



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

Exploring the Botanical Origins, Traditional Uses, and Extraction Methods of Cannabidiol: Role in Pain, Inflammation, Anxiety, Depression, and Neurological Health

Rama Tyagi¹, Vikram Sharma¹, Neeraj Kumar², Gayatri Khosla^{1*}, Nadeem Ahmad Siddique³

1. Galgotia College of Pharmacy, Greater Noida, U.P., 201310, India

2. Department of Pharmacognosy & Phytochemistry, School of Pharmaceutical Education and Research, Jamia Hamdard, New Delhi, 110062, India

3. Department of Pharmaceutical Chemistry, College of Pharmacy, University of Hafar Al-Batin, Hafr Al-Batin 31991, Saudi Arabia

ABSTRACT

This review provides an in-depth exploration of Cannabidiol (CBD), a substance originating from the Cannabis species with noteworthy therapeutic potential. It comprehensively covers CBD's botanical origins, diverse extraction methodologies, and the emerging significance of nanoformulations in addressing a wide spectrum of health conditions, including pain, inflammation, anxiety, depression, and neurological disorders. The section on botanical origins delves into the sources of CBD within the Cannabis plant, highlighting the chemical variations among different strains and the Biosynthesis of the cannabidiol in *cannabis sativa*. The historical significance of CBD is elucidated, offering insights into its traditional uses across various cultures and historical contexts. The review paper extensively discusses various extraction techniques employed for CBD isolation, presenting a comparative analysis of their efficacy, safety, and environmental implications. Special attention is devoted to advanced extraction methodologies designed to optimize CBD yield while minimizing the content of psychoactive constituents, such as THC (delta-9-tetrahydrocannabinol). Additionally, this paper emphasizes the burgeoning domain of CBD nanoformulations, elucidating how nanotechnology augments CBD's bioavailability, stability, and targeted delivery. This advancement in drug delivery systems enhances CBD's therapeutic potential in the management of pain, inflammation, anxiety, depression, and neurological disorders. By offering information ranging from CBD's botanical origins to cutting-edge nanoformulations, this review paper is an invaluable resource for researchers, healthcare professionals, and policymakers. This review aims to deliver a succinct overview of the pharmacological, extraction technologies, phytochemical, botanical and ethnopharmacological regarding Cannabidiol.

Keywords: Cannabidiol (CBD), *Cannabis Sativa*, Extraction Methods, Therapeutic effect.

*Corresponding Author Name: Gayatri Khosla

Received 30 August 2026, Accepted 21 September 2026

Please cite this article as: Khosla G M *et al.*, A Detailed Review On Artificial Intelligence In Pharmacy Exploring the Botanical Origins, Traditional Uses, and Extraction Methods of Cannabidiol: Role in Pain, Inflammation, Anxiety, Depression, and Neurological Health. American Journal of PharmTech Research 2026.

INTRODUCTION

Cannabis is one of the oldest and most enduring crops in human history, having grown for over 6000 years. Systematically studied subspecies is *Cannabis sativa*, which is the one that blooms widely in Western countries. *Cannabis sativa* is a tall, without branches species with fragile leaves that can grow to 5 to 18 feet¹. The cannabis sativa plant, an annual herb of the Cannabaceae family, is among the earliest plants humans have ever encountered². These were the earliest plants used by humans for sustenance, health care, worship, or leisure. Among the illicit substances with an extensive history of consumption by humans is cannabis, which can also be utilized medicinally. Since ancient times, people have utilised cannabis, one of the first developed plants, fiber, hemp seeds, and active ingredients. Cannabis is said to have originated in Central Asia and cultivated for more than 12,000 years with a broad spread that stretches from China and Siberia to the Caspian and Himalayas. Hemp has been used for many uses since ancient times, such as producing fibre, seeds, and psychotropic compounds. One of the earliest types of hemp to be cultivated is hemp. Most of the expansion started in the steppes of Central Asia, especially in southern Siberia and Mongolia. However, many theories describes that it might have risen in the Hindu Kush mountains, Afghanistan, South Asia, the Huang He River valley. Between 1400 and 2000 BC, it might have shown up in the Middle East most likely as the outcome of increased Aryan arrivals to the region. Three primary subspecies of cannabis are *Cannabis indica*, *Cannabis sativa*, and *Cannabis ruderalis*, have been identified by botanists based on physical characteristics. *Cannabis indica* stands out among them because its 2-4 foot height, compact branching, large oblanceolate leaves, and numerous blooming buds give it a bushier appearance. *Cannabis ruderalis* is constantly symbiotic with other plants, frequently small and branchless, and typically low in tetrahydrocannabinol (THC). Hundreds of different chemical compounds have been identified in *Cannabis sativa*, and new ones are continuously being found. As prospective lead chemicals for future nutraceutical and pharmaceutical development, secondary metabolites such as cannabinoids and terpenes are currently being studied, as they are crucial in maintaining a plant's environment³.

In this review, we will explore the botanical origins of Cannabis, its distribution across different regions, and its traditional uses throughout history. We will also examine various extraction methods employed to obtain its compounds, the synthesis processes involved, and its therapeutic applications in managing pain, alleviating inflammation, and treating various neurological disorders.

Traditional uses

Over a hundred phytocannabinoids have been identified so far, and they represent a structurally diverse class of cannabis organically produced chemical components. Tetrahydrocannabinol (THC), the primary active ingredient and psychoactive phytocannabinoid, was originally identified and published in 1964 by researchers Gaoni and Mechoulam. Another significant advance occurred in 1992 when de Meijer *et al.* published their initial observations that plants from the same population had different proportions of THC and cannabidiol⁴. The significant cannabinoids extracted from the *Cannabis species* is cannabidiol. CBD has a good safety record and no psychotropic side effects⁵. CBD is a lipid-soluble, low-toxic cannabinoid that is present in cannabis. Because of its suspected health advantages, it is utilized in well-known supplements. In both laboratory and clinical settings, researchers have examined its biological properties and those relate to gastrointestinal illnesses, malignancies, psychiatric problems, and neurological disorders. According to a poll, an extensive number of people in the US turned to CBD products in 2019 to treat their pain, anxiety, insomnia, and arthritis⁶. CBD is a cannabinoid that is incredibly fascinating and widely recognized for its known pharmacological effects in a variety of pathologies, such as inflammation, neurodegenerative illnesses, epilepsy, autoimmune disorders including multiple sclerosis and arthritis, as well as schizophrenia and cancer⁷. Since the 1960s, cannabidiol has made up to 40% of the extract and has assumed its position as the major cannabinoid. Cannabinoid receptors and anandamide, an endocannabinoid with binding sites for CB1 and CB2 receptors, were discovered because of the discovery of CBD and THC⁸. This system includes the CB1 and CB2 cannabinoid receptors as endocannabinoids, which are natural compounds produced within our bodies. Anandamide (AEA) and 2 arachidonoyl glycerol (2AG) are two endocannabinoids derived from the acid⁹. Cannabidiol show its action by antagonizing CB1 and CB2 receptor agonists which inhibits the reuptake of endocannabinoid anandamide and antagonize the activity of fatty acid amide hydrolase (FAAH)^[2]. The precise mechanisms of CBD's biological effects are yet unknown as of 2019. Therefore, CBD is known to have less affinity for CB1 or CB2 receptors¹⁰. A non-specific cation channel involved in nociceptive signaling, the vanilloid type 1 receptor (TRPV1), has been reported to be stimulated by CBD. TRPV1 gets activated by CBD, which raises intracellular Ca²⁺¹¹. Additional receptors, such as GPR55, subtype 5-HT1A, and D2 receptor may participate in the mechanisms of action of CBD, according to different studies¹². Among the various pharmacological effects, CBD possesses anti-inflammatory, antiepileptic, antipsychotic, anticonvulsant, and immunomodulatory properties¹³. The 5-HT1A serotonin receptor is one of CBD's biological targets. Moreover, CBD showed an agonistic effect at higher dosages via inducing [35S] GTP-S binding¹⁴.

