

## Cannabinoids in pain management

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World Journal of Advanced Research and Reviews, 2025, 25(03), 876-884

Publication history: Received on 30 January 2025; revised on 07 March 2025; accepted on 10 March 2025

Article DOI: <https://doi.org/10.30574/wjarr.2025.25.3.0762>

### Abstract

Chronic pain is a complicated experience that includes physical sensations, thoughts, and emotions, creating significant challenges for individuals. Approximately 1.5 billion people worldwide suffer from chronic pain. Managing this condition can be difficult and traditional pain medications, such as opioids, may not always be effective. As a result, researchers are actively studying new pain treatments that use the endocannabinoid system (ECS), which has been linked to different functions that contribute to homeostasis i.e. stability of your internal environment. For example, if some outside force like pain or fever imbalances your body's homeostasis, your ECS comes in to help your body return to its ideal operation. There is ongoing study that aims to change how pain signals are processed, showing promise in treating difficult pain conditions.

In modern times, cannabis use has changed greatly for spiritual and business reasons, influenced by shifts in culture, religion, and economics. According to ancient Indian scriptures called the Vedas, cannabis is considered one of the five special plants with spiritual and healing importance. It is referred to as a remedy for various ailments in Ayurveda. Cannabis was once thought to be beneficial for both short-term and long-lasting pain relief, but recent research has raised doubts about these claims. Limited evidence supports various types of chronic pain like nerve and joint pain, and headache; some evidence of chronic pain related to multiple cerebro-spinal sclerosis and also medical profession acknowledge the potential therapeutic benefits of cannabis for treatment of specific conditions, such as cancer.

**Keywords:** Chronic pain; Cannabinoid; Ayurveda; Potential therapeutic benefits.

### 1. Introduction

This review explores the effect of cannabis on persistent pain control, discussing its historical significance, chemical composition, mechanism of action, and ability to reduce pain in various chronic pain conditions.

Historic texts like Atharva Veda speak many testimonies and events which include the role of hashish in rituals and lifestyle, and highlight the unique significance of hashish in Indian subculture. In accordance to the conventional beliefs, hashish became a vital element in the preparation of Somaras throughout the Vedic duration, highlighting its historic and religious significance [1]. In line with Atharva Veda, hashish is considered as one of the five sacred plants because it's use is related to the feeling of happiness and freedom, and can assist to manage persistent pain. Moreover, offering cannabis in the form of Bhang to Lord Shiva is reported in our ancient stories. Ingesting hashish during the celebration of Indian festivals like Mahashivratri and Holi holds cultural importance. In addition to marijuana, different famous cannabis products include charas, ganja, and weeds.

A substance derived from the hashish plant, hashish sativa, originating in Central or South Asia, exhibits psychoactive properties. Cannabis is a part of the Cannabaceae family. Cannabis consists of over one hundred compounds called

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cannabinoids, the primary psychoactive element of which is tetrahydrocannabinol (THC). Currently, unlike many different flora, the cultivation of the cannabis plant is unlawful in many countries.

