

Review Article

Therapeutic uses, pharmacological and clinical importance of *Cannabis sativa*: a review article

Pramod Chandra Dwivedi^{1*}, Pulsi Pande², Madan Mohan Sharma¹, Amit Kumar¹

¹Central Council for Research in Ayurvedic Sciences, Regional Ayurveda Research Institute, Gwalior, Madhya Pradesh, India

²Government Ayurved College, Rewa, Madhya Pradesh, India

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*Correspondence:

Dr. Pramod Chandra Dwivedi,

E-mail: dpramod825@gmail.com

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ABSTRACT

Hempro Cannabis is a commonly used herbaceous plant, *Cannabis sativa* L., or hemp, is a plant that has been used multifunctionally in the past as a medicine, nutritional, and industrial crop since ancient times. Throughout the last few decades, its medicinal properties have acquired new scientific interest because of the development of phytochemistry and the identification of an endocannabinoid system in humans. The plant has a vast array of bioactive compounds with the majority of cannabinoids, terpenoids, flavonoids, all contributing to the various pharmacological effects of it. Among them, Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD) are the most researched constituents with unique physiological action. The effects of THC are mainly psychoactive, analgesic, antiemetic and muscle relaxant by acting mediated by the CB1 receptors in the central nervous system. CBD in its turn, has anti-inflammatory, neuroprotective, antioxidant, anxiolytic and anti-epileptic effects without psychoactive adverse effects, by regulating multiple non-cannabinoid receptors and ion channels. The Mult synergy between cannabinoids, together with other minor constituents, results in a so-called encouragements effect, which improves the effects of therapy, reducing the number of adverse effects. According to the pharmacological studies, *Cannabis sativa* and its active components have a plethora of biological systems in that they can exert effects on the nervous, immune, metabolic and gastrointestinal systems.

Keywords: Cannabis sativa, Cannabinoid, Endocannabinoid system, Medicine, Pharmacology, Clinical trials, Review

INTRODUCTION

Cannabis sativa L., which is also referred to as hemp or cannabis, is one of the oldest and highly diverse plant species that has ever been known to humanity. Thousands of years have passed, and it has been used and developed as food, fibre, oil and medicine among other things. It has been in use since time immemorial and in both historical documents and conventional medical systems of various cultures to relieve pain, aid in digestion, a clear state of mind and appetite enhancement. The plant is referred to as Vijaya or Bhang in Indian traditional medicine

(especially Ayurveda), it is referred to as such due to its psychoactive effects, analgesic effects, and therapeutic effects when used in moderation.¹

Cannabis sativa is an herb, which is an annual and is a member of the family Cannabaceae. Its main distinctive features are palmately compound leaves, resinous inflorescence and a strong aromatic smell. It is a dioecious plant that is, male and female flowers are present on different plants. The glandular trichomes of the female flowers produce a distinct group of bioactive compounds known as cannabinoids that form the root causes of most of the pharmacology effects of the resin.²

During the course of centuries, *Cannabis sativa* has gained medicinal as well as social meanings. Its psychoactive effects have seen it being a controversial plant which has been limited in most cases by legal systems. But now the revival of scientific interest in the 20th and 21st centuries has changed all that the intoxicating effects of it were forgotten, and its therapeutic value was observed. Discovery of the human body endocannabinoid system comprising of cannabinoid receptors (CB1 and CB2), endogenous ligands as well as the enzymes involved in its metabolism - has transformed the current knowledge of how cannabinoids can interact with the human physiology. It is an important system in aiding the internal balance or homeostasis by controlling various processes including pain perception, mood, appetite, memory and immune response.³

The major active components of the *Cannabis sativa* are the Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD). THC has been found to be a psychoactive drug, nonetheless, it has also analgesic, antiemetic and antispasmodic uses. CBD, however, does not have a psychoactive effect, demonstrate a great deal of anti-inflammatory, antioxidant and neuroprotective properties. Their combination with other minor cannabinoids and aromatic molecules (terpenes and flavonoids) contributes to the summative effect of cannabis on therapy, a phenomenon also known as the entourage effect.⁴ *Cannabis sativa* has a wide range of activity, with action on the nervous, immune and endocrine systems, pharmacologically.