Extraction process

Cannabidiol is a bicyclic phytocannabinoid found to be highly lipophilic and concentrated in the glandular trichomes of the *Cannabis sativa* plant. By the action of cannabigerolic acid synthase, aryl carboxylic acid, also known as cannabidiolic acid (CBDA) is generated¹⁵. A critical step in establishing effective generation of the medicinally active ingredient cannabidiol (CBD) is the decarboxylation of cannabidiolic acid (CBDA) (Figure 1). When heated, acidic cannabinoids (ACBs) easily undergo conversion to neutral cannabinoids by releasing carbon dioxide¹⁶. Cannabidiolic acid (CBDA) undergoes decarboxylation to produce relative alcoholic cannabidiol (CBD). In plant tissues, this reaction typically occurs spontaneously which can speed up with the change in exposure to heat, light or storage conditions¹⁷.

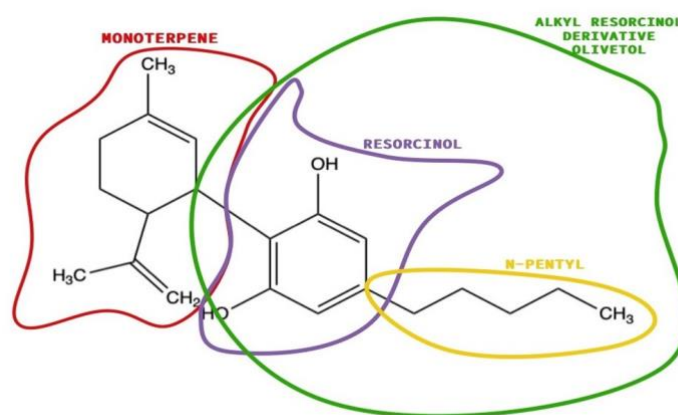


Figure 1: The bicyclic core of CBD is thought to be an adduct generated by the monoterpene, p-cymene and the alkyl resorcinol derivative olivetol. This structure is known as a tetrahydro biphenyl skeleton.⁷⁷

Cannabis-based medicinal treatments are either produced from resin that has been extracted or are ingested as oils. In this situation, the raw cannabis needs to be treated before or while the extraction process is going on Table-1. Because non-polar molecules and limited aqueous solubility, extraction of cannabinoids with variety of diverse organic solvents, like alcohols, hexane, etc¹⁸. The decision regarding the use of a solvent depends upon the characteristics of the solute, such as acid dissociation, hydrophobicity, molecular weight, solubility, and vapour pressure. These are also chosen based on the principle "Like Dissolves Like." To increase desired component yield, these procedures are continually optimized. Supercritical fluid extraction (SFE) techniques and conventional solvent extraction are two different approaches for phytocannabinoid extraction and separation (Figure 2)¹⁹.

Table 1: Different extraction process for cannabidiol

Extraction Methods	Plant Parts	Solvents	Conditions	Isolation	Ref.
Pressurized liquid extraction	Leaves, seeds, small inflorescence, and stalk of industrial hemp consisting of around 20% CBD.	Ethanol	Temperature 120°C Pressure: -11MPa Two static cycles that lasted three minutes each.	Flash chromatography: C18 Column Mobile phase: Water and ethanol UV detection at 210nm	[22]
Pressurized propane and dimethyl-ether extraction	Flower buds with some leaves.	Solvents: Dimethyl-ether and unscented propane (purity> 89.9%)	Temperature: 55oC Pressure: - 40 bar	LCMS-MS: Biphenyl Column Mobile phase: 0.1% formic acid in methanol	[23]
Green extraction using supercritical CO2	Dried biomass of inflorescences of the hemp cultivar Finola.	Supercritical CO2 Gas.	Temperature: - 60oC & 80OC Pressure: 380 bar Eight cycles comprising 10min creation in static and dynamic conditions separately. Constant flow rate of gas of 0.28 SCMH.	Ultra-performance liquid: C18 Column Mobile phase: water with 0.1% formic acid in methanol (20:80) Temperature: 35oC Wavelength at 225nm.	[24]
Optimized Microwave assisted extraction using a central composite design	Female <i>Cannabis sativa</i> hemp inflorescences.	Equipment: - 2.45 GHz multimode microwave reactor with two magnetrons each producing 950 W and an infrared temperature sensor.	Atmospheric Pressure.	GC and FID combined: Carrier gas Hydrogen Gas flow in the column 3.7 mL/min Temperature from 60oC to 340oC in 15.60 mins.	[17]
Soxhlet Extraction	The hemp dust residue of <i>cannabis sativa</i> .	Heptane 250ml. 2006T thermocouple	Ambient Temperature Reflux for 4 hours.	High Temperature-gas chromatography: - ZB-5HT capillary column. Carrier Gas helium. Constant pressure: - 22.35psi Temperature: - 360oC (Initially 60oC)	[25]

Green Extraction Using Deep Eutectic Solvents	The leaves of industrial hemp.	Materials for DES Preparation: Choline chloride ($\geq 98\%$): D-sorbitol ($\geq 98\%$) With molar ratio- 1:1- Betaine ($\geq 98\%$): Urea ($\geq 99.5\%$) With molar ratio- 1:2	Hemp-leaves powder and DES aqueous solution with concentration 50%-90% Solid-liquid ration (1:10-1:30). Different temperature.	HPLC: - Syncronis C18 column. Mobile phase: - Methanol: H ₂ O (78:22) Flow rate: 0.8mL/min. Wavelength 220nm. Room Temperature 15°C.	[13]
Ultrasound- Assisted Extraction	FM2 cannabis in dry powered form prepared at 120°C	Refined Olive oil. Siliconil bath	Maceration: -20ml olive oil Fixed temperature 100°C for preheated solvent 30mL Stirred for 40 mins Ultrasound assisted extraction: - 20mL olive oil Room temperature 25-27°C 2mm sonotrode(S26d). Sonication times 10,20 and 30mins with 60% amplitude.	HPLC: - 2.7 μ m analytical column. Eluents: water and acetonitrile containing 0.085% phosphoric acid. Flow rate: - 1.6mL/min. Column temperature 35°C Wavelength 220nm.	[10]