## 2. How cannabis works in the body

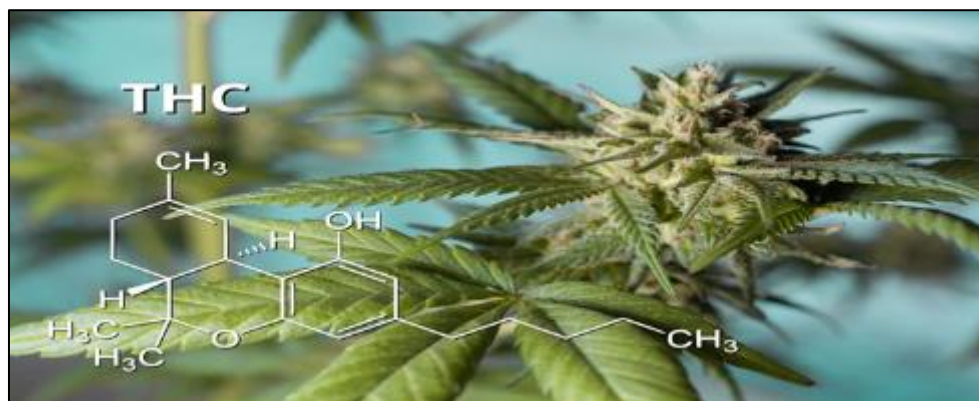
Marijuana consists of around one hundred one of a kind compounds referred to as cannabinoids, and each has extraordinary results within the body. The two maximum mighty cannabinoids are delta-nine-tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is responsible for the psychoactive outcomes of marijuana, at the same time CBD has been proven to have clinical features like anxiolytic, and ache-relief. The endocannabinoid system (ECS), is responsible for regulating many physiological phenomena, inclusive of ache, urge for food, temper, and sleep. With the aid of interacting with the ECS, cannabis can help in keeping stability and homeostasis in the body. While hashish is used to deal with continual pain, unique cannabinoids like THC spark off receptors within the mind and nerves that play a role in restoration. Research has proven the benefits of using hashish to treat the aches[2].



**Figure 1** Psychoactive and non-psychoactive constituents of Cannabis

## 3. Know the components of cannabis: THC, CBD, and minor cannabinoids

### 3.1. THC-tetrahydrocannabinol



**Figure 2** Tetrahydrocannabinol

Cannabis contains chemicals called cannabinoids that interact with the human body's natural endocannabinoid system. More research is needed concerning Cannabis and the many different types of pain.

THC, or tetrahydrocannabinol, is one of the two major cannabinoids found in cannabis. THC has been shown to relieve central and neuropathic pain. THC can modulate pain at the level of the spinal cord and brain by directly activating CB1 receptors and indirectly by increasing opioid receptor activation. Like several other chemical components in cannabis, THC has anti-inflammatory properties that can contribute to pain reduction too.

### 3.2. CBD – cannabidiol



**Figure 3** Cannabidiol

Cannabidiol or CBD is another vital cannabinoid that has been proven to relieve aches for neuropathic and inflammatory conditions. CBD also blocks the infection by means of growing tiers of endocannabinoids like 2-Arachidonoylglycerol (2-AG) and anandamide and also reduces infection.

### 3.3. Benefits of using THC and CBD together



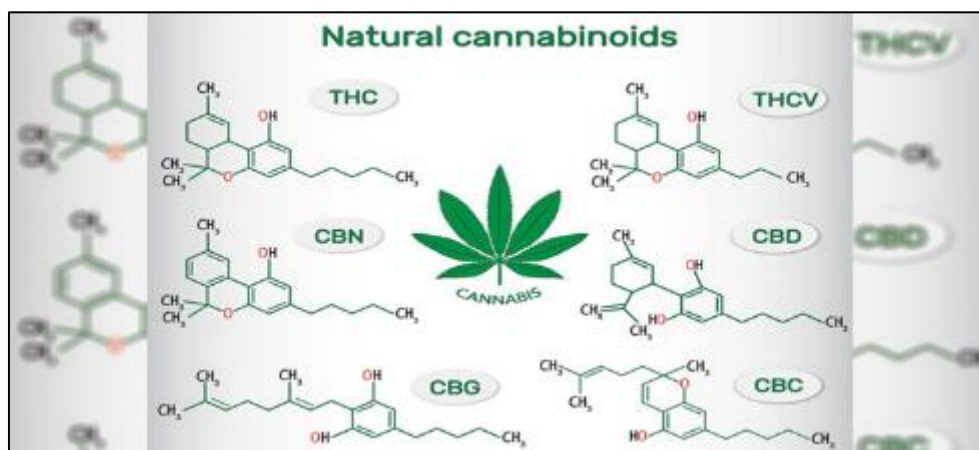
**Figure 4** THC and CBD Combination

The combination of THC (tetrahydrocannabinol) and CBD (cannabidiol) has been shown to provide more effective ache relief than the use of either of these cannabinoids alone.

