Therapeutic Characteristics and Fundamental Pharmacology</p> <p>One of the most popular drugs in Western society is Cannabis sativa, a member of the flowering plant genus Cannabis. The two main phytocannabinoids that affect the central nervous system are THC, which causes the euphoric and altered state of consciousness, and CBD, which has no such psychoactive effects. CBD has been shown in preclinical and clinical trials to have a variety of therapeutic qualities, such as antipsychotic, analgesic, neuroprotective, anticonvulsant, antiemetic, antioxidant, anti-inflammatory, anti-arthritic, and antineoplastic effects (see reviews in [9, 10, 14-17]). CBD was well tolerated throughout a wide dose range, up to 1500 mg/day (orally), according to an assessment of probable side effects in humans, with no observed psychomotor slowdown, adverse mood effects, or abnormal vital sign findings [18].</p>
<p>2.2</p>	<p>The Endocannabinoid System</p> <p>The endocannabinoid system (ECS) is a neuromodulatory system responsible for partial regulation of cognitive and emotional processes in the human central nervous system such as behavior, mood disorders, and neurologic disorders such as epilepsy [20].</p> <p>Even if you don't consume cannabis, the ECS is still present and functioning in your body. You have ECS receptors all over your body. In order to communicate with the ECS that something</p>

needs to be done, endocannabinoids attach to them. The two primary endocannabinoid receptors are CB1 receptors, which are largely present in the central nervous system, and CB2 receptors, which are mostly present in the peripheral nervous system, particularly immune cells. Both receptors can be binded by endocannabinoids. The location of the receptor and the endocannabinoid it binds to determine the outcomes.

For example, endocannabinoids might target CB1 receptors in a spinal nerve to relieve pain. Others might bind to a CB2 receptor in your immune cells to signal that your body's experiencing inflammation, a common sign of autoimmune disorders.

Research has linked the ECS to the following processes: appetite and digestion, metabolism, chronic pain, inflammation and other immune system responses, mood, learning and memory, motor control, sleep, cardiovascular system function, muscle formation, bone remodeling and growth, liver function, stress, skin and nerve function, and reproductive system function.

These functions all contribute to homeostasis, which refers to stability of your internal environment. For example, if an outside force, such as pain from an injury or a fever, throws off your body's homeostasis, your ECS kicks in to help your body return to its ideal operation. Today, experts believe that maintaining homeostasis is the primary role of the ECS [73].

One of the several cannabinoids obtained from the Cannabis sativa plant, which produces hemp, is CBD. Tetrahydrocannabinol is a well-known cannabinoid (THC). However, compared to THC, CBD has special qualities that make it appealing for therapeutic applications. Pharmacologically speaking, CBD has no overtly intoxicating (psychotropic) effects and no risk of excitotoxicity, two factors that are very important when choosing a treatment.

Homeostasis, metabolism, inflammation, pain-sensation, mood, memory, and many other physiological and mental functions are all balanced and controlled by the Hypothalamic-Pituitary-Adrenal (HPA) axis and ECS working together. It's interesting to note that THC can directly connect to CB receptors, preferring the CB1 receptors because they are more numerous in the central nervous system and are the cause of THC's psychoactive effects. However, CBD affects cellular function indirectly by interacting with other cells, which in turn interact with these receptors and other receptors.

The endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG), which are based on arachidonates, are also found in the ECS, along with the enzymes fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL), which degrade AEA and 2-AG respectively.

CBD increases the body's levels of AEA and 2-AG by acting as a competitive inhibitor that binds to FAAH and MAGL. Endocannabinoid levels in the body can be raised to help the ECS function properly and maintain balance during times of stress or change. The fight-or-flight response, also known as acute hyperarousal, is a physiological response to a perceived threat.

or stressor, whether or not it is actual. In short, when the cerebral cortex detects an external stress signal, the hypothalamus begins to release corticotrophin-releasing hormone (CRH) which then triggers the pituitary gland to release adrenocorticotropic hormone (ACTH), which cascades to the adrenal glands and causes the release of cortisol, epinephrine, and norepinephrine. This enables the body to react in an enhanced manner, but persistent activation of this system might cause long-term harm. Additionally, the hippocampus and amygdala have regions that are heavily populated with CB1 receptors. The primary functions of the amygdala in the body are intelligence and emotion processing, including stress, anxiety, fear, and PTSD.