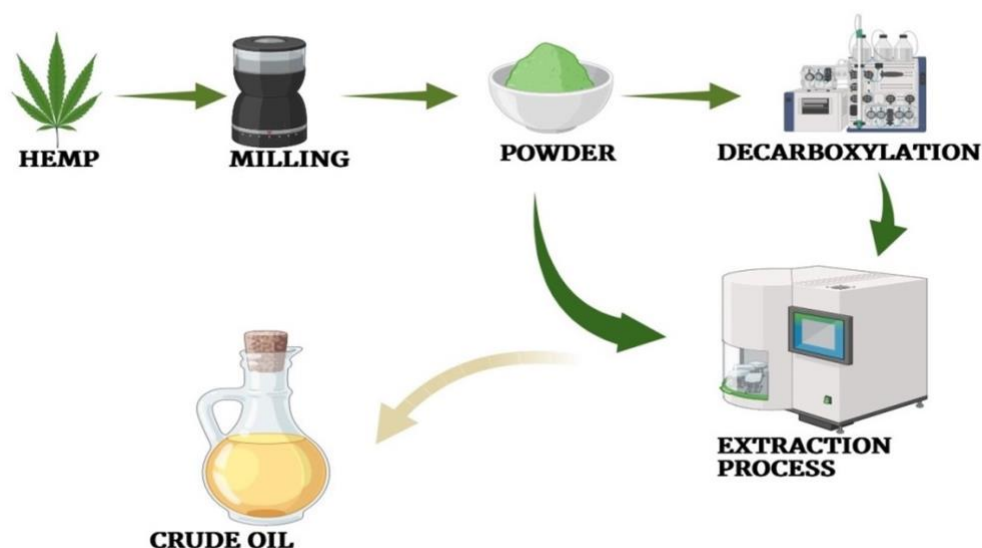


Figure 2: Basic Extraction process

Currently, the most popular approach for extracting cannabis for medical purposes is solid-liquid extraction (SLE) using organic solvents. Supercritical fluid extraction (SCF), avoids the involvement of harmful solvents, delivers superior extracts, and at lesser working durations²⁰. This process, the supercritical fluid (SCF) separates or dissolves plant matrix constituents by their solvating characteristics. By altering the temperature and pressure above the critical point, the solvating property of extracting the component may be preserved¹⁹. Cannabinoids may be extracted effectively using ultrasound or microwave treatments (UAE), with UAE being the best option due to its quicker processing time, lower energy usage, and cheaper prices. The ideal parameters for maximizing CBD output while utilizing UAE are 130 W power, 15 minutes of treatment duration, and 80% methanol as the solvent. Waves produced by cavitation help to lyse cells and dissolve chemical connections, which speeds up the extraction procedure²¹. Despite the partial conversion of CBDA into its neutral form brought on by the high extraction temperature attained by microwave-assisted extraction (MAE), this technique is useful for extracting CBD. However, dynamic maceration with EtOH turned shown to be the most efficient method for extracting cannabinoids from hemp when compared to both ultrasounds.

Botanical sources

Cannabis sativa's therapeutic and depressant properties have long been recognized. This plant yielded many secondary metabolites, the majority of which were utilized medicinally. *Cannabis sativa* contains more than 100 terpene-phenol chemicals known as phytocannabinoids. Cannabis has several psychotropic components, one of which is cannabidiol (CBD), which is the

phytocannabinoid that is found in the highest concentration in cannabis²⁶. The herbaceous plant *Cannabis sativa* L. is a member of the Cannabaceae family.

Cannabis sativa can be categorized into two primary forms: narcotic marijuana and medicinal hemp. Hemp normally has less than 0.3% psychotropic chemicals, but marijuana typically has over 20%, including CBD and 9-THC. Hemp is a valuable plant that is produced inside controlled environments, frequently in greenhouses or vertical farms using artificial lighting to control its development²⁷. Marijuana, on the other hand, contains a high concentration of THC but only a comparatively low amount of CBD. In contrast, hemp contains a considerable amount of CBD but a lower concentration of THC²⁸. The cultivation of cannabis, on the other hand, was first documented in East Asia²⁹⁻³⁰ and it was also documented in Eastern Europe at least eight thousand years ago. China has been a big hemp-growing nation and possibly the plant's presumed origin country on account of its largest hemp farming area and the development of numerous acres of land for cannabis cultivation³¹.

Biosynthesis of CBD in *Cannabis sativa*

Most of these cannabinoids are found in the leaves and inflorescences of plants. Tetrahydrocannabinol, cannabidiol, and cannabigerol were found to be the primary cannabinoids present in seed oil, but some cannabinoids were present in the hydroalcoholic maceration of seeds. Since cannabinoids are neither synthesized nor transmitted to the seeds, these results are most likely the effect of inflorescence resins contaminating the seeds³². Many cannabinoid-producing plants start the resorcinolic core's production with an aryl-containing beginning component. This includes the addition of acetate units in a systematic manner, which is then followed by aromatization of the aldol type. Therefore, a part of resorcinol that has been substituted with phenethyl is produced³³. Acidic cannabinoids are the by-product of cannabinoid production. When reactions like oxidation, decarboxylation, and cyclization occur, further cannabis alterations result through spontaneous breakdown or conversion. Due to the limited oxidative stability of alkylic cannabis, these modifications occur³⁴. The cannabis plant does not contain significant amounts of natural phytocannabinoids. Instead, the plant manufactures and stores carboxylic acid-containing variations of these compounds within its glandular trichomes. Some examples of these variants are 9-tetrahydrocannabinol acid, cannabidiol acid. Both THCA and CBDA are produced from a similar precursor, CBGA, through distinct oxidoreductase enzymes, namely THCA synthase and CBDA synthase, respectively. One of the processes that leads to the production of CBGA itself involves the use of olivetolic acid. Following this, the neutral forms are created through a process known as non-enzymatic decarboxylation of the acid forms, which results in the output of carbon

dioxide (CO₂). This transition occurs by a process that occurs in a solid state and is accelerated by factors that are external to the system, such as temperature, light, and oxygen. With time, CBDA gets converted into CBD as shown in Figure 3²³.