The combination may help alleviate pain in cancer patients who did not respond to opioid medicines. These hashish-primarily based treatments were usually nicely tolerated, and patients no longer wanted to increase their dosages over the years, in contrast to opioids. Cannabis use is not risk-free, nor it is a panacea, the risks the cannabis poses of dependence and accidental overdose compared with opioids are significantly lower [3]. In fact, fatal overdose with cannabis has not been documented and is thought to be probably impossible [4].

Further, patients who used the THC/CBD combination reported improvements in their quality of life and sleep, unlike those relying solely on opioids. This suggests that cannabis may offer a safer alternative for managing pain in cancer patients, without the risks of tolerance or addiction that often accompany opioid use.

### 3.4. Minor cannabinoids

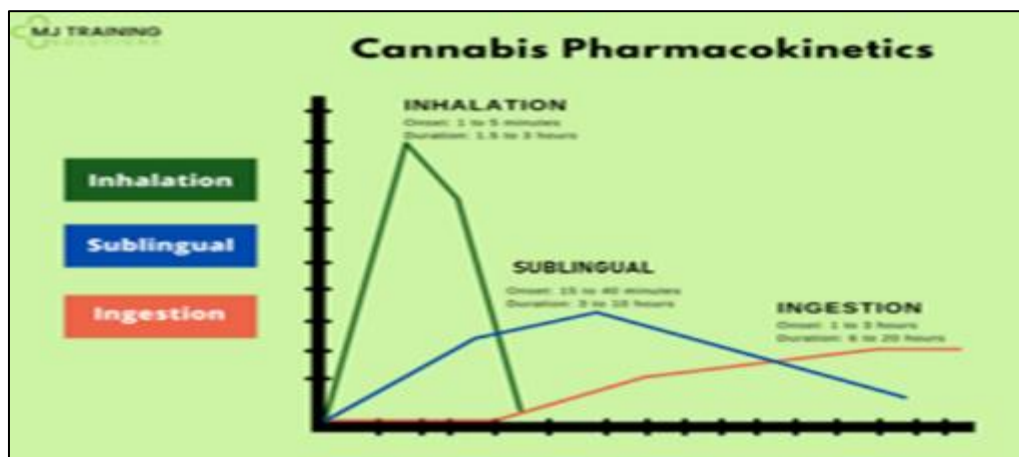


**Figure 5** Minor cannabinoids

In addition to THC and CBD, more than 130 minor cannabinoids have been found, and some of these have shown beneficial effects in reducing chronic pain symptoms.

For example, preclinical studies have demonstrated the therapeutic properties of **Cannabichromene(CBC)**, **Cannabigerol (CBG)**, and **Cannabinol(CBN)**.

## 4. Choosing dosage forms of cannabis



**Figure 6** Choosing dosage forms of cannabis

### 4.1. Dosage forms of Cannabis

The onset and duration of action from different cannabis dosage forms can range appreciably. In many instances, aggregate healing procedures might also be more effective. For sufferers with persistent aches, long-acting hashish products which include tinctures or pills tend to offer the more sustained comfort over the years. Starting with a low dose and progressively increasing the dose to achieve exceptional healing effects is advocated.

Additionally, inhalable products along with long-acting dosage forms give more control.

Topical hashish products, like creams and lotions, also can be effectively used for localized pain relief in case of joint pain and muscle spasm [5].



## 5. Different Uses of Cannabis

Pain is processed in the brain, although it can originate anywhere in the body. Nerve pathways begin with receptor cells that react to environmental changes, signaling the brain to interpret the pain. Both experimental and clinical research suggests that cannabinoids can interfere with these nerve signals, reducing pain. CBD, in particular, has been shown to enhance the immune system by lowering proinflammatory cytokines, which are small proteins involved in inflammation—and also influence the peripheral nerves. The way cannabinoids modulate pain can vary depending on the region of the brain, from peripheral areas to the cerebral cortex. In fact, CBD is considered an immunomodulator, meaning it can regulate the immune system depending on the situation, potentially boosting a weakened immune system or suppressing an overactive immune system [6].

In some cases, medical marijuana can be used alongside opioids to manage pain, helping to reduce opioid side effects.