Most stress and anxiety are physiologically caused by the bed nucleus of the stria terminalis (BNST) working with the amygdala to coordinate a stress-based response. Here, serotonin related 5HT-1a receptors and the amygdala's BNST are both activated by CBD to create its anxiolytic effects. It's crucial to remember that CBD only slightly raises AEA levels. This has been demonstrated to provide sufficient stimulation to reduce FAAH levels and the neurotransmitter glutamate, alleviating stress and enabling the brain to react to stress in an efficient manner.

Both the HPA axis and the ECS are out of balance and dysfunctional during conditions of persistent stress and inflammation. The deficiency of endocannabinoids must be addressed and the HPA axis must be restored to equilibrium. By increasing AEA and lowering glutamate by reducing CRH and FAAH with exogenous cannabinoids like CBD, the ECS can be corrected. Wellness, mood, and stress response are all directly connected with higher amounts of AEA. By concentrating on reducing cortisol and CRH levels through stress, food, and sleep management the HPA axis can be corrected.

All things considered, CBD is a great approach to increase endocannabinoid signalling enhance control over the HPA axis, and support a healthy endocrine system. Naturally, CBD raises ECS tone, which enhances the HPA axis's ability to regulate homeostasis. ECS and HPA axis equilibrium can be preserved with the use of CBD, a potent dietary supplement that is non-toxic and non-psychoactive. Together with its anti-inflammatory, anti-stress, and anti-anxiety effects, it also has antioxidant and neuroprotective characteristics [74].

2.3 Human Experiment

The experiment was carried out on both male and female human among 7 volunteered adult respondents in Thailand. All respondents were living separately and were given a bottle of RAKSA Full Spectrum CBD Oil from Golden Triangle Group Co., Ltd (GTG). The given CBD oil is a medical grade and toxin-free high-quality cannabis distillate with 5% concentration of CBD (500mg per 10ml). The THC content is less than 0.2% giving no psychoactive effect. The given CBD oil is fully licensed and tested to assure quality of the product every time, making it qualified to treat various health issues. Throughout the duration of the experiment, respondents were free to practice their usual diets.

3 Results

Experiment: CBD's potential as a treatment for anxiety-related diseases and CBD's potential for a quick and lasting antidepressant-like effects

Table 1 lists result from the experiment in no specific order. Observation on the existing anxiety-related concern from each respondent is used to study the effects of CBD. Anxiolytic effects detected at moderate level.

Respondent	Age	Weight	Route	Dose	Effect
Female	28	58 kg	Sublingual	272 mg per day	1. Instantly feel relaxed in 15-20mins. 2. Controlled panic attack within 7 days consumption. No hands trembling.
Male	30	72 kg	Sublingual	318 mg per day	1. Instantly feel relaxed in 15-30mins. 2. Recorded 4 hours deep sleep every night (used to be 1-2 hours).
Male	47	76 kg	Sublingual	363 mg per day	1. Instantly feel relaxed in 20-30mins. 2. Recorded 6 hours deep sleep every night (used to be 3-4 hours).
Female	36	63 kg	Sublingual	272 mg per day	1. Instantly feel relaxed in 15-30mins. 2. Controlled stress on a daily basis. No panic attack symptoms

					after 7 days consumption.
Female	56	62 kg	Sublingual	272 mg per day	1. Instantly feel relaxed in 25-30mins. 2. Controlled panic attack after 7 days consumption.
Male	34	80 kg	Sublingual	363 mg per day	1. Instantly feel relaxed in 25-30mins. 2. Controlled anger and aggression within 7 days consumption.
Female	58	55 kg	Sublingual	272 mg per day	1. Instantly feel relaxed in 20-30mins. 2. Improved sleeping hours to average 6 hours after 7 days (used to be average 3 hours).

Table 1

The CBD dosage is generally calculated by the day based on the weight of the person taking it. The following CBD dosage chart is based upon recommendations from multiple sources. The wide ranges are due to more than just weight variations. Some conditions call for using lower amounts of CBD than others.