It has an analgesic and anti-inflammatory effect which makes use viable with chronic pain, arthritis, and neuropathic disorders. Epilepsy, multiple sclerosis, and neurodegenerative diseases such as Parkinson or Alzheimer neuroprotective desired side effects have been investigated. Moreover, cannabinoids have been proposed to be effective in controlling chemotherapy-related nausea, anorexia in cachectic patients, and in the treatment of spasticity in neurological patients.⁵

This increased medical cannabis acceptance around the globe is now causing new scientific research, clinical trials and more standardised formulations. Nevertheless, there are still issues of quality regulation, proper dosage and sustainability in terms of safety. *Cannabis sativa* has dual nature by being both a likely medicine and a potential substance of abuse, thus requiring a delicate balance to be achieved between its application as a treatment and its control as a substance of abuse.⁶ Cannabinoids are currently seen in the field of modern medicine as new therapeutic agents that can supplement or even replace the traditional medications in some chronic and refractory illnesses.

This is because their multimodal action mechanism, which involves the use of several signalling pathways, offers comprehensive disease management. However, the inconsistency in chemical makeup of various cannabis

varieties, non-standardisation and psychoactive side effects remain the key challenges to its large-scale use in clinical practice.⁶ To conclude, cannabis sativa is a special pharmacological material that is between the traditional and modern healing systems and biomedical science.

Modern pharmacological understanding has proven its usefulness in drug development by allowing it to have a wide variety of therapeutic effects to which it can be used as a development candidate in the future. This review will give a unified view of a combination of the therapeutic use of the plant, pharmacological characteristics, and clinical significance of the plant and its possibilities as well as limitations in contemporary medicine.⁷

Botany, traditional uses and phytochemistry

C. sativa is an annual herb, with considerable variation in chemotype and morphology. Ethnobotanical surveys indicate traditional uses of various parts: the leaves, roots, seeds and inflorescences have been employed for rheumatism, epilepsy, asthma, skin disorders, pain, gestational/post-partum uses, gastrointestinal disorders, circulatory and nervous-system complaints.⁸ For example, roots used in birthing/post-partum, leaves for analgesic/sedative effects, seeds/oil as food, etc.

METHODS

Type of study

A narrative and systematic review of the available literature was conducted.

Data sources

An extensive literature search was conducted using electronic databases: PubMed, Scopus, ScienceDirect, SpringerLink, and Google Scholar. Traditional knowledge sources and ayurvedic pharmacognosy texts were also screened.

Phytochemistry

C. sativa contains a complex mixture of bioactive metabolites: over 550 different molecules have been reported, including cannabinoids, terpenoids, flavonoids, lignan amides, stilbenoids etc.⁹ The most studied cannabinoids are Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD). Beyond these, "minor" cannabinoids (e.g., cannabigerol CBG, cannabichromene CBC, tetrahydrocannabivarin THCV) and numerous terpenes play roles. Biosynthetically, cannabinoids derive from cannabigerolic acid (CBGA).

Endocannabinoid system and receptor biology

The endocannabinoid system includes CB1 (primarily central nervous system) and CB2 (mainly immune/

peripheral) receptors. Cannabinoids act via these and also via other targets (TRP channels, PPARs, serotonin receptors etc) particularly the minor cannabinoids.¹⁰ Thus, the diversity of targets provides a mechanistic basis for the range of pharmacological effects seen.

Pharmacological activities¹¹

C. sativa and its constituents exhibit multiple pharmacological activities. The following summarises principal actions, with mechanistic notes where available.

Analgesic/anti-pain and spasticity

Cannabinoids have demonstrated analgesic effects in chronic pain (especially neuropathic pain), and benefit in spasticity (e.g., in multiple sclerosis). Mechanistically, CB1 activation in central pain pathways modulates neurotransmitter release; CB2 may suppress inflammatory pain via immune cell modulation.¹²

Anti-emetic and appetite stimulation

THC and synthetic cannabinoids have been used as anti-emetics (notably in chemotherapy-induced nausea/vomiting) and appetite stimulants in AIDS/cachexia.

Anti-seizure/anti-epileptic

CBD has significant evidence in certain childhood epilepsies (e.g., Dravet syndrome). More broadly, cannabinoids show potential anticonvulsant activity.¹³ Mechanistically, modulation of excitatory/inhibitory neurotransmission via CB1 and other targets may be involved.

Anti-inflammatory/immunomodulatory

Cannabinoids and cannabis extracts show anti-inflammatory, immunomodulatory, neuroprotective activities (e.g., in neuroinflammation, arthritis).¹⁴ CB2-mediated immune cell modulation, PPAR activation, inhibition of cytokine release and oxidative stress are among proposed mechanisms.