### 5.1. CBD for Pain Relief

Cannabidiol (CBD), has much less potential to cause side effects compared to tetrahydrocannabinol (THC).

Cannabinoids like CBD interact with receptors in the endocannabinoid machine. For the past years, scientists have been testing the effectiveness of CBD, with desirable outcomes. While research continues, so far we understand a way to use CBD oil to alleviate aches. For instance, it is approved in the United Kingdom for the treatment of multiple sclerosis (MS) and Canada for the treatment of most cancer pain. Ongoing research indicates that CBD oil may also provide therapeutic benefits, such as decreasing arthritis aches and controlling fibromyalgia aches. Some illnesses can't be handled with only CBD, however may be useful when combined with THC [7].

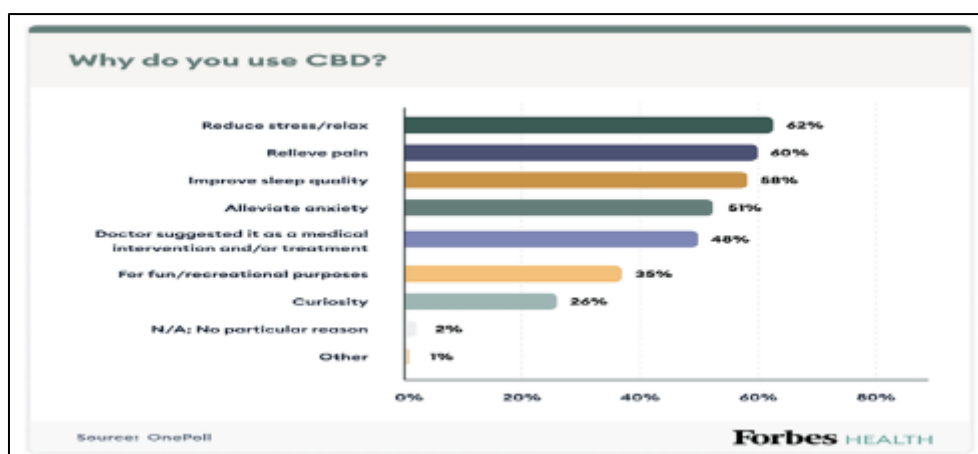


Figure 7 Uses of CBD

### 5.2. CBD for Chronic Pain

Chronic or continual pain is defined as a circumstance that lasts longer than some months. Studies have shown that CBD, often in combination with THC, is a powerful pain reliever for a no. of ailments [8] such as multiple sclerosis and cancer. It has been proven to be particularly powerful in neuropathic pain [9].

### 5.3. CBD for arthritis and joint pain

Arthritis is an extensive term that encompasses many joint illnesses and conditions, usual signs of which include joint swelling, pain, and stiffness which can worsen through the years. CBD has proven promise as a drug useful in the remedy of arthritis [10] [11] [12] [13]. Studies have proven that a single inhalation of CBD-THC medicine is more powerful than a placebo and the drug itself [14].

### 5.4. CBD for Neuropathic Pain

Multiple sclerosis (MS) is a common reason of neuropathic ache. This disorder destroys myelin, an aggregate of proteins and phospholipids that surround the nerve cell. Studies support a median dose of eight sprays a day for patients with MS, which provides about 20 milligrams of CBD and 21.6 milligrams of THC [15]. A study also tested topically administered CBD oil as a treatment for patients with peripheral neuropathy, or damage to the peripheral nervous

system, which sends information throughout your body from the central nervous system [16]. When compared to placebo, the topical CBD significantly reduced patients' intense pain and sharp pain, as well as cold and itchy sensations.

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## **6. Forms of Chronic pain**

Persistent ache is defined as pain that persists for more than 12 weeks. The ache can occur in almost any part of your body. It is able to sense sharp or dull pain, or that causing a burning or aching sensation. It may be resulting from numerous clinical situations, which include most cancers, arthritis, headaches, and others. The maximum common varieties of persistent ache consist of [17]:

### **6.1. Headache**

Chronic day by day complications are people who arise 15 days or extra a month and persist for longer than three months. The analgesic properties of Cannabis along with its anti-inflammatory properties are helpful in treating headache disorders. Cannabis also possesses anti-epileptic properties that influences migraine-induced nausea. A recent research by Washington State University showed that cannabis reduced self-reported migraine severity by 49.6%.

