

A Narrative Review

Medical Cannabis for Chronic Pain: A Narrative Review of the Evidence, Challenges, and Future Directions.

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ABSTRACT

Background: Chronic pain is a major global health concern that significantly affects quality of life and increases healthcare burden. Conventional treatments, particularly opioids, are associated with limited efficacy and substantial adverse effects. Medical cannabis has emerged as a potential alternative, attracting increasing clinical and research interest due to its analgesic properties.

Objectives: To evaluate the efficacy and safety of medical cannabis in the management of chronic pain and to explore its role as an alternative to conventional therapies.

Methods: This narrative review analyzed recent literature on medical cannabis for chronic pain management. Relevant studies, including randomized controlled trials, systematic reviews, and clinical guidelines, were identified through electronic databases. The review focused on the pharmacological mechanisms, clinical effectiveness, safety profile, and potential role of cannabis in reducing opioid use.

Results: Evidence suggests that cannabis-based medicines provide modest pain relief in patients with chronic pain, particularly neuropathic pain. Cannabinoids such as tetrahydrocannabinol (THC) and cannabidiol (CBD) interact with the endocannabinoid system to modulate pain pathways. Several studies reported improvements in pain intensity and quality of life, along with a potential opioid-sparing effect. However, adverse effects, including dizziness, sedation, and cognitive impairment, were commonly reported.

Conclusion: Medical cannabis shows promise as an adjunct or alternative therapy for chronic pain management. While evidence supports its potential benefits, variability in study outcomes and safety concerns highlight the need for further high-quality research. Careful patient selection and clinical monitoring are essential for optimizing therapeutic outcomes.

INTRODUCTION

Chronic pain is a major global health challenge, affecting millions of individuals and significantly impairing physical, psychological, and socioeconomic well-being. It is commonly defined as pain persisting beyond normal tissue healing time, typically exceeding three months, and is associated with reduced quality of life, functional disability, and increased healthcare utilization [1]. Conventional pharmacological treatments, particularly opioids, remain widely used for moderate to severe chronic pain. However, their long-term use is associated with substantial risks, including tolerance, dependence, overdose, and increased mortality, raising serious concerns regarding their safety and effectiveness [2]. In response to these limitations, there has been growing interest in alternative and adjunctive therapies for chronic pain management. Among these, medical cannabis has emerged as a promising option due to its potential analgesic, anti-inflammatory, and neuromodulatory properties [3,4]. Medical cannabis comprises a diverse group of compounds, primarily tetrahydrocannabinol (THC) and cannabidiol (CBD), which exert their effects through interaction with the endocannabinoid system. This system plays a crucial role in regulating pain perception, inflammation, mood, and immune responses [5]. THC acts as a partial agonist at cannabinoid receptors, producing both analgesic and psychoactive effects. In contrast, CBD is non-intoxicating and exhibits complex pharmacological actions, including modulation of neurotransmitter systems and anti-inflammatory pathways [6]. Recent years have witnessed increasing clinical and public interest in the use of cannabis-based therapies, particularly for conditions that are difficult to manage with conventional treatments, such as neuropathic pain, fibromyalgia, and cancer-related pain [7]. Several observational studies and clinical trials have reported improvements in pain intensity, sleep quality, and overall quality of life among patients using medical cannabis [8]. Additionally, the potential opioid-sparing effect of cannabis has been highlighted in multiple studies, suggesting a reduction in opioid consumption among patients receiving cannabinoid therapy [9]. Despite these encouraging findings, the clinical evidence supporting medical cannabis remains inconsistent and heterogeneous. High-quality randomized controlled trials (RCTs) have produced conflicting results, with some studies demonstrating modest analgesic benefits while others show no significant difference compared to placebo [10]. Variability in cannabis formulations, dosing regimens, routes of administration, and patient populations further complicates interpretation and limits the generalizability of findings [11]. Moreover, concerns regarding adverse effects, including cognitive impairment, psychiatric symptoms, and potential dependency, pose additional challenges for clinicians [12]. Regulatory and legal barriers also contribute to the complexity of integrating medical cannabis into routine clinical practice. Differences in legislation, product standardization, and prescribing guidelines across regions create uncertainty for healthcare providers and patients alike [13]. Furthermore, the lack of robust long-term safety data and standardized dosing protocols underscores the need for cautious, evidence-based use. Given these challenges, medical cannabis presents both an opportunity and a clinical conundrum in chronic pain management. Therefore, this narrative review aims to critically evaluate the current evidence on the efficacy, safety, and clinical applicability of medical cannabis for chronic pain, while identifying

key limitations and future research directions to support its optimal integration into healthcare practice [14].