Neurodegenerative and neuroprotective

Pre-clinical evidence suggests potential in neurodegenerative conditions (Parkinson's, Alzheimer's) and neuroprotection through anti-oxidant/anti-inflammatory pathways.¹⁵

Anticancer/anti-tumour

Some in vitro and animal studies show cannabinoids inducing apoptosis, inhibiting angiogenesis and metastasis in certain cancers. However, clinical translation remains limited.

Metabolic, cardiovascular, gastrointestinal effects

Early evidence indicates effects on glucose metabolism, hypertension, bone loss and inflammatory bowel disease.¹⁶ Mechanistic links include modulation of inflammation, oxidative stress and endocannabinoid signalling.

Clinical evidence and therapeutic applications

Evidence strength and major indications

A systematic review (2022) of medical cannabinoids found overall positive therapeutic effect for epilepsy, chronic pain, spasticity, appetite, Parkinson's disease, sleep, substance use disorders and Tourette's syndrome but with varying levels of evidence (from low to moderate).

Another scoping review across 72 systematic reviews concluded that many findings are mixed, with heterogeneity of trials, inconsistent reporting and significant adverse-event rates; many conclusions emphasised the need for higher-quality evidence.

Selected clinical applications

Chronic pain/neuropathic pain/spasticity: Moderate evidence supports cannabinoid use (e.g., nabiximols, dronabinol) in neuropathic pain and MS spasticity.

Epilepsy: High/moderate evidence for CBD in specific epilepsies.

Chemotherapy-induced nausea/vomiting (CINV): Some evidence supports cannabinoids as anti-emetic, but not as first-line.

Other indications: Appetite stimulation, sleep disorders, Tourette's, neurodegeneration evidence is less robust.

Cancer symptoms: Some relief of pain/nausea; anti-tumour clinical evidence is currently weak.

Safety, adverse effects and limitations

Cannabinoids are not without risk. Mild adverse effects (drowsiness, dizziness, dry mouth, nausea) are common; serious adverse events (psychosis, seizures, urinary tract infection) have been reported.¹⁷

Many clinical trials vary in formulation (THC vs CBD vs combinations), dose, route of administration, duration, and patient population — making meta-analysis and guideline development difficult.

Also, recreational use findings (especially long-term) report risks of cognitive impairment, psychosis, addiction important when interpreting therapeutic claims.

Pharmacological/mechanistic insights relevant to therapeutic use

Receptor/target engagement

CB1 receptor (CNS) and CB2 receptor (immune/peripheral) are primary cannabinoid targets. Minor cannabinoids act also on TRP channels, PPARs, serotonin-1A receptors, and voltage-gated ion channels.¹⁸ Thus, the therapeutic effects likely arise from a combination of receptor interactions, signalling modulation and downstream cellular effect (anti-inflammation, neuroprotection, modulation of excitability etc).¹⁹

Table 1: Pharmacological actions.

Pharmacological action	Mechanism of action	Relevance
Analgesic and anti-spasmodic	CB1 receptor-mediated central inhibition of nociceptive signals	Chronic pain, multiple sclerosis
Anti-seizure	Modulation of GABAergic/ glutamatergic neurotransmission	Epilepsy, Dravet syndrome
Anti-inflammatory	CB2 receptor activation, cytokine inhibition	Arthritis, IBD
Anti-emetic and appetite stimulant	CB1-mediated action on brainstem	Chemotherapy-induced nausea
Neuroprotective	Anti-oxidant and anti-excitotoxic mechanisms	Parkinson's, Alzheimer's
Anti-cancer	Induction of apoptosis, inhibition of angiogenesis	Breast, lung, and glioma models

Anti-oxidant, anti-inflammatory and immunomodulation

Cannabinoids reduce oxidative stress and pro-inflammatory cytokine release, inhibit microglial activation, modulate immune cell function.²⁰ These mechanisms provide rationale for application in inflammatory diseases, neurodegeneration, cardiovascular/metabolic disorders.

Neurotransmission and neuromodulation

Via CB1 and other targets, cannabinoids influence GABAergic/glutamatergic balance, reduce excitotoxicity, modulate ion channel activity relevant in epilepsy, pain, spasticity.²¹

Cell-growth, apoptosis and tumour-modulation

In vitro/animal data show cannabinoids induce apoptosis, inhibit angiogenesis, modulate tumour-

microenvironment; although translation to humans remains limited.