Weight	CBD Recommended Dose
35 kg to 45 kg	180 mg to 450 mg
45 kg to 55 kg	225 mg to 545 mg
55 kg to 65 kg	272 mg to 636 mg
65 kg to 75 kg	318 mg to 727 mg
75 kg to 85 kg	363 mg to 818 mg
85 kg to 95 kg	409 mg to 909 mg
95 kg to 100 kg	454 mg to 600 mg
100kg and above	Up to 600 mg per day

Table 2

4 Discussions

Overall, the experiment shows the CBD oil gives instant relieving reaction and also has positive long-lasting effect. All respondents benefit from the experiment and intent to continue the CBD intake. All of them are already on antidepressant medication previously and strongly prefer CBD oil as substitute due to no side effects impacting their normal daily routine.

Existing preclinical research also strongly suggests that CBD may be used to treat anxiety disorders. Anxiolytic, panicolytic, and anticomulsive actions, as well as a reduction in autonomic arousal, a reduction in the expression of conditioned fear, an enhancement of fear extinction, a blockade of reconsolidation, and a prevention of the long-term anxiogenic effects of stress are just a few of the diverse actions that CBD demonstrates that are relevant to multiple symptom domains. As there are very few studies that are relevant and have yielded inconsistent results, including both anxiolytic and anxiogenic outcomes, more research is also needed to determine the effectiveness of CBD when delivered in chronic doses.

Preclinical research also favours the use of systemic CBD as an acute treatment for GAD, SAD, PD, OCD, and PTSD. It also implies that CBD has the advantage over other medications in that it does not produce anxiogenic effects at larger doses. Results, in particular, point to possibilities for treating a variety of PTSD symptom categories, such as lowering arousal and avoidance, avoiding the long-term negative consequences of stress, and improving the extinction of persistent fear memories while preventing their reconsolidation.

Human Experimental and Clinical Studies: Evidence from Acute Psychological Studies

CBD demonstrated similar efficacy to ipsapirone (a 5-HT_{1A}R agonist) or diazepam in reducing anxiety related to a simulated public speaking test in healthy people and in subjects with SAD [55, 58]. In both healthy and SAD participants, CBD also lessened the anticipated anxiety related to undertaking a single-photon emission computed tomography (SPECT) imaging procedure [56, 57]. In particular, inhaled CBD given before or after extinction training in a contextual fear conditioning paradigm led to a trend-level enhancement in the reduction of skin conductance response during reinstatement and a significant reduction in expectancy (of shock) ratings during reinstatement [59]. Finally, CBD improved the extinction of fear memories in healthy volunteers.

Human Experimental and Clinical Studies: Evidence from Epidemiological and Chronic Studies

Epidemiological studies of various neuropsychiatric disorders indicate that a higher CBD content in chronically consumed cannabis may protect against adverse effects of THC, including psychotic symptoms, drug cravings, memory loss, and hippocampal gray matter loss [60–69] (reviewed in [64]). As THC acutely causes anxiety, this pattern might also be noticeable for symptoms of ongoing anxiety. Two studies, including an uncontrolled retrospective study of PTSD patients who were civilians [65] and a case study of a patient with severe PTSD caused by sexual abuse [66], demonstrated that regular cannabis use significantly lessens PTSD symptoms. These studies, however, did not provide information on the THC:CBD ratio.

Benzodiazepines Refusal During Dispensing Process Among Patients Diagnosed With Depression or Schizophrenia in Malaysia

Psychiatric patients frequently receive prescriptions for benzodiazepines (BZDs). Few research have examined BZD rejection among patients with psychiatric disorders throughout the dispensing procedure, making it difficult to pinpoint the causes of this behaviour. From May to June 2018, a study was carried out at Jerantut Hospital's Specialist Clinic Pharmacy in Malaysia. Following the dispensing procedure, the researchers determined the BZD refusal status and gathered general BZD data using a questionnaire they had created. The Malaysian Medication Adherence Scale was used to measure medication adherence (MALMAS). 75 people with psychiatric problems take part in the trial as a whole. The average duration of BZD treatment for participants was 32.8 ± 21.6 months. The 38.7% BZD refusal rate was highly correlated with a number of variables [67].

Significant correlations between BZD rejection and demographic variables like older age, male gender, and single status as well as diagnosis variables like schizophrenia diagnosis and abstinence from illicit drug usage were found. Therefore, it is important to periodically assess whether certain patient groups still require BZD. BZDs may be helpful for sedating and calming agitated schizophrenic patients in the short term. Additionally, it was discovered that BZD use for up to four weeks among individuals with depression improved antidepressant medication adherence.