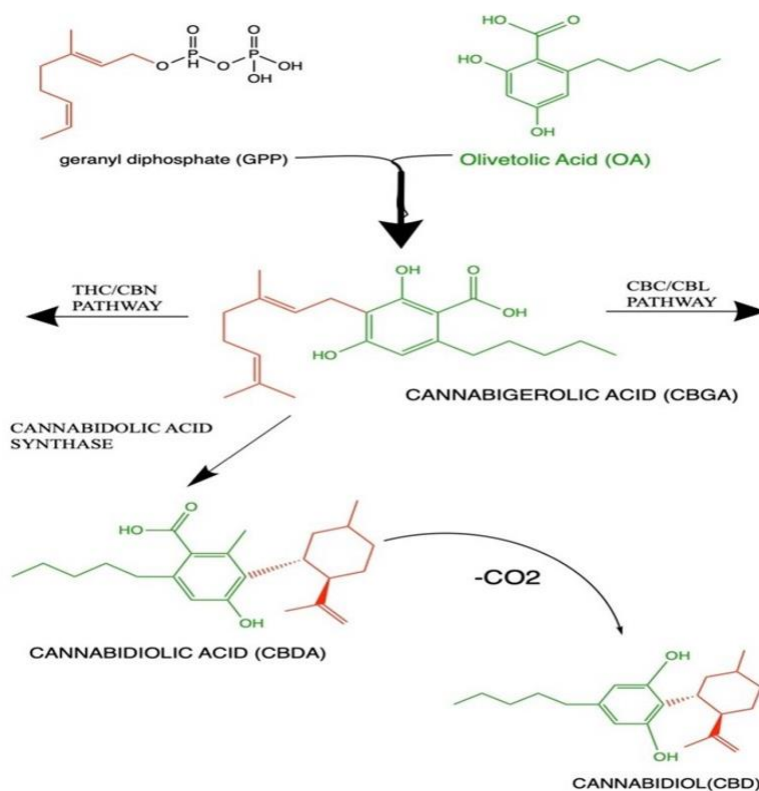


Figure 3: Biosynthesis of cannabidiol

Non-*Cannabis sativa*

After being extracted from the aerial parts of *Helichrysum umbraculigerum* L., which had been gathered in Natal, South Africa, cannabigerol, its acidic precursor CBGA, and related chemicals from the anomalous series were found. These discoveries were made after the two substances were separated from one another³³. *Trema orientalis* flower extracts may include cannabinoids, which are known as the chemical signatures of cannabis. This tropical African and Asian shrub has a long history of use in traditional medicine as an anti-infective drug. It has been demonstrated that the inflorescences of this plant contain both cannabidiol (CBD) and nine-tetrahydrocannabinol (9-THC). According to the GC-MS report, CBD was found to be 5.22 mg/Kg³⁵.

In the Humulus family, a unique plant called *Humulus Kriya* has been created that can produce cannabidiol. Research has shown that the effects of CBD present in *H. kriya* and cannabis are equivalent. In CBD experiments, *H. Kriya* shows promise as a good cannabis alternative, also removing the worry of THC contamination. Even, The Food Safety and Standards Authority of India has certified the CBD from *H. Kriya* as a safe food component, thus establishing its safety³⁶.

Traditional uses

There is a lengthy history of cannabis being used in several civilizations throughout the world. It was originally utilized as a food source, for medicine, to make fibres, ropes, paper, and textiles³⁷. Cannabis sativa has been indicated to contain more than 150 cannabinoids, including Δ^9 -THC and CBD, in addition to thousands of other compounds including flavonoids, terpenoids, and alkaloids which are increasing attention of the pharmaceutical industry toward Cannabis to elevate its significance in medical research (Figure 4) because these substances traditionally possess beneficial qualities discussed in Table 2³⁸.

Table 2: Medicinal uses of active constituents for various diseases

Medicinal Use	Disorder	Cannabis Component	Ref.
Chronic Pain Relief	Chronic Pain	THC	[39]
Seizure Reduction	Epilepsy (Dravet and Lennox-Gastaut Syndromes)	CBD	[40]
Neuropathic Pain Relief	Neuropathic Pain	THC/CBD	[41]
Appetite Stimulation	HIV/AIDS-Related Anorexia	THC	[42]
Anxiolytic	Anxiety Disorders	CBD	[43]
PTSD Symptom Reduction	Post-Traumatic Stress Disorder	THC/CBD	[44]
Symptom Relief	Inflammatory Bowel Disease	THC/CBD	[45]
Tic Reduction	Tourette Syndrome	THC	[46]
Intraocular Pressure Reduction	Glaucoma	THC	[47]
Behavioural Improvement	Alzheimer's Disease	THC	[48]
Symptom Management	Amyotrophic Lateral Sclerosis	THC/CBD	[49]
Pain Relief	Arthritis	THC/CBD	[50]
Pain and Stiffness Reduction	Fibromyalgia	THC/CBD	[51]
Migraine Relief	Migraine Headaches	THC/CBD	[52]
Symptom Management	Huntington's Disease	CBD	[53]

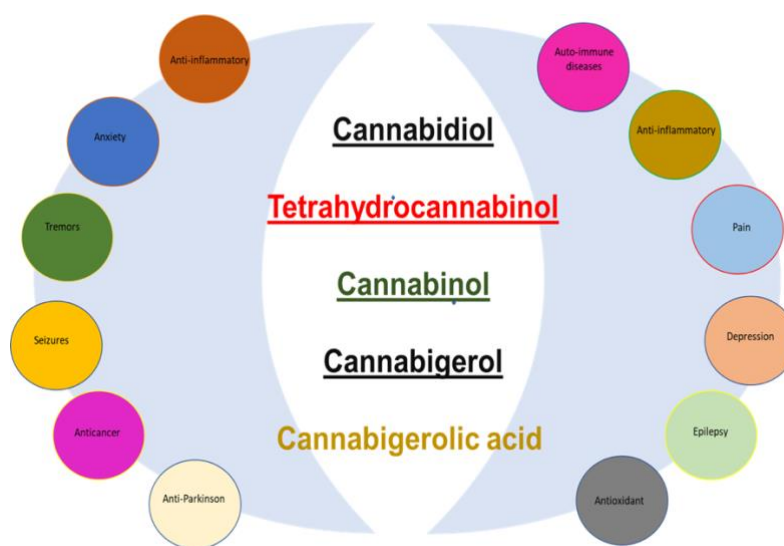


Figure 4: Medicinal uses of various chemical constituents of Cannabis species

Parkinson's disease**Pain**

Since the beginning of the twenty-first century, clinical trials have been done to investigate the efficacy of cannabidiol (CBD) as a treatment for chronic pain. The results reveal that CBD is incredibly useful. This CBD appeared to be useful in treating chronic pain brought on by kidney transplantation or chronic pain experienced by fibromyalgia patients. Additionally, formulations containing both CBD and THC, such as Sativex (1:1), have proven effective in reducing average pain scores among individuals suffering from chronic pain^[55]. According to research, CBD affects the transient receptor potential cation channel TRPV1 as well as the opioid receptors to relieve pain present in the CNS. But as discussed above CBD falls under Class II BCS classification so it has low penetration in CNS. Researchers created a CBD formulation employing polymer-coated nanoparticles (also known as PCNPs) to overcome this problem. Within just 10 minutes of administration, this CBD formulation reached a considerable concentration in the brain, demonstrating a notable preference for retention in the spinal cord. It was demonstrated that the CBD PCNPs had a peak concentration (C_{max}) of 94 ng/g at 30 minutes (T_{max}), which highlights the potential for rapid transport of the compound to the brain through the utilization of PCNPs. A two-fold nanoprecipitation process was used to create the CBD PCNPs⁵⁶.