Relevance in clinical practice and therapeutic areas

From the current evidence, the most justifiable therapeutic uses of *C. sativa*/cannabinoids (in appropriate, regulated form) include:

Neuropathic chronic pain and spasticity (MS)

Specific forms of epilepsy (e.g., CBD in childhood epilepsies). Chemotherapy-induced nausea/vomiting and appetite stimulation (in selected cases). Possibly adjunctive in neurodegenerative and inflammatory disorders (pending further research).

However, clinicians must weigh benefits against risks, pay attention to formulation (THC vs CBD), route, dose, patient factors (age, psychiatric history, comorbidities). Standardisation remains a major gap. Regulatory context (varies by country) adds complexity.

Table 2: Therapeutic applications and clinical significance.

Therapeutic indication	Preparation cannabinoid	Clinical evidence	Evidence level
Neuropathic pain	THC+CBD (nabiximols)	Pain reduction and improved sleep	Moderate
Epilepsy (Dravet syndrome)	Cannabidiol (epidiolex)	Reduced seizure frequency	Strong
Chemotherapy induced nausea	Dronabinol, nabilone	Reduced vomiting and nausea	Moderate
Multiple sclerosis spasticity	Nabiximols	Improved mobility and muscle tone	Strong
Parkinson's disease	CBD	Reduction in tremor and rigidity	Limited
Anxiety disorders	CBD	Anxiolytic and sedative effects	Emerging

Gaps, limitations and future directions

Standardisation and formulation: Many studies use different cannabinoid combinations, varying purity, dose and route — making comparison difficult.

Long-term safety: Much of the evidence is short-term; long-term effects (especially in medical populations) need more study.

Regulatory/legal issues: Even in countries where medical cannabis is legal, product quality, dose control and clinical guidelines are still evolving.

Large, well-constructed RCTs: Large and good-quality RCTs are admittedly absent, particularly with non-pain indications (ex: cancer, neurodegeneration, or metabolic disorders).

Mechanistic specificity: Further studies are required to identify the best cannabinoid (major and minor) to give which indications and what the entourage effect adds.

Combining with other therapies: Since you are interested in Ayurveda, an avenue of *C. sativa* research as a component of integrative therapies (herbal medicine, cannabinoid-plant synergy) can be a useful area.²²

One of the most impressive instances of the convergence of the old and the new medicine is the pharmacological and therapeutic profile of *Cannabis sativa*, which finds the same level of implementation by both conventional medicine and advanced pharmacology. The plant that merely was seen as a recreational or ritualistic drug just a few decades ago has the tendency to appear again as an object of serious biomedical studies. The endogenous receptors and metabolic enzymes of the endocannabinoid system (ECS) including endogenous ligands, cannabinoid receptors (CB1 and CB2) and other related metabolic enzymes have formed a very strong scientific platform through which the various effects of *Cannabis sativa* on human physiology can be explained. The ECS is linked to homeostasis in various systems of the body and they include the nervous system, immune system and endocrine system and hence the broad range of therapy of the plant.²³

Cannabis sativa has multimodal mechanisms of action, pharmacologically. The most significant psychoactive cannabinoid, which is known as THC, also has such actions in that of analgesia, anti-spasmodic activity, and the stimulation of appetite by binding CB1 receptors in the central nervous system and CB2 receptors in peripheral tissues. The non-psychoactive cannabinoid (CBD) reacts to serotonin (5-HT1A), TRPV1, and PPAR, and has anxiogenic, neuroprotective, and anti-inflammatory effects. Besides, there is a synergistic pharmacodynamic process between cannabinoids, terpenoids and flavonoids that is called the entourage effect. Such a complicated interplay maximizes efficacy and minimizes adverse effects which is usually not the case with single-molecule pharmacotherapy.²⁴

Cannabinoid-based therapies have been shown to have a considerable potential in the treatment of neuropathic and chronic pain, seizures, and spasticity in multiple sclerosis, chemotherapy-induced nausea and vomiting, and cachexia clinically. The clinical significance and usefulness of non-psychoactive cannabinoids have been confirmed by the formulation of cannabidiol (Epidiolex)

to control refractory epilepsy approved by FDA. Equally, the use of nabiximols (a solution of THC: CBD extract) has been effective in multiple sclerosis, which makes *Cannabis sativa* an effective adjunct treatment in neurodegenerative and autoimmune conditions.²⁵