However, there are a number of problems with BZD therapies, including over-prescribing by doctors, prolonged usage (exceeding four weeks) in 40% of antidepressant patients, dependence in around 47.6% to 60% of patients, and misuse. Additionally, it was discovered that long-term BZD use did not increase older individuals with depression's adherence to antidepressant treatment. Therefore, monitoring BZD use is essential.

BZDs are among the pharmaceuticals that are most frequently provided to people with psychiatric disorders. Diazepam and lorazepam were the most often prescribed BZDs, with 37.3% (n=28) and 32% (n=24), respectively. According to the research, people with depression were up to 52% more likely to become dependent on BZD than patients with schizophrenia, who were between 0 and 20% more likely to do so. Patients with depression may become dependent on BZDs due to problematic BZD usage, disobedience to medical advice, personality issues, and problematic BZD use. On the other hand, the current study's schizophrenia patients' unwillingness to take BZDs may have been caused by their knowledge of the dangers of BZD dependence associated with long-term BZD therapy.

Cannabis Strains for CBD Oil R&D in Malaysia

With the proven medicinal properties of CBD, researchers need to find the right Cannabis strain for hemp cultivation in Malaysia aligned with the country's law and regulations to be able to further explore the plant's potential in the medical field. Our recent visit to the Asia International Hemp Expo 2022 in Bangkok has open doors for Malaysia to deep dive into CBD research and development. Engagement with international seed banks such as Resin Seeds enables us to explore unlimited high CBD and low THC seed strains fit for producing medical grade CBD oil. Example of high CBD and low THC strains: Cannatonic, Strawberry Cake, Bioshot and more. These strains could produce up to 15% CBD with proper cultivation [8].

Meanwhile engagement with well established medical grade CBD brands such as Salus Bioceutical have provided important insight to control THC content in CBD oil extraction utilising the correct machinery and equipment through the right process. Available process to practice is the THC remediation in developing a compliant distillate end product.

Malaysian Climate Suitability for Cannabis Cultivation

Cannabis sativa, also known as hemp, is a versatile industrial crop that is primarily grown in temperate climates. In many regions, like Malaysia and other Asian nations where it is now prohibited to cultivate hemp, there is growing interest due to the tremendous potential for economic returns for its seeds and fibre.

A framework comprises crop modelling (current and future yields under climate change) suitability evaluation (climate and soil), and economic analysis (net present value (NPV), NPV benefit (NPVB), and benefit-cost ratio) (BCR) was conducted. Hemp was categorised as a crop that could be grown on the majority of the country's land by the land suitability evaluation. In simulations and prospective yield mapping, the AquaCrop model, parameterized from secondary data gathered from literature, was employed. At six locations between 2010 and 2019, the prospective average seed and fibre yield was predicted to be 1.61 ± 0.25 and $2.78 \pm 0.39 \text{ t ha}^{-1}$, respectively. Future yields in Malaysia indicated a rise in the majority of the areas using five general circulation model (GCM) simulations [68].