Anxiety

Anxiety constitutes an emotional condition marked by sensations of unease, preoccupying thoughts, and physiological alterations like heightened blood pressure and heart rate. While the exact process through which CBD reduces anxiety is not fully understood, previous clinical encounters have initially showcased the anxiolytic impacts of CBD⁹. The potential anti-anxiety benefits of CBD may result from its capacity to inhibit the neurotransmitter AEA from becoming inactive as well as from its interactions with 5-HT_{1A} receptors^[57]. The first clinical trials assessing CBD's anxiolytic effects were in 1974 and 1982, indicating its potential to relieve THC-induced anxiety. Further, double-blind studies examined CBD's impact on healthy individuals, revealing that oral CBD administration reduced anxiety during simulated public speaking tests. CBD significantly decreased the level of subjective anxiety and increased the amount of mental sedation, which was related to a decrease in activity in the left amygdala-hippocampal complex as well as the left posterior cingulate gyrus⁵⁸. CBD might even help mitigate THC's negative effects⁵⁹.

Depression

Depression is linked to neuron loss in mood-regulating brain regions. Men and women react differently to stressors due to hormonal, cultural, and biological factors. Both genders can be

equally affected by stress-related depression, but triggers and responses may vary. Another possible symptom is reduced energy or fatigue⁶⁰. The findings demonstrate that via shortening stagnation time, high-dose orally and low-dose via IV. CBD have antidepressant-like actions. However, because of its minimal orally its bioavailability the lower-dose oral dosage did not enhance behaviour related to depression. Additionally, ongoing utilization of CBD has been shown to mitigate signs of depression and chronic stress, which lends credence to the notion that long-term intake of CBD is necessary to sustain the drug's long-lasting antidepressant benefits⁶¹. CBD usage reduced depression-like symptoms and increased cognitive processes linked to changing attention, gaining language skills, and recalling information among frequent cannabis users. Nabiximols, a THC/CBD combination, was used as a therapeutic to simulate the impact of agonists during cannabis withdrawal⁶².

Neurological disorder

Epilepsy

Anticonvulsant drugs are commonly necessary for epileptic patients to reduce the risk of repeated seizures. However, it's important to highlight that a sizeable portion roughly 30% of these individuals show resistance to traditional antiseizure pharmacological treatments and do not respond well⁶³. Positive outcomes from meticulously executed investigations known as randomized controlled trials (RCTs) led to the granting of these permits⁶⁴. These studies shown that CBD significantly lowers seizures in persons with severe and challenging-to-treat epilepsy (Devinsky et al. 2017). Epidiolex, a highly pure CBD oral solution, received formal clearance from the US Food and Drug Administration (FDA) on June 25, 2018⁶⁵.

Both problems with movement and non-motor dysfunction characterize the neurodegenerative disorder of Parkinson's disease. Utilizing many drugs is frequently necessary for the management of its symptoms⁶⁶. According to a preliminary study, CBD may help treat and manage Parkinson's disease. Six Parkinson's patients with persistent psychotic symptoms participated in pilot research that showed a substantial decrease in psychotic symptoms after receiving flexible dosages of CBD tablets containing over 99.9% pure CBD over four weeks. Notably, CBD did not worsen patients' motor deficits and may have even improved their general health, as seen by a decline in patients⁶⁷. As a result of the limited number of participants in the study, it is not yet known if cannabidiol (CBD) is effective in alleviating the neurological symptoms associated with Parkinson's disease. Larger clinical trials with more patients are needed to evaluate its effectiveness and safety in this situation.

Essential tremors

The most common movement issue in the USA is essential tremor (ET). The torso or upper limbs may tremble, which may be rather irritating because it happens both while you're still and when you move. Because CBD interacts with the cerebellum's CB1 receptors, which are involved in controlling communication between many types of brain cells, this might be a viable new therapeutic approach. More research on humans is required to ascertain how CBD affects Essential Tremor (ET). Studies on mice have demonstrated the endocannabinoid system's contribution to tremor control. To learn how CBD can be used to treat ET in people, however, additional study is needed⁶⁸.

Inflammation

Memory, speech, and other CNS processes can be affected by neurological diseases. They are the outcome of several factors, including neuroinflammation often. For these disorders, reducing CNS inflammation is a feasible course of action⁵.

Inflammation is a normal immunological reaction brought on by infections and cell injury, among other things. It is essential for protection against infections and poisons. However, chronic conditions including cancer, atherosclerosis, asthma, and multiple sclerosis can be brought on by excessive inflammation. Lipopolysaccharide (LPS), a component of Gram-negative bacteria, is a significant initiator of inflammation because it activates Toll-like receptor 4 (TLR4) on macrophages⁶⁹. While inflammation is a natural defense mechanism against harmful stimuli, it can also damage cellular and tissue tissue⁷⁰. The scientific community has recently focused a lot of attention on CBD's potential anti-inflammatory and immunomodulatory benefits. In terms of its mechanism of action, CBD reduces inflammation and the resulting cytokine production by influencing the immune system and dampening immune responses⁷¹. In contrast to THC, it does not cause psychoactive effects; however, it does offer a variety of pharmacological benefits that are beneficial⁷². In particular, CB1 and CB2 cannabinoid receptors are activated by CBD. As a result, CBD could have other anti-inflammatory mechanisms unrelated to these receptors⁷³. Because CBD has a low affinity for CB1 and CB2 receptors, it is believed that the pharmacological effects of CBD occur independently of these receptors. Instead, it has been demonstrated that cannabidiol (CBD) affects the transient receptor potential vanilloid1 channel (TRPV1), which is a pro-inflammatory channel. Particularly noteworthy is the fact that it has been proven that the anti-inflammatory and immune-suppressive effects of CBD can be negated by the utilization of TRPV1 antagonists⁷⁴. TNF, Interferon (IFN), Interleukin-1 (IL-1), Interleukin-2 (IL-2), and IL-6 are examples of inflammatory cytokines that have been shown to block the JAK/STAT pathway in vitro and preclinical experiments⁷⁵. The effectiveness of CBD and its

derivatives in relieving chronic pain was demonstrated in a study utilizing animals with CFA-induced inflammatory pain. Additionally, CBD increased the anti-inflammatory cytokine IL-10 while decreasing levels of pro-inflammatory cytokines including IL-6 and TNF in two different animal models of induced inflammation. The NF- κ B and interferon beta (IFN- γ) pathways are linked to their anti-inflammatory properties⁷⁶.

CONCLUSION

In summary, this article delved into the world of Cannabidiol (CBD), examining its origins in plants, traditional uses, methods of extraction, and its growing relevance through nanoformulations for treating conditions such as pain, inflammation, anxiety, depression, and neurological disorders. CBD, celebrated for its historical medicinal value and lack of psychoactive effects, stands out as a promising therapeutic choice. The discussion also highlighted the critical need for sustainable extraction practices as the demand for CBD surges. Additionally, incorporating nanotechnology into CBD products offers encouraging prospects for enhancing their effectiveness in addressing specific health concerns. As research in this field advances, it becomes increasingly vital for both healthcare practitioners and the general public to stay well-informed. Moreover, regulatory frameworks must evolve to ensure the safe and responsible use of CBD and its nanoformulations. Looking ahead, the potential impact of CBD and its innovative formulations on natural medicine cannot be understated. It holds the promise of providing renewed hope and improved well-being to countless individuals grappling with various health challenges. Given its multifaceted potential in the realms of healthcare and scientific research, CBD remains a topic of utmost significance.