### **6.2. Post-surgical pain**

Persistent post-surgical pain (CPSP) is not unusual. To help get better without using prescription painkillers with significant side effects, medical hashish is being prescribed for holistic restoration. Medicinal cannabis can assist lessen postoperative pain.

### **6.3. Post-Trauma ache**

Pain that happens after a traumatic damage is disturbing. In line with current studies, cannabinoids may additionally help to deal with PTSD in two therapeutic ways. First, hashish can decrease activity within the amygdala, the part of the brain associated with fear responses to threats. Secondly, the plant's cannabinoids may want to play a function in extinguishing worrying memories of the trauma.

### **6.4. Lower back pain**

It is a common painful condition affecting the lower portion of the spine. A balanced ratio of CBD: THC has been found effective for chronic pain and chemotherapy-induced neuropathic pain. Some of the natural Cannabis medicine for alleviating pain that affects mobility, like neck and backache. It is efficacious for most muscular spasms and sciatica pain.

### **6.5. Cancer ache**

Ache is a commonplace and dreadful symptom among most cancer sufferers and survivors. Cannabinoids along with THC and CBD in a balanced ratio assist the patients relieve ache. It produces analgesia by acting on multiple pain targets in the peripheral and Central nervous system at the site of the activation of CB1 and CB2 receptors.

### **6.6. Arthritis ache**

Continual pain stemming from systemic infection, along with arthritis, is benefitted by the results of clinical cannabis. Hashish oil for ache remedy is more and more being utilized by patients.

### **6.7. Neurogenic pain (pain as a result of nerve harm)**

Neurogenic pain is any sort of discomfort or pain that can be caused by lesions and damage to the nervous system of the body. This can result from the damage done to the peripheral nervous system, spinal system or the supraspinal nervous system.

It can be caused by trauma, disorder, or underlying neurological conditions. Natural hashish medication for chronic inflammation is available elsewhere and is used to soothe aching joints, strengthen bones, and promoting cartilage regeneration. Neurogenic pain can be very challenging and painful and even life-threatening for patients. While you might be able to avoid neurogenic pain, you can also have it treated too.

### **6.8. Psychogenic pain (pain that isn't because of disease, damage, or nerve harm)**

Psychogenic pain is specially attributed to psychological elements, together with despair or anxiety. There are methods in which cannabis help alleviate psychogenic pain. First, it helps relieve the pain due to its analgesic properties. Secondly, it reduces nausea related to chronic ache and its medicines. Additionally, it has strong anti-tension characteristic as well as improving the sleep.

There may be no magic pill for chronic ache, but the situation may be managed effectively. To increase a safe and effective ache control plan with holistic advantages, consider incorporating a combination of medical treatments, lifestyle adjustments, and alternative therapies. Medical hashish is proven to lessen nausea, ache, and irritation. Hashish drugs in India are widely trusted as an herbal opportunity as their side effects are minimal and are secure.

#### **Possible dangers and side effects of using cannabis for ache:**

Most cannabis side effects are related to THC and include:

- Pink eyes
- Expanded urge for food
- A "high" or intoxicated feeling
- Dizziness
- Drowsiness
- Slowed sense of time
- Increased coronary heart
- Diarrhea (CBD-related)

These consequences can frequently be avoided by means of following a dosing time table that slowly increases your dose over time. If these results occur, they're generally simple to manage on your own and could go away because the hashish dose wears off.

Moreover, there are large dangers associated with hashish use, in most cases attributed to the effect of THC on the brain. THC can cause some symptoms, especially in higher doses:

- Emotions of fear or anxiety
- Impaired wondering and coordination
- Issues with cognitive function
- Seeing, listening to, or feeling matters that aren't real
- Irrational feelings and thoughts

Use of cannabis high in THC also can be habit-forming.