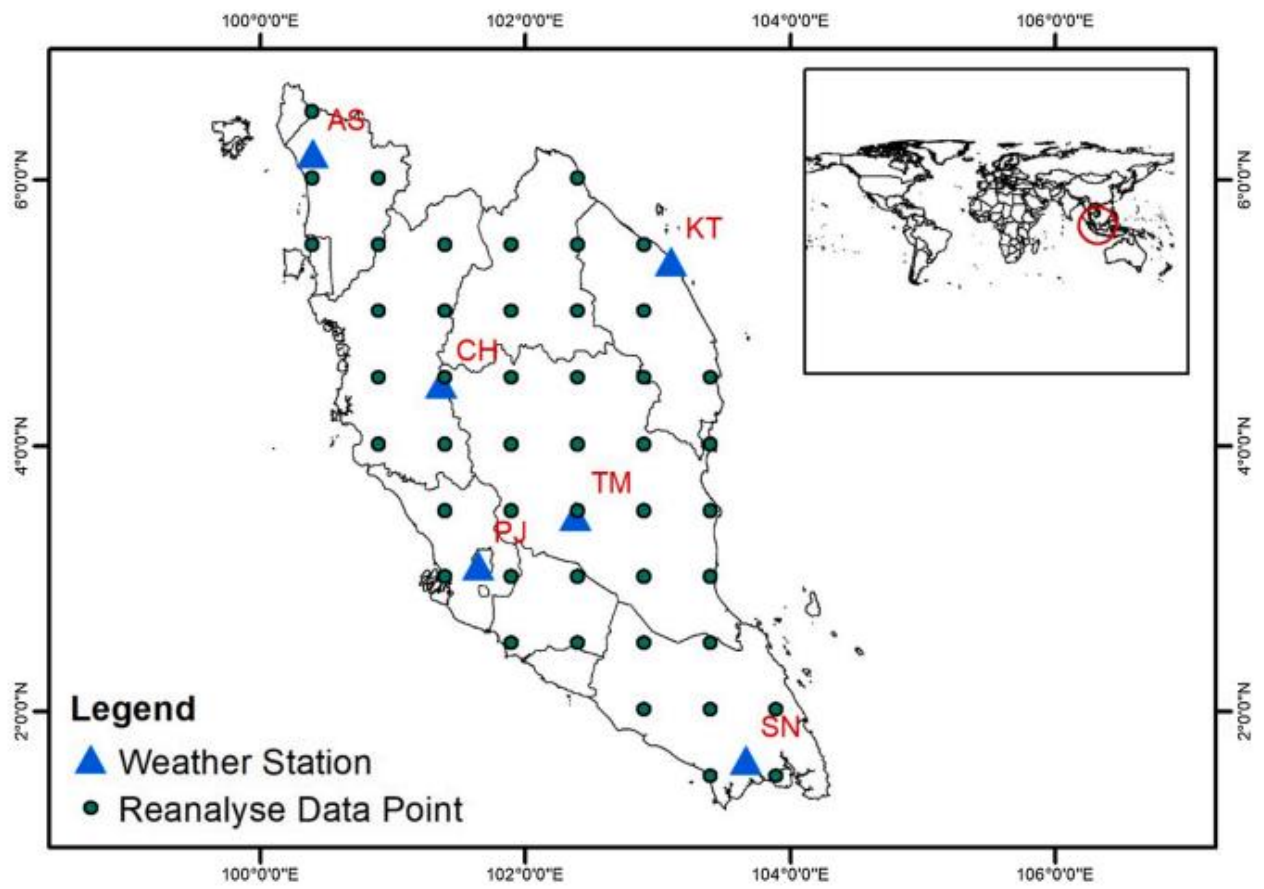


Fig. 2. Map of Peninsular Malaysia with locations used in yield simulations marked. Weather stations are marked as AS = Alor Setar, CH = Cameron highlands, KT = Kuala Terengganu, PJ = Petaling Jaya, TM = Temerloh and SN = Senai

Six meteorological stations of the Malaysian Meteorological Department's observations of daily rainfall and minimum and maximum temperatures were collected from 2010 to 2019. Tropical rainforest climate is the standard classification for all places.