Declaration

The authors declare that there is no conflict of interest.

Funding None

Authors' contributions The authors confirm contribution to the paper as follows: Study conception and design: RA.; data collection: V.S.; analysis and interpretation: N.K.; draft manuscript and editing: N. A. S, resources and data curation: GK

Statement for the use of AI

Artificial intelligence (AI) tools were used solely for basic grammar correction and language refinement in the preparation of this manuscript. Specifically, OpenAI's ChatGPT was employed to improve the readability and linguistic clarity of the English text. All scientific content, data interpretation, and conclusions were developed independently by the author. The authors have thoroughly reviewed and edited the AI-assisted text to ensure its accuracy and accept full responsibility for the manuscript's content.

REFERENCES

1. Li H, Liu Y, Tian D, Tian L, Ju X, Qi L, et al. Overview of cannabidiol (CBD) and its analogues: Structures, biological activities, and neuroprotective mechanisms in epilepsy and Alzheimer's disease. *European Journal of Medicinal Chemistry* [Internet] 2020;192:112163. Available from: <https://doi.org/10.1016/j.ejmech.2020.112163>
2. dos Santos RG, Hallak JEC, Zuardi AW, de Souza Crippa JA. Cannabidiol for the Treatment of Drug Use Disorders [Internet]. Elsevier Inc.; 2017. Available from: <http://dx.doi.org/10.1016/B978-0-12-800756-3/00113-7>
3. O'Croinin C, Garcia Guerra A, Doschak MR, Löbenberg R, Davies NM. Therapeutic Potential and Predictive Pharmaceutical Modeling of Stilbenes in Cannabis sativa. *Pharmaceutics* 2023;15(7).
4. Montgomery BW, Allen J. Cannabis Policy in the 21st Century: Mandating an Equitable Future and Shedding the Racist Past. *Clinical Therapeutics* [Internet] 2023;45(6):541–50. Available from: <https://doi.org/10.1016/j.clinthera.2023.05.001>
5. Eydelman I, Zehavi N, Feinshtein V, Kumar D, Ben-Shabat S, Sintov AC. Cannabidiol-Loaded Nanoparticles Based on Crosslinked Starch: Anti-Inflammatory Activity and Improved Nose-to-Brain Delivery. *Pharmaceutics* 2023;15(7).
6. Story G, Briere CE, McClements DJ, Sela DA. Cannabidiol and Intestinal Motility: a Systematic Review. *Current Developments in Nutrition* [Internet] 2023;7(10):101972. Available from: <https://doi.org/10.1016/j.cdnut.2023.101972>
7. Pisanti S, Malfitano AM, Ciaglia E, Lamberti A, Ranieri R, Cuomo G, et al. Cannabidiol: State of the art and new challenges for therapeutic applications. *Pharmacology and Therapeutics* [Internet] 2017;175:133–50. Available from: <http://dx.doi.org/10.1016/j.pharmthera.2017.02.041>
8. Low ZXB, Lee XR, Soga T, Goh BH, Alex D, Kumari Y. Cannabinoids: Emerging sleep modulator. *Biomedicine and Pharmacotherapy* [Internet] 2023;165(June):115102. Available from: <https://doi.org/10.1016/j.biopha.2023.115102>
9. Peng J, Fan M, An C, Ni F, Huang W, Luo J. A narrative review of molecular mechanism and therapeutic effect of cannabidiol (CBD). *Basic and Clinical Pharmacology and Toxicology* 2022;130(4):439–56.
10. Shahbazi F, Grandi V, Banerjee A, Trant JF. Cannabinoids and Cannabinoid Receptors: The Story so Far. *iScience* [Internet] 2020;23(7):101301. Available from:

<https://doi.org/10.1016/j.isci.2020.101301>

11. Gingrich J, Choudhuri S, Cournoyer P, Downey J, Muldoon Jacobs K. Review of the oral toxicity of cannabidiol (CBD). Food and Chemical Toxicology [Internet] 2023;176(April):113799. Available from: <https://doi.org/10.1016/j.fct.2023.113799>
12. Galaj E, Xi ZX. Possible receptor mechanisms underlying cannabidiol effects on addictive-like behaviors in experimental animals. International Journal of Molecular Sciences 2021;22(1):1–14.
13. Cai C, Wang Y, Yi Y, Li F, Tan Z. Ionic liquids simultaneously used as accelerants, stabilizers and extractants for improving the cannabidiol extraction from industrial hemp. Industrial Crops and Products [Internet] 2020;155(June):112796. Available from: <https://doi.org/10.1016/j.indcrop.2020.112796>
14. Assadpour E, Rezaei A, Das SS, Krishna Rao BV, Singh SK, Kharazmi MS, et al. Cannabidiol-Loaded Nanocarriers and Their Therapeutic Applications. Pharmaceuticals 2023;16(4):1–26.
15. Chandra S, Lata H, ElSohly MA. L . - Botany and Biotechnology. 2017.
16. Seo C, Jeong M, Lee S, Kim EJ, Rho S, Cho M, et al. Thermal decarboxylation of acidic cannabinoids in Cannabis species: identification of transformed cannabinoids by UHPLC-Q/TOF-MS. Journal of Analytical Science and Technology [Internet] 2022;13(1). Available from: <https://doi.org/10.1186/s40543-022-00351-4>
17. Fiorini D, Molle A, Nabissi M, Santini G, Benelli G, Maggi F. Valorizing industrial hemp (*Cannabis sativa* L.) by-products: Cannabidiol enrichment in the inflorescence essential oil optimizing sample pre-treatment prior to distillation. Industrial Crops and Products [Internet] 2019;128(May 2018):581–9. Available from: <https://doi.org/10.1016/j.indcrop.2018.10.045>
18. Rochfort S, Isbel A, Ezernieks V, Elkins A, Vincent D, Deseo MA, et al. Utilisation of Design of Experiments Approach to Optimise Supercritical Fluid Extraction of Medicinal Cannabis. Scientific Reports [Internet] 2020;10(1):1–7. Available from: <http://dx.doi.org/10.1038/s41598-020-66119-1>
19. Qamar S, Manrique YJ, Parekh HS, Falconer JR. Development and optimization of supercritical fluid extraction setup leading to quantification of 11 cannabinoids derived from medicinal cannabis. Biology 2021;10(6):1–20.
20. Pino S, Espinoza L, Jara-Gutiérrez C, Villena J, Olea AF, Díaz K. Study of Cannabis Oils

Obtained from Three Varieties of *C. sativa* and by Two Different Extraction Methods: Phytochemical Characterization and Biological Activities. *Plants* 2023;12(9).