Materials and Methods

Literature Search Strategy

The online databases PubMed, Scopus, Web of Science, and Google Scholar were used for a thorough literature review, which identified relevant studies from April 1, 2020, to March 31, 2025. Searches were conducted using combinations of Medical Subject Headings (MeSH) terms, as well as free-text keywords such as medical cannabis, cannabinoids, tetrahydrocannabinol (THC), cannabidiol (CBD), chronic pain, neuropathic pain, fibromyalgia, arthritis, efficacy, and safety, between April 1 and April 10, 2025. Boolean operators (AND/OR) were used as an optimization technique for the search strategy.

Study Selection and Screening

Titles and abstracts of all retrieved records were screened for relevance by two independent reviewers. All full-text articles were then evaluated based on the established inclusion criteria. Disagreements about the choice of studies were discussed, and consensus was reached, with a third reviewer consulted if required. Publications and studies that were duplicated and did not meet inclusion criteria were discarded.

Data Extraction

The reviewers independently extracted data using the data extraction form they developed and used for the eligible studies. The data obtained included the first author, publication year, country, study design, characteristics of the study sample, intervention, comparator (if any), primary outcome, adverse events, and the main conclusions regarding the efficacy and safety of medical cannabis in the treatment of chronic pain.

Quality Assessment

This is a narrative review, but the methodological quality and scientific relevance of the included studies were critically assessed. Randomized controlled trials, systematic reviews, and meta-analyses were emphasized for finding high-quality evidence. The methodological rigor, risk of bias, sample size, consistency of findings, and the study's overall relevance to the review's aims were evaluated.

Data Synthesis

Due to substantial variability across studies in population, type of cannabis, method of administration, outcome measures, and study design, the findings were synthesized narratively. The evidence was presented in thematic categories, such as: pharmacological mechanisms; clinical efficacy; safety profile; opioid-sparing; and clinical challenges regarding the use of medical cannabis for chronic pain.

Inclusion Criteria

Studies were included if they were randomized controlled trials, systematic reviews, meta-analyses, or observational studies evaluating the efficacy or safety of medical cannabis or cannabinoids in chronic pain management. Only English-language human studies published between April 2020 and March 2025 involving adolescents and adults were considered.

Exclusion Criteria

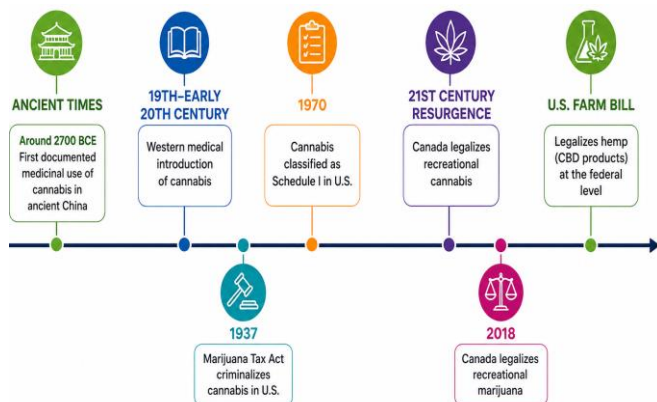
Studies were excluded if they were preprints, editorials, conference abstracts, or non-peer-reviewed articles. Animal studies, duplicate

publications, and studies unrelated to chronic pain or cannabis were also excluded. Articles with insufficient data, unclear outcomes, or lacking clinical relevance were not considered for inclusion in this review.