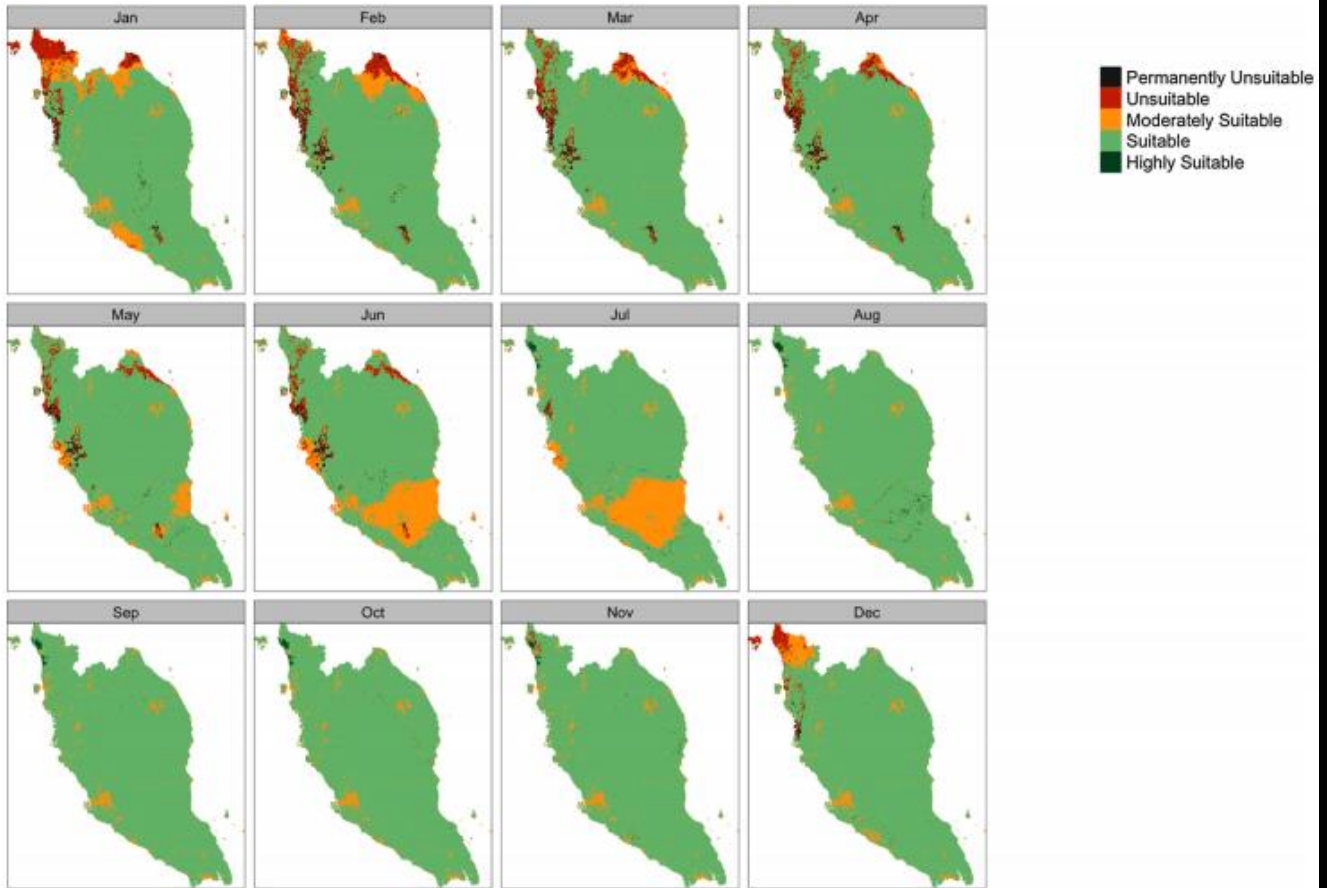


Fig. 3. Total climate and soil suitability for hemp across peninsular Malaysia

According to these maps, hemp could be farmed across Peninsular Malaysia all year long. In terms of temperature and total seasonal precipitation, the climate in Malaysia is generally favourable for hemp, however regions of the peninsula that experience precipitation levels above or below a threshold of 600 to 1200 mm during particular seasons are thought to be less suitable. The majority of Malaysia is "compatible" when combining soil and climate (a weighted average of total pedoclimatic appropriateness).

