

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

Ahtisham Ali¹, Muhammad Haris¹, Ayesha Islam¹, Nusrat Iqbal¹, Yarfa Khurram¹, Fiza Hussain¹

¹. Riphah International University, Islamabad, Pakistan

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 Structured 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.

Keywords: Medical cannabis; THC; CBD; cannabinoids; chronic pain; pain management

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Corresponding Author: Muhammad Haris

Department of Medicine Riphah International University, Islamabad, Pakistan

Email: muhammadharisriu@gmail.com

ORCID: <https://orcid.org/0009-0002-8781-0139>

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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, whereas 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 highlights the need for cautious and 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 regarding the efficacy, safety, and clinical applicability of medical cannabis in chronic pain, while also identifying key limitations and future research directions necessary for its optimal integration into healthcare practice [14].

MATERIALS AND METHODS

This Structured Narrative Review synthesizes current evidence on the role of medical cannabis in chronic pain management. A comprehensive literature search was conducted by the Department of Medicine, Rupiah International University, Islamabad, covering the period from April 1, 2020, to March 31, 2025. The search strategy incorporated key terms and Boolean operators as follows: (“medical cannabis” OR “cannabinoids” OR “CBD” OR “THC”) AND (“chronic pain” OR “neuropathic pain” OR “nociceptive pain” OR “fibromyalgia” OR “arthritis”) AND (“efficacy” OR “safety” OR “clinical trials” OR “adverse effects” OR “treatment outcome”). Filters were applied to include free full-text articles, English-language publications, human studies, and relevant age groups (adolescents [13–18 years] and adults [≥ 19 years]). Eligible study designs included randomized controlled trials (RCTs), systematic reviews, meta-analyses, observational studies, and clinically relevant review articles, while preprints and non-peer-reviewed sources were excluded. The search yielded a broad range of potentially relevant literature. For the purpose of this narrative review, data synthesis was based primarily on a curated selection of high-quality sources, supplemented by additional database searches and reference screening to ensure comprehensive coverage. The included studies comprised randomized controlled trials evaluating efficacy and safety, systematic reviews and meta-analyses summarizing existing evidence, observational studies and case series providing real-world insights, and selected preclinical studies elucidating underlying mechanisms. This approach ensured a balanced and evidence-based overview of the current role of medical cannabis in chronic pain management.

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

A comprehensive literature search identified a total of 172 records, including 119 from database searches (PubMed = 15, Scopus = 104) and 53 additional records from manual and reference screening. After removing duplicates, 148 records remained for screening. Following title and abstract screening, 92 records were excluded due to irrelevance, leaving 56 full-text articles assessed for eligibility. Of these, 24 studies were excluded based on predefined criteria, including lack of clinical relevance, insufficient data, or non-peer-reviewed sources. Finally, 32 studies were included in the narrative synthesis. The included studies comprised randomized controlled trials (RCTs), systematic reviews, meta-analyses, and observational studies, providing a broad

evidence base for evaluating the efficacy and safety of medical cannabis in chronic pain management. Most studies focused on neuropathic pain, fibromyalgia, and cancer-related pain, with outcomes including pain reduction, quality of life, and adverse effects. Overall, the findings indicate that medical cannabis provides modest but clinically relevant pain relief, particularly in treatment-resistant cases. Several studies also reported improvements in sleep quality and patient-reported outcomes. However, variability in study design and cannabis formulations contributed to inconsistent findings across trials. Adverse effects were commonly reported but were generally mild to moderate in severity. The most frequent side effects included dizziness, sedation, and gastrointestinal symptoms, with higher incidence observed in THC-dominant formulations.

Figure 1: Historical timeline of cannabis use and regulation.

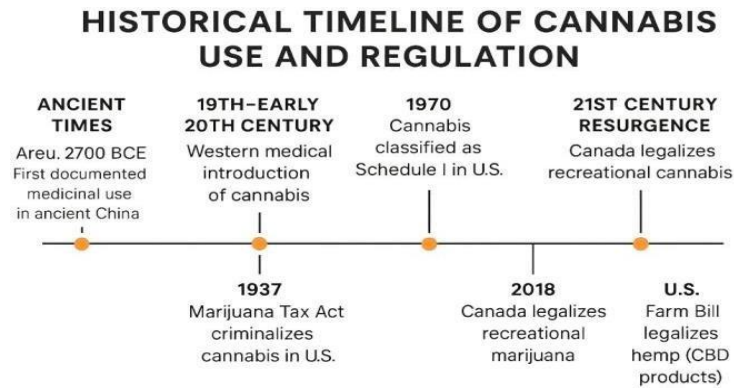


Figure 2: Endocannabinoid system and cannabinoid interactions.