Results

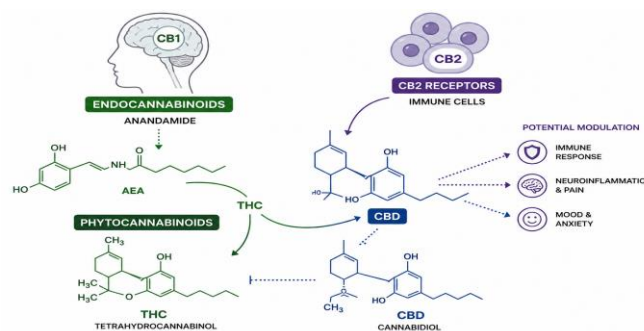
The literature search revealed a wide variety of publications on the use of medical cannabis for the management of chronic pain. After the titles and abstracts were screened, the most suitable and methodologically sound studies were included following full-text review. Randomized controlled trials, systematic reviews, and meta-analyses, as well as high-quality observational studies and evidence-based clinical guidelines, published between 2020 and 2025, were prioritized. This literature review examined the efficacy, safety, pharmacological mechanisms, and clinical uses of medical cannabis in different chronic pain disorders such as cancer-related pain, arthritis, fibromyalgia, and neuropathic pain. The evidence was consistently supportive of the potential for small improvements in pain intensity, sleep quality, and general quality of life from cannabis-based medicines, especially for those with treatment-resistant pain. Several studies also indicated there might be an opioid-sparing effect, but the evidence was moderate for some, and weak for others. Adverse events were mostly mild to moderate, and included dizziness, sedation, dry mouth, nausea, and transient cognitive impairment. There was substantial variation across studies in terms of the formulation of cannabis, the quantities of cannabinoids (THC/CBD ratio), dosing, route of administration, and outcome measures, making comparisons between studies difficult. Thus, the results are reported as a narrative synthesis to offer a comprehensive evidence-based overview of the current place of medical cannabis in chronic pain management.

Figure 1: Historical timeline of cannabis use and regulation.



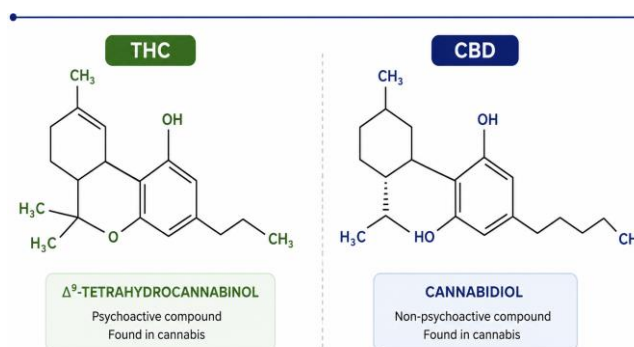
This figure illustrates the major historical milestones in the medical and regulatory evolution of cannabis, from its earliest documented medicinal use in ancient China (approximately 2700 BCE) to modern legislative developments, including the 1937 Marijuana Tax Act, Schedule I classification in the United States (1970), Canada's legalization of recreational cannabis (2018), and the U.S. Farm Bill legalizing hemp-derived cannabidiol (CBD) products.

Figure 2: Overview of the Endocannabinoid System and Cannabinoid Interactions.



This schematic illustrates the principal components of the endocannabinoid system, including endogenous cannabinoids (anandamide), cannabinoid receptors (CB1 and CB2), and plant-derived cannabinoids (Δ^9 -tetrahydrocannabinol [THC] and cannabidiol [CBD]). It demonstrates their interactions and potential roles in modulating pain perception, immune responses, neuroinflammation, and mood regulation.

Figure 3: Chemical Structures of Δ^9 -Tetrahydrocannabinol (THC) and Cannabidiol (CBD).



This figure presents the molecular structures of the two major phytocannabinoids found in *Cannabis sativa*. Δ^9 -Tetrahydrocannabinol (THC) is the principal psychoactive constituent, whereas cannabidiol (CBD) is a non-psychoactive compound with potential analgesic, anti-inflammatory, and neuroprotective properties.