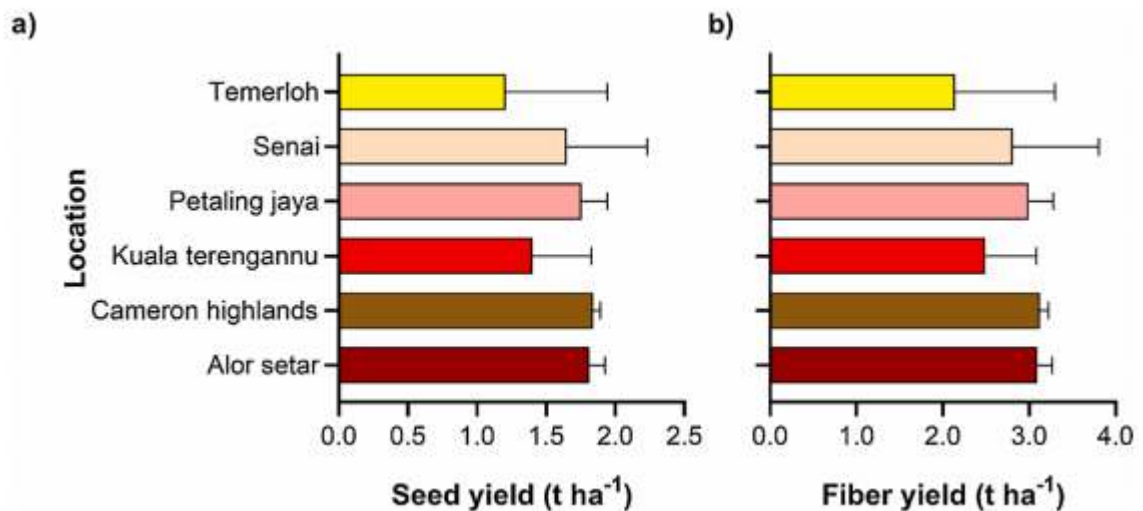


Fig. 4. Average hemp (a) seed and (b) fiber yield of selected locations throughout 2010-2019 period

Cameron Highlands recorded the highest seed output of 1.84 t ha⁻¹ under the investigated conditions, followed by Alor Setar (Fig. 4). According to this framework, hemp may be a profitable new crop for much of peninsular Malaysia where rice and the plantation sector (oil palm and rubber) already play significant roles. New industrial crops could aid in diversifying the Malaysian economy and agricultural sector in light of the growing effects of climate change on agriculture, deforestation, and other environmental and socioeconomic difficulties with plantations. In Malaysia, the utilisation of non-wood fibre crops like kenaf has already been tried with varying degrees of success. To our knowledge, however, this is the first study on the viability of hemp, a crop with multiple uses and economic worth in both its seed and fibre.

Hemp Farm Security

There are multiple established systems created to monitor and record all hemp plant movement in a farm. Riosol System is one example we could incorporate. The system is the outcome of advanced applied research and development, from an in-depth understanding of the agricultural processes of growing cannabis, complying with regulations, and extensive experience in industrial processes. It is an optimal solution to document the growing process from the earliest stage until the dry flower, with an array of application that meets all of a farmer's needs, in full compliance with the regulations.

The system documents all stages of the process while collecting, displaying, and analyzing the information, enabling complete traceability. From the mother plant and the propagation stages including the botanical and genetic material - everything is documented, and all the history is available. Measures of each stage, what treatments were conducted, what sprayings and by whom and more, all the information is accessible for analysis, monitoring and reporting purposes.

5 Clinical Protocol

To explore CBD compound further, we are planning for a Pre-Clinical Research under the project Local Hemp Cultivation for CBD Oil R&D As Antidepressants Substitute. The following is the suggested protocol:

Title: 24 weeks, double blind, randomized controlled trial comparing outcomes of cannabidiol (CBD) isolate versus antidepressant pills among Anxiety Disorders and Trauma and Stressor-Related Disorders in Malaysia.

Study Population: A total of 200 adults with Anxiety Disorders and Trauma and Stressor-Related Disorders are planned to be enrolled in the study. Aged 18 years and above with written consent, fulfilled DSM-5 diagnostic criteria for Anxiety Disorders and Trauma and Stressor-Related Disorders in University of Malaya Medical Centre (UMMC), Hospital Selayang (HS), Hospital Tunku Azizah (HTA) and Hospital Canselor Tuanku Muhriz UKM (HCTM).

Study Design: The study design is randomized clinical controlled clinical trial with double blind, parallel group, 24 weeks follow up, two arms with CBD treatment versus antidepressant pills.

General Objective: To investigate the effectiveness of CBD versus antidepressant pills among adults with Anxiety Disorders and Trauma and Stressor-Related Disorders.

Specific Objectives: 1) To investigate the tolerability of CBD among adults with Anxiety Disorders and Trauma and Stressor-Related Disorders. 2) To investigate the evidence for anxiolytic effects of CBD in humans.

Study Endpoint/Outcomes: 1) To determine the quality of life (QoL) of adults with Anxiety Disorders and Trauma and Stressor-Related Disorders using CBD treatment. 2) To Improve the behavior among adults with Anxiety Disorders and Trauma and Stressor-Related Disorders.

Sample Size: 200 subjects

Study Duration: 24 weeks

Anxiety Disorders in Malaysia

In Malaysia anxiety is one of the most commonly reported and growing mental health problems. According to the Fourth National Health Morbidity Survey (NHMS-IV), the prevalence rate of generalised anxiety disorder (GAD) was 1.7%, which is comparable with international figures (1.9%–2.5%). Based on the systematic review by Abdul Khaiyom, the prevalence rates of anxiety among students, general and clinical populations in Malaysia range between 1% to 67.6%, (unpublished data). This indicates the paramount need to ensure that patients with AD receive treatments with immediate sustainable effect, least disturbing side effects, and not affecting daily activities.