Even with these developments, there are significant challenges towards the clinical translation of cannabis-based therapies. Unpredictability of the efficacy of the therapy is often witnessed by variability in chemical composition, non-standardised dosing and non-uniform extraction processes. Depending on the cultivar, the environment the cannabinoids are grown, the active cannabinoids may vary by a great deal. In addition, cultural and government regulations and stigmatization of cannabis have traditionally constrained the clinical research, which subsequently in turn has resulted in dearth of a large proportion of long-term, placebo-controlled, and large-scale studies. Such constraints are impediments to the development of clear clinical guidelines and the incorporation of cannabis-based therapeutics into primary healthcare.²⁶

Other important issues are safety and adverse effects. Although mostly benign to toleration, at most perversely, THC is capable of causing psychoactive effects, cognitive impairment and dependence in the chronic use and at high doses. Mental results like anxiety, paranoia and psychosis have been reported in predisposed persons. Moreover, medications that are affected by the hepatic cytochrome P450 enzymes require caution especially when used in polypharmacy patients. The therapeutic index of cannabis is extensive yet relative and hence clinical oversight and education to patients is necessary to avoid misuse.²⁷

According to Ayurveda, Vijaya (*Cannabis sativa*) is said to have a Tikta (bitter) taste, Katu (pungent), Ushna Veerya (hotness) taste, and it has Laghu (light) and Ruksha (dry) qualities. It mainly balances Vata and Kapha doshas and is thus adequate in the management of conditions that are accompanied by pain, stiffness, and neurological disorders. This classical perception is in line with its noted analgesic and antispasmodic effects of use in contemporary medicine. There are Ayurvedic preparations of Vijaya, which traditionally find use in insomnia, gastroenterology, and chronic pains, in which cannabinoid effectiveness is however substantiated in modern clinical studies. Therefore, the point of convergence between the traditional and modern knowledge is a holistic picture of therapeutic potential of the plant.²

The significance of cannabis research in the future will involve the development of evidence-based standardized preparations that will optimise therapeutic effect at low psychoactivity potential. The expanded therapeutic uses of the cannabinoid-medicines are likely to be expanded by new biotechnological discoveries, including the isolation of minor cannabinoid molecules (like CBG and CBC) as well as the creation of synthetic analogs.

Moreover, the emergence of customised medicine and the regulation of phytopharmaceuticals offers an arena on which the incorporation of cannabinoids with individualised treatment protocols can be executed. The coming decade will see a marked growth of clinical evidence and rational therapeutic use of *Cannabis sativa* due to increasing societal acceptance and medical legalization.²⁹

In conclusion, it can be stated that the discussed plant *Cannabis sativa* is a pharmacologically promising plant with a long history of use, but also with a solid scientific basis. However, it is impossible to realise the full therapeutic potential of it without focusing on standardisation, clarity of regulations and effective clinical trial in order to establish the safety levels, effectiveness and dose range of the drug in various groups of people.

CONCLUSION

Cannabis sativa may be characterized as the plant that is abundant in its pharmacological properties and also has a long history of its usage through the civilizations. Its curative potential has again been found by the recent studies where cannabinoids have been identified to be main figures in controlling human physiology when they interact with endocannabinoid system. The plant has demonstrated good effects on chronic pain, epilepsy, muscle spasticity and nausea during chemotherapy although there is increasing evidence on its application in neurodegenerative and inflammatory disease.

Though it has demonstrated promising therapeutic prospects, formulation, psychoactive side effects and legal uncertainty still remain the bane of its further medical use. Ensuring the homogeneity of the cannabinoid content and developing explicit dosage guidelines and evidence-based clinical guidelines are paramount to driving cannabis into the mainstream health administration system. Also, it is essential to educate clinicians and patients on safe use, potential drug interactions, and side effects in the long term.

Scientific rigor and ethics should be employed in integrating *Cannabis sativa* in therapeutic practice. The communication gap in traditional and modern biomedical knowledge can represent a one-of-a-kind chance to establish safer and more efficient plant-based medicine. Since the world is changing its mind image on the medical uses of cannabis, interdisciplinary investigations should go on with the aim of harnessing its full potential and making its responsible and evidence-based use. *Cannabis sativa* becomes a symbol of the dynamic association between the traditional medicine and the modern science - a botanical resource that under the exactness, deference, and control can serve as a significant contributor to the development of integrative and patient-oriented healthcare.

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