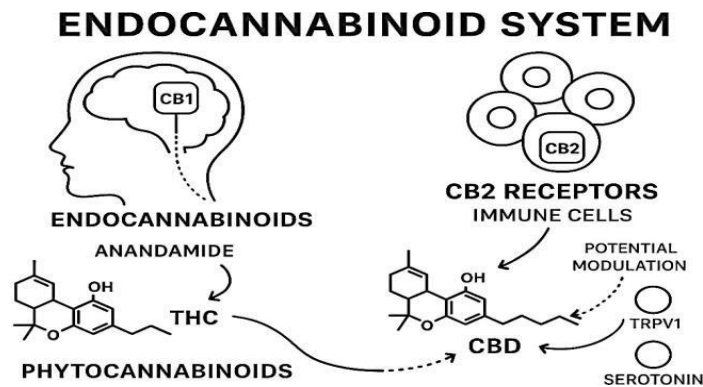


Figure 3: Chemical structures of THC and CBD.

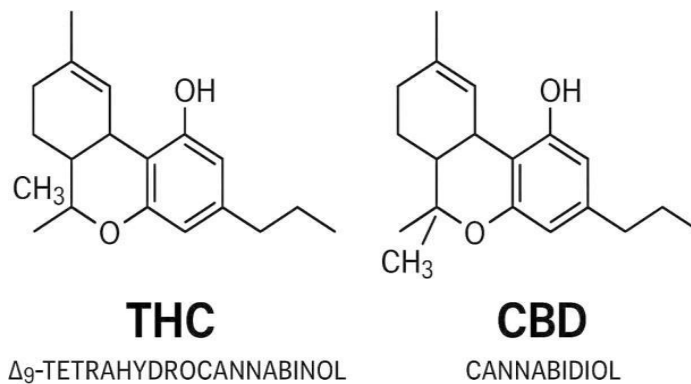


Table 1. Characteristics of Included Studies

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 highlights the complex and evolving role of medical cannabis in chronic pain management. The available evidence suggests that cannabinoids may have modest analgesic effects in specific patient groups, but the overall clinical efficacy is still inconsistent. This inconsistency indicates high levels of heterogeneity on 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 non-significant 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 anticipations 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, always been found in all studies, and the evidence of 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 on 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 dose. Cannabis products are different in their composition, which can include variations in the levels of THC and CBD, routes of delivery, pharmacokinetic profile [23,24]. This inconsistency complicates setting of best dosing guidelines and comparisons across studies. In contemporary clinical practice, the use of titration strategies aimed at individualization is common, and it is commonly summarized as start low and go slow, which, although supported

by practical guidelines, is not well-supported by evidence-based techniques [25,26,27]. Medical cannabis use is further complicated by the regulatory and legal factors. The variations in laws among countries and regions impose obstacles to research, restrict the utilization of standardized products, and prevent the formation of clear clinical guidelines [28,29]. Moreover, the absence of stringent quality checks in certain markets brings up the issue of safety and uniformity of products, especially in over-the-counter CBD products [30]. Comparatively, medical cannabis can have some benefits to a traditional treatment. 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 cautiously applied with regards to the possible 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, big, well-designed RCTs using standardized formulations, well-defined dosing schedules, and extended follow-ups are necessary. Furthermore, studies on the investigation of individualized methods, such as pharmacogenomics and individual treatment plan, could improve treatment and reduce the negative effects. To sum up, medical cannabis is an effective yet multifaceted treatment option of chronic pain. Although it might have small benefits in some populations, its application is restricted by the inconsistent evidence, safety issues, and non-standardization. Selecting patients carefully, treating them individually, and monitoring patients throughout are critical in maximizing the results [34]. To close the gap between the emerging evidence and clinical practice, researchers, clinicians, and policymakers will need to collaborate in order to make medical cannabis safe and effective integration into healthcare systems.

LIMITATIONS

This Structured 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, as the inclusion of literature was not based on a fully standardized protocol. Although efforts were made to include high-quality and relevant studies, the possibility of overlooking pertinent evidence cannot be excluded. 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. Third, a substantial proportion of the available evidence is derived from observational studies and small-scale clinical trials, which may be prone to bias and confounding factors. High-quality randomized controlled trials remain

limited, particularly for long-term outcomes. Additionally, variations in regulatory frameworks and product standardization across regions may influence both study outcomes and real-world applicability. The lack of standardized dosing guidelines and consistent formulations further complicates interpretation and clinical translation. Finally, long-term safety data on medical cannabis use remain insufficient, particularly regarding dependency, cognitive effects, and potential interactions with other medications. These gaps highlight the need for further rigorous, large-scale research.

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, along with improvements in patient-reported outcomes such as 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 Contribution

Concept & Design of Study: Ahtisham Ali

Drafting: Muhammad Haris

Data Collection & Critical Review: Ayesha Islam, Nusrat Iqbal Yarfa Khurram, Fiza Hussain

Final Approval of Version: All authors approved the final version of the manuscript.

CONFLICT OF INTEREST: Not applicable.

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ETHICAL STATEMENT

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.

AI USAGE STATEMENT

AI tools (e.g., ChatGPT) were used for language editing and structuring of the manuscript. The authors take full

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DATA AVAILABILITY STATEMENT

All data analyzed in this study were derived from previously published literature and are available in the cited references.

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