Table 1. Characteristics of Included Studies

Study Type	Number of Studies	Key Focus Area
Randomized Controlled Trials (RCTs)	10	Efficacy and safety
Systematic Reviews	8	Evidence synthesis
Meta-analyses	6	Comparative outcomes
Observational Studies	8	Real-world effectiveness

This table summarizes the types of studies included in the review and their primary focus areas.

Table 2. Clinical Outcomes of Medical Cannabis

Outcome	Findings
Pain Reduction	Moderate improvement (~ 20%)
Sleep Quality	Improved in the majority of studies

Quality of Life	Positive patient-reported outcomes
Opioid Reduction	Potential but inconsistent evidence

This table presents the key clinical outcomes associated with the use of medical cannabis in chronic pain management.

Table 3. Reported Adverse Effects of Medical Cannabis

Category	Common Effects
Neurological	Dizziness, sedation
Psychiatric	Anxiety, confusion
Gastrointestinal	Nausea, dry mouth
Cardiovascular	Tachycardia

This table outlines the commonly reported adverse effects of medical cannabis, categorized by system involvement.

Discussion

The current review indicates the complex and evolving role of medical cannabis in chronic pain management. The available evidence suggests that cannabinoids may have modest analgesic effects in certain patient groups, but overall clinical efficacy remains inconsistent. This inconsistency indicates high levels of heterogeneity in study designs, cannabis preparations, dosage schedules, and patient variables that make it hard to interpret and constrain the extrapolation of results [11]. Among the main findings of this review is the difference in the outcomes of observational studies and randomized controlled trials (RCTs). Clinically significant changes in pain intensity, quality of life, and sleep outcomes are often reported in observational studies, and some studies show that pain scores change by an average of 20 percent over time [12]. On the contrary, the quality RCTs usually present modest or nonsignificant improvements over placebo, especially in disease states like peripheral neuropathy and pain in HIV [13,14]. This heterogeneity can be explained by the dissimilarity in study groups, placebo effects, and the real-world settings of cannabis therapy, in which personalized therapy and patient expectations can affect the results. Another significant finding is the possible opioid-sparing effect of medical cannabis. Multiple observational studies indicate that cannabis use might be related to a lower rate of opioid use, especially given the current opioid crisis [15,16,17]. This effect has not, however, been found in all studies, and evidence from controlled trials is scarce. Moreover, co-administration of cannabinoids with opioids does not always improve analgesic efficacy and can lead to more adverse events, which means that it requires special attention to patient selection and monitoring [18]. The safety profile of medical cannabis is also a major issue, even though there might be certain positive effects. Adverse effects are common and include dizziness, sedation, impaired thinking, and gastrointestinal disturbances, but tend to be mild or moderate in nature and can impact daily functioning [19,20]. Anxiety, confusion, and, in some exceptional instances, hallucinations are some of the psychiatric effects of THC-containing products, and should be paid due attention, particularly in vulnerable groups [21,22]. There is a lack of long-term safety data, and issues of dependency and cognitive decline have not been addressed, which underscores the importance of future studies. One of the significant difficulties in clinical use of medical cannabis is the absence of standardization of formulations and doses. Cannabis products are different in their composition, which can include variations in the levels of THC and CBD, routes of delivery, and pharmacokinetic profile [23,24]. This inconsistency