21. Brighenti V, Protti M, Anceschi L, Zanardi C, Mercolini L, Pellati F. Emerging challenges in the extraction, analysis and bioanalysis of cannabidiol and related compounds. *Journal of Pharmaceutical and Biomedical Analysis* [Internet] 2021;192:113633. Available from: <https://doi.org/10.1016/j.jpba.2020.113633>
22. Olejar KJ, Kinney CA. Evaluation of thermo-chemical conversion temperatures of cannabinoid acids in hemp (*Cannabis sativa* L.) biomass by pressurized liquid extraction. *Journal of Cannabis Research* 2021;3(1).
23. Moreno T, Dyer P, Tallon S. Cannabinoid Decarboxylation: A Comparative Kinetic Study. *Industrial and Engineering Chemistry Research* 2020;59(46):20307–15.
24. Marzorati S, Friscione D, Picchi E, Verotta L. Cannabidiol from inflorescences of *Cannabis sativa* L.: Green extraction and purification processes. *Industrial Crops and Products* 2020;155(April).
25. Attard TM, Bainier C, Reinaud M, Lanot A, McQueen-Mason SJ, Hunt AJ. Utilisation of supercritical fluids for the effective extraction of waxes and Cannabidiol (CBD) from hemp wastes. *Industrial Crops and Products* 2018;112(July 2016):38–46.
26. Cassano T, Villani R, Pace L, Carbone A, Bukke VN, Orkisz S, et al. From *Cannabis sativa* to Cannabidiol: Promising Therapeutic Candidate for the Treatment of Neurodegenerative Diseases. *Frontiers in Pharmacology* 2020;11(March):1–10.
27. Hahm S, Lee B, Bok G, Kim S, Park J. Diniconazole Promotes the Yield of Female Hemp (*Cannabis sativa*) Inflorescence and Cannabinoids in a Vertical Farming System. *Agronomy* 2023;13(6).
28. Sawler J, Stout JM, Gardner KM, Hudson D, Vidmar J, Butler L, et al. The genetic structure of marijuana and hemp. *PLoS ONE* 2015;10(8):1–9.
29. McPartland JM, Hegman W, Long T. Cannabis in Asia: its center of origin and early cultivation, based on a synthesis of subfossil pollen and archaeobotanical studies. *Vegetation History and Archaeobotany* [Internet] 2019;28(6):691–702. Available from: <https://doi.org/10.1007/s00334-019-00731-8>
30. Ren G, Zhang X, Li Y, Ridout K, Serrano-Serrano ML, Yang Y, et al. Large-scale whole-genome resequencing unravels the domestication history of *Cannabis sativa*. *Science Advances* 2021;7(29):1–12.

31. Zhang Q, Chen X, Guo H, Trindade LM, Salentijn EMJ, Guo R, et al. Latitudinal adaptation and genetic insights into the origins of cannabis sativa L. *Frontiers in Plant Science* 2018;871(December):1–13.
32. Ni B, Liu Y, Dai M, Zhao J, Liang Y, Yang X, et al. The role of cannabidiol in aging. *Biomedicine and Pharmacotherapy* [Internet] 2023;165(June):115074. Available from: <https://doi.org/10.1016/j.biopha.2023.115074>
33. Hanuš LO, Meyer SM, Muñoz E, Taglialatela-Scafati O, Appendino G. *Phytocannabinoids: A unified critical inventory*. 2016.
34. Gülck T, Möller BL. *Phytocannabinoids: Origins and Biosynthesis*. *Trends in Plant Science* [Internet] 2020;25(10):985–1004. Available from: <https://doi.org/10.1016/j.tplants.2020.05.005>
35. Napiroon T, Tanruean K, Poolprasert P, Bacher M, Balslev H, Poopath M, et al. Cannabinoids from inflorescences fractions of *trema orientalis* (L.) blume (cannabaceae) against human pathogenic bacteria. *PeerJ* 2021;9:1–15.
36. Cushing D, Kristipati S, Shastri R, Joseph B. Measuring the bioactivity of phytocannabinoid cannabidiol from cannabis sources, and a novel non - cannabis source. *Journal of Medical Phyto Research* 2018;1:10–25.
37. Balant M, Gras A, Ruz M, Vallès J, Vitales D, Garnatje T. Traditional uses of Cannabis: An analysis of the CANNUSE database. *Journal of Ethnopharmacology* 2021;279.
38. Jin D, Dai K, Xie Z, Chen J. Secondary Metabolites Profiled in Cannabis Inflorescences, Leaves, Stem Barks, and Roots for Medicinal Purposes. *Scientific Reports* 2020;10(1):1–14.
39. Strand N, D'souza RS, Karri J, Kalia H, Weisbein J, Kassa BJ, et al. Medical Cannabis: A Review from the American Society of Pain and Neuroscience. *Journal of Pain Research* 2023;16(November):4217–28.
40. Devinsky O, Cross JH, Laux L, Marsh E, Miller I, Nabbout R, et al. Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome. *New England Journal of Medicine* 2017;376(21):2011–20.
41. Mücke M, Phillips T, Radbruch L, Petzke F, Häuser W. Cannabis-based medicines for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2018;2018(3).
42. Lutge EE, Gray A, Siegfried N. The medical use of cannabis for reducing morbidity and

- mortality in patients with HIV/AIDS. *Cochrane Database of Systematic Reviews* 2013;2013(4).
43. Blessing EM, Steenkamp MM, Manzanares J, Marmar CR. Cannabidiol as a Potential Treatment for Anxiety Disorders. *Neurotherapeutics* 2015;12(4):825–36.
44. Bujarski SJ, Feldner MT, Lewis SF, Babson KA, Trainor CD, Leen-Feldner E, et al. Marijuana use among traumatic event-exposed adolescents: Posttraumatic stress symptom frequency predicts coping motivations for use. *Addictive Behaviors* [Internet] 2012;37(1):53–9. Available from: <http://dx.doi.org/10.1016/j.addbeh.2011.08.009>
45. Shah ND, Parian AM, Mullin GE, Limketkai BN. Oral Diets and Nutrition Support for Inflammatory Bowel Disease: What is the Evidence? *Nutrition in Clinical Practice* 2015;30(4):462–73.
46. Müller-Vahl KR. Treatment of Tourette Syndrome with cannabis-based medicine. *Nervenheilkunde* 2020;39(5):314–9.
47. Tomida I, Perlwee RG, Azuara-Blanco A. Cannabinoids and glaucoma. *British Journal of Ophthalmology* 2004;88(5):708–13.
48. Lotan I, Treves TA, Roditi Y, Djaldetti R. Cannabis (Medical Marijuana) treatment for motor and non-motor symptoms of parkinson disease: An open-label observational study. *Clinical Neuropharmacology* 2014;37(2):41–4.
49. Amtmann D, Weydt P, Johnson KL, Jensen MP, Carter GT. Survey of cannabis use in patients with amyotrophic lateral sclerosis. *American Journal of Hospice and Palliative Medicine* 2004;21(2):95–104.
50. Blake DR, Robson P, Ho M, Jubb RW, McCabe CS. Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis. *Rheumatology* 2006;45(1):50–2.
51. Fiz J, Durán M, Capellà D, Carbonell J, Farré M. Cannabis use in patients with Fibromyalgia: Effect on symptoms relief and health-related quality of life. *PLoS ONE* 2011;6(4):3–7.
52. Rhyne DN, Anderson SL, Gedde M, Borgelt LM. Effects of Medical Marijuana on Migraine Headache Frequency in an Adult Population. *Pharmacotherapy* 2016;36(5):505–10.
53. Consroe P, Sandyk R, Snider SR. Open label evaluation of cannabidiol in dystonic movement disorders. *International Journal of Neuroscience* 1986;30(4):277–82.