Year	2019		2020		2021		2022	
Case	New	Follow Up	New	Follow Up	New	Follow Up	New	Follow Up
Total	737	5000	764	4609	739	4106	856	3913

Table 2. Attendance of patients to Psychiatrist and Mental Health Clinic in year 2019-2022

Canabidiol (CBD)

One of the numerous compounds in the cannabis plant is CBD. It's linked to health advantages like pain reduction, better sleep, and recovery from addiction and anxiety disorders.

There are few types of CBD which is Full Spectrum, Broad Spectrum and CBD Isolate. Tetrahydrocannabinol (THC) and the rest of the cannabis plant's constituents are all present in Full Spectrum CBD. However, Full Spectrum CBD products that are approved by the federal government will never include more than 0.3% THC. Broad Spectrum CBD contains every element found in the cannabis plant except for THC. Without any other components from the cannabis plant, CBD Isolate is pure CBD. In this research, researcher focus on CBD Isolate to treat Anxiety Disorders and Trauma and Stressor-Related Disorders.

Methodology

This is a randomized clinical controlled clinical trial with double blind, parallel group, 24 weeks follow up, two arms with CBD treatment versus antidepressant pills. We are targeting participation at four sites namely in University of Malaya Medical Centre (UMMC), Hospital Selayang (HS), Hospital Tunku Azizah (HTA) and Hospital Canselor Tuanku Muhriz UKM (HCTM). The eligible subjects will be screened for substance used by using DSM-5.

The subject numbers were increase based on stat calculation methods. This study has two comparison groups CBD (Experimental) versus Antidepressants (Comparator), sample size calculation depends on the type of percentage of Anxiety Disorders and Trauma and Stressor-Related Disorders in Malaysia Hospitals.

Subject Selection

To participate in the study, each potential subject must fulfil all of the following requirements:

- a) Adults aged 18 years and above that fulfilled DSM-5 diagnostic criteria of Anxiety Disorders and Trauma and Stressor-Related Disorders
- b) Written consent of the subject
- c) Not on regular CBD treatment prior to study enrollment
- d) No known allergies to CBD products
- e) No acute psychotic/medical problems

Ethics

The investigator is in charge of making sure that the clinical trial is carried out in compliance with the protocol, Good Clinical Practice (GCP) standards, and any relevant regulatory requirements.

6 Conclusions

The potential of CBD as a treatment for anxiety disorders is well supported by evidence from the conducted experiment. At oral doses ranging from 200 to 400 mg, CBD decreases and gradually eliminates symptoms relating to various anxiety disorders in the respondents. The

experiment's findings show that CBD has both immediate and sustained antidepressant impact.

Preclinical data clearly show CBD's effectiveness in lowering anxiety behaviours associated with a variety of diseases, including PTSD, GAD, PD, OCD, and SAD, with no discernible anxiogenic effects. Preclinical findings are supported by results from human experiments, which also point to a lack of sedative effects, a low level of anxiogenic effects, and a very good safety profile. Further research is necessary to determine whether chronic CBD dose has similar effects in pertinent clinical populations because current preclinical and human findings mostly focus on acute CBD dosing in healthy subjects. Overall, this analysis highlights the potential benefits and necessity of future research into CBD's ability to treat anxiety disorders.

CBD has to be made an optional substitute to available antidepressants considering the current refusal rate for prescribed antidepressants at the moment due to its side effects. To compare:

Substance	CBD	Antidepressants (BZD)
Effectiveness	Within 30 mins for acute effect & 7 days for sustained effect	Within 4-8 weeks
Dosage	200 milligrams to 600 milligrams a day	1 milligram to 6 milligrams a day
Side Effects	Dry mouth, diarrhea, reduced appetite, drowsiness, and fatigue	Drowsiness, withdrawal, somnolence, fatigue, depression, sedation, and dizziness

Table 2

Given on average, more than 95 % of the country could be suitable for hemp cultivation, it is time for Malaysia to develop front to end research on CBD potential locally for the rising mental health issues in the country.

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