complicates the setting of best dosing guidelines and comparisons across studies. In contemporary clinical practice, the use of titration strategies aimed at individualization is common. It is often summarized as "start low and go slow," which, although supported by practical guidelines, is not well supported by evidence-based techniques [25,26,27]. The regulatory and legal factors further complicate medical cannabis use. Variations in laws across countries and regions pose obstacles to research, limit the use of standardized products, and hinder the development of clear clinical guidelines [28,29]. Moreover, the absence of stringent quality checks in certain markets raises concerns about product safety and uniformity, especially for over-the-counter CBD products [30]. Comparatively, medical cannabis can have some benefits compared to traditional treatments. Cannabinoids have reduced chances of respiratory depression compared to opioids and can serve as a safer option in a few patients [31]. Nevertheless, they do not seem as effective in terms of analgesia and cannot be regarded as a direct alternative to standard treatment. Equally, although cannabis can be a helpful option among contraindicated patients to nonsteroidal anti-inflammatory drugs (NSAIDs), especially those with impaired kidney function, there is little evidence to support its superiority [32]. The concept of medical cannabis incorporation into multimodal pain management techniques is a promising solution. Cannabinoids can be used as a supplement to the current treatment methods and enhance the outcomes of patients by alleviating various aspects of chronic pain, such as sleep disturbances, anxiety, and well-being [33]. Nonetheless, this method must be applied cautiously regarding potential drug interactions, patient-specific factors, and treatment objectives. Future studies ought to work on the existing gaps in the evidence base. To determine the effectiveness and safety of medical cannabis, large, well-designed RCTs using standardized formulations, well-defined dosing schedules, and extended follow-ups are necessary. Furthermore, studies investigating individualized approaches, such as pharmacogenomics and individualized treatment plans, could improve treatment outcomes and reduce adverse effects. To sum up, medical cannabis is an effective yet multifaceted treatment option for chronic pain. Although it might offer small benefits in some populations, its application is limited by inconsistent evidence, safety concerns, and lack of standardization. Selecting patients carefully, treating them individually, and monitoring them throughout are critical to maximizing results [34]. To close the gap between the emerging evidence and clinical practice, researchers, clinicians, and policymakers will need to collaborate to make medical cannabis a safe and effective integration into healthcare systems.

Limitations

This narrative review has several limitations that should be acknowledged. First, as a narrative synthesis rather than a systematic review, the study may be subject to selection bias because the literature was included without a fully standardized protocol. Although efforts were made to include high-quality, relevant studies, the possibility of overlooking pertinent evidence cannot be ruled out. Second, the included studies demonstrated considerable heterogeneity in terms of study design, patient populations, cannabis formulations, dosing regimens, and outcome measures. This variability limits the comparability of findings and restricts the ability to draw definitive conclusions regarding the efficacy and safety of medical cannabis.

Conclusion

Medical cannabis represents a promising yet complex therapeutic option in the management of chronic pain. Evidence suggests that cannabinoids may provide modest analgesic benefits, particularly in neuropathic and treatment-resistant pain conditions, as well as improvements in patient-reported outcomes, including sleep and quality of life. However, the current evidence base remains heterogeneous and, in some cases, inconclusive. Variability in study designs, formulations, and dosing strategies, coupled with limited high-quality randomized controlled trials, poses challenges in establishing clear clinical guidelines. Additionally, concerns regarding adverse effects, long-term safety, and regulatory inconsistencies must be carefully considered. Despite these limitations, medical cannabis may serve as a valuable adjunct in selected patients who do not respond adequately to conventional therapies. Its potential role in reducing opioid dependence further underscores its clinical relevance. Future research should focus on well-designed, large-scale clinical trials with standardized formulations and long-term follow-up to better define efficacy, safety, and optimal therapeutic use. A balanced, evidence-based approach is essential to ensure the safe and effective integration of medical cannabis into chronic pain management strategies.

Authors' Contributions (ICMJE)

Ahtisham Ali: Conceptualization, study design, literature review, data interpretation, and manuscript preparation.

Muhammad Haris: Literature search, data extraction, manuscript drafting, and critical revision for important intellectual content.

Ayesha Islam: Literature screening, data collection, data interpretation, and manuscript review.

Nusrat Iqbal: Quality assessment of included studies, data interpretation, and critical manuscript revision.

Yarfa Khurram: Data collection, literature review, manuscript editing, and reference verification.

Fiza Hussain: Manuscript review, language editing, final proofreading, and administrative support.

All authors made substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data; participated in drafting or critically revising the manuscript; approved the final version for publication; and agreed to be accountable for all aspects of the work in accordance with the ICMJE authorship criteria.

Conflict of Interest: The authors declare no conflict of interest.

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Ethical Approval

This study is a narrative review based exclusively on previously published literature and publicly available data. It did not involve human participants, patient data, or any form of clinical intervention. Therefore, ethical approval from an institutional review board was not required in accordance with standard research guidelines.

Copyright Statement

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Data Availability Statement

Data Availability Statement: All data analyzed in this narrative review were obtained from previously published studies cited in the reference list. No new datasets were generated or analyzed during this study.

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