Successful pain management with cannabis includes the usage of it responsibly and at the lowest effective dose. High-CBD or balanced CBD to THC products are favored for ache control to lessen the above dangers.

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## **7. Legalizations of Cannabis in India?**

It's ironic having forced India to shut its Cannabis Industry, different countries legalized cannabis in the majority of their states. India is in a state of economic limbo. The Coronavirus is the biggest emergency since Independence, and the World Bank and credit rating agencies have downgraded India's 2021 fiscal year growth with India's lowest figures seen since the 1990s liberalization. It is time for India to rise and legalize the medical use of cannabis.

### **7.1. The Reasons to Legalize Cannabis**

The plant is not only used as a medical boon, but hemp can be refined into a variety of commercial items, including paper, textiles, clothing, biodegradable plastics, paint, insulation, biofuel, food, and animal feed. Opening India to the whole new \$100 billion market.

The legalization of this plant in India will reduce the potential harms of the drug's use, put a dent in corruption and crime, and provide our country with the economic boost it needs. Our distressed Indian farmers can use this cash crop since it takes bare minimum time and water to grow.

The legalization of cannabis for commercial and medical purposes in Colorado has created 10,000 new jobs in the region. There is a plethora of employment that can be created by the cannabis industry and help reduce India's unemployment rate.

The legalization would ensure that better quality cannabis is sold to customers. In India, traffickers sometimes combine hash and cannabis with chemicals or other drugs such as afeem to enhance the taste, colour, texture or 'high' of the product. Legalizations would increase the quality of cannabis sold to consumers as the government would control the manufacture and distribution of the drug.

The laws on cannabis in India are obsolete and necessitate long-awaited reconsideration. The increasing number of start-up cannabis and hemp companies and the rising mainstream support for the legalization of plants are promising, although legalizations are still far from achievable. Given the medical and economic reasons for cannabis legalization, the full potential of legalization could not be long before the Indian Government has legalized cannabis.

"High time for India to embrace the health, business, and broader societal benefits that legally regulating cannabis can bring".

Nowadays, the world is accepting cannabis and legalizing its consumption by researching on the benefits the plant holds. Cannabis is a plant with psychoactive properties. India has been using Cannabis for industrial, medical, and religious purposes since aeons. In India, several names have been given to this plant, popular ones such as Ganja, Bhang, Hemp and Charas. Nevertheless, the most widely used type of cannabis in India is in the form of bhang which is used to make "Thandai", an auspicious drink consumed during the festivals of Holi, Maha Shiv Ratri and the Hola Mohalla Sikh Festival, and other festive forms. However, the focal concern in uncertainty is whether Cannabis Legal in India?

The legal status of cannabis in India reflects a balance between tradition, regulation, and modern challenges. While bhang enjoys cultural acceptance and legal protection, marijuana and hashish remain criminalized under the NDPS Act. As global attitudes toward cannabis evolve, India has the opportunity to harness its economic and medicinal potential through reform and regulation. A nuanced approach that respects cultural practices while promoting industrial and medicinal use could pave the way for a progressive cannabis policy in the future [18].

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## 8. Conclusion

An article suggests that cannabis may be effective in reducing both pain severity and pain interference while also improving quality of life, general health, mood and sleep in patients with chronic pain. The current scientific understanding of cannabinoids, coupled with a better understanding of the endocannabinoid system, has activated patient advocacy groups and the medical community to reconsider legislative policy and reshape cultural bias. High-quality studies are needed to determine if cannabinoids are effective in many painful conditions and if there are opioid-sparing effects.

The legalization of cannabis is highly required for medicinal, industrial, and some other uses. Though cannabis is illegal, India has witnessed the consumption of cannabis in a huge quantity. This creates a black market for cannabis. If legalization takes place, people would legally buy the product and pay revenue to the government, improving the condition of the Indian economy. Furthermore, many cannabis sellers also sell adulterated cannabis, mixed with other similar-looking harmful products. This is because there are no regulations to have control over these malpractices.

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

The authors have stated that they do not have any conflicts of interest.

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