54. Boyaji S, Merkow J, Elman RNM, Kaye AD, Yong RJ, Urman RD. The Role of Cannabidiol (CBD) in Chronic Pain Management: An Assessment of Current Evidence. *Current Pain and Headache Reports* 2020;24(2):2–7.
55. Argueta DA, Ventura CM, Kiven S, Sagi V, Gupta K. A Balanced Approach for Cannabidiol Use in Chronic Pain. *Frontiers in Pharmacology* 2020;11(April):1–7.
56. Muresan P, Woodhams S, Smith F, Taresco V, Shah J, Wong M, et al. Evaluation of cannabidiol nanoparticles and nanoemulsion biodistribution in the central nervous system after intrathecal administration for the treatment of pain. *Nanomedicine: Nanotechnology, Biology, and Medicine* [Internet] 2023;49:102664. Available from: <https://doi.org/10.1016/j.nano.2023.102664>
57. Patel S, Hill MN, Cheer JF, Wotjak CT, Holmes A. The endocannabinoid system as a target for novel anxiolytic drugs. *Neuroscience and Biobehavioral Reviews* [Internet] 2017;76:56–66. Available from: <http://dx.doi.org/10.1016/j.neubiorev.2016.12.033>
58. García-Gutiérrez MS, Navarrete F, Gasparyan A, Austrich-Olivares A, Sala F, Manzanares J. Cannabidiol: A potential new alternative for the treatment of anxiety, depression, and psychotic disorders. *Biomolecules* 2020;10(11):1–34.
59. Skelley JW, Deas CM, Curren Z, Ennis J. Use of cannabidiol in anxiety and anxiety-related disorders. *Journal of the American Pharmacists Association* [Internet] 2020;60(1):253–61. Available from: <https://doi.org/10.1016/j.japh.2019.11.008>
60. Paykel ES. Basic concepts of depression. *Dialogues in Clinical Neuroscience* 2008;10(3):279–89.
61. Solowij N, Broyd SJ, Beale C, Prick JA, Greenwood LM, Van Hell H, et al. Therapeutic Effects of Prolonged Cannabidiol Treatment on Psychological Symptoms and Cognitive Function in Regular Cannabis Users: A Pragmatic Open-Label Clinical Trial. *Cannabis and Cannabinoid Research* 2018;3(1):21–34.
62. Xu C, Chang T, Du Y, Yu C, Tan X, Li X. Pharmacokinetics of oral and intravenous cannabidiol and its antidepressant-like effects in chronic mild stress mouse model. *Environmental Toxicology and Pharmacology* [Internet] 2019;70(May):103202. Available from: <https://doi.org/10.1016/j.etap.2019.103202>
63. Dini G, Tulli E, Dell’Isola GB, Mencaroni E, Di Cara G, Striano P, et al. Improving Therapy of Pharmacoresistant Epilepsies: The Role of Fenfluramine. *Frontiers in Pharmacology* 2022;13(May):1–7.

64. Abu-Sawwa R, Scutt B, Park Y. Emerging use of Epidiolex (Cannabidiol) in epilepsy. *Journal of Pediatric Pharmacology and Therapeutics* 2020;25(6):485–99.
65. Ożarowski M, Karpiński TM, Zielińska A, Souto EB, Wielgus K. Cannabidiol in neurological and neoplastic diseases: Latest developments on the molecular mechanism of action. *International Journal of Molecular Sciences* 2021;22(9).
66. Leehey MA, Liu Y, Hart F, Epstein C, Cook M, Sillau S, et al. Safety and Tolerability of Cannabidiol in Parkinson Disease: An Open Label, Dose-Escalation Study. *Cannabis and Cannabinoid Research* 2020;5(4):326–36.
67. Chayasirisobhon S. The Role of Cannabidiol in Neurological Disorders. *Permanent Journal* 2021;25(2):1–6.
68. Fiani B, Sarhadi KJ, Soula M, Zafar A, Quadri SA. Current application of cannabidiol (CBD) in the management and treatment of neurological disorders. *Neurological Sciences* 2020;41(11):3085–98.
69. Kim JH, Hong M, Han JH, Ryu BR, Lim YS, Lim JD, et al. In Vitro and In Vivo Anti-Inflammatory Effects of Cannabidiol Isolated from Novel Hemp (*Cannabis sativa* L.) Cultivar Pink Pepper. *Molecules* 2023;28(18).
70. Luz-Veiga M, Azevedo-Silva J, Fernandes JC. Beyond Pain Relief: A Review on Cannabidiol Potential in Medical Therapies. *Pharmaceuticals* 2023;16(2):26–8.
71. Robaina Cabrera CL, Keir-Rudman S, Horniman N, Clarkson N, Page C. The anti-inflammatory effects of cannabidiol and cannabigerol alone, and in combination. *Pulmonary Pharmacology and Therapeutics* [Internet] 2021;69(June):102047. Available from: <https://doi.org/10.1016/j.pupt.2021.102047>
72. Atalay S, Jarocka-karpowicz I, Skrzydlewska E. Antioxidative and anti-inflammatory properties of cannabidiol. *Antioxidants* 2020;9(1):1–20.
73. Tran VN, Strnad O, Šuman J, Veverková T, Sukupová A, Cejnar P, et al. Cannabidiol nanoemulsion for eye treatment – Anti-inflammatory, wound healing activity and its bioavailability using in vitro human corneal substitute. *International Journal of Pharmaceutics* 2023;643(June).
74. Castillo-Arellano J, Canseco-Alba A, Cutler SJ, León F. The Polypharmacological Effects of Cannabidiol. *Molecules* 2023;28(7).
75. Peyravian N, Deo S, Daunert S, Jimenez JJ. The Anti-Inflammatory Effects of Cannabidiol (CBD) on Acne. *Journal of Inflammation Research* 2022;15(March):2795–801.

76. Martinez Naya N, Kelly J, Corna G, Golino M, Abbate A, Toldo S. Molecular and Cellular Mechanisms of Action of Cannabidiol. *Molecules* 2023;28(16):1–24.
77. Nelson KM, Bisson J, Singh G, Graham JG, Chen SN, Friesen JB, Dahlin JL, Niemitz M, Walters MA, Pauli GF. The Essential Medicinal Chemistry of Cannabidiol (CBD). *J Med Chem.* 2020; 12;63(21):12137-12155.

AJPTR

American Journal of PharmTech Research



**PEER-REVIEWED**

**BIMONTHLY**

**RAPID PUBLICATION**

SUBMIT YOUR MANUSCRIPT

 Submit your manuscript at:
editor@ajptr.com

 Visit our site:
<https://ajptr.com/>