Medical cannabis in the management of musculoskeletal pain: a systematic review of clinical trials

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Abstract

Background: Cannabinoids not only act through classical cannabinoid receptors but also influence a wide range of physiological processes via numerous cellular signaling pathways. In this paper, we focus on two of the most extensively studied cannabinoids: delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). Recent scientific findings suggest that cannabinoids may be therapeutically beneficial for conditions such as neurodegenerative disorders, seizures, nausea and vomiting, insomnia, neuropathic pain, excessive muscle tension, fibromyalgia, osteoarthritis (OA), rheumatoid arthritis (RA), and chronic wounds.

Aims: The aim of this study was to summarize the current state of knowledge regarding the therapeutic potential of medical cannabis in the management of musculoskeletal pain.

Materials and Methods: We conducted a systematic search of scientific databases (PubMed, Medline, Google Scholar, and the PEDro Database) as well as gray literature sources for articles published between January 1, 2013, and January 1, 2024. Eligible publications were full-text English-language reports that examined various approaches to medical cannabis therapy for musculoskeletal pain, including diverse cannabinoid formulations and adminis-

Key words

musculoskeletal pain, musculoskeletal disorders, cannabinoids, medical cannabis, medicinal cannabis.

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tration methods. Outcomes of interest included pain intensity, motor function, sleep quality, and health-related quality of life.

Results: The search yielded 148 articles, of which 13 met the inclusion criteria. Overall, medical cannabis was generally well tolerated and was associated with significant pain reduction, improved motor function, enhanced sleep quality, and overall improvements in health-related quality of life.

Conclusions: Although early clinical evidence supports the efficacy of medical cannabis in managing musculoskeletal pain, the methodological quality of the included studies limits the strength of these conclusions. Larger and more rigorously designed randomized controlled trials are needed to further clarify the role of medical cannabis therapy in musculoskeletal pain management.

Introduction

Chronic pain and pain-related diseases are leading causes of disability, limited mobility, restrictions in daily activities, and global disease burden [1]. Among these, musculoskeletal pain has consistently ranked as a primary cause of disability worldwide [2].

Cannabinoids are a class of compounds found in various species of the cannabis plant (*Cannabaceae Endl.*). Although some suggest that cannabis may have been used medicinally for over 12,000 years, definitive historical evidence remains inconclusive [3]. The pharmacological actions of cannabis are influenced by phytocannabinoids specific to Cannabis sativa and Cannabis indica, as well as synthetic cannabinoids, which are designer drugs that bind to the same receptors as the plant-derived cannabinoids [4].

The discovery of the endocannabinoid system as a modulator of nociception broadened the scope of cannabis research in pain management. Numerous mechanisms have been proposed for endocannabinoid signaling and synaptic function. Cannabinoid-induced antinociception affects multiple levels of the pain sensory pathway, including the peripheral and supraspinal structures, primarily through cannabinoid (CB) receptors CB1 and CB2. These receptors, along with endogenous cannabinoid ligands and endocannabinoid-metabolizing enzymes, appear to be integral to pain modulation. At the spinal level, the analgesic effect of cannabinoids may be partly mediated by the opioid OP2 receptor [5]. This may explain why tetrahydrocannabinol (THC) can reduce the minimum effective dose of opioids, especially codeine (by 96%) and methadone (by 75%) [6, 7].

Cannabinoids also exhibit anti-inflammatory properties by reducing levels of tumor necrosis factor-alpha (TNFα), reactive oxygen species, and lipoxygenases. They may improve tissue perfusion and oxygenation through direct vasodilation and nitric oxide-related mechanisms [8, 13].

Beyond their antinociceptive and anti-inflammatory effects, cannabinoids influence a wide range of physiological processes via classical cannabinoid receptors (CB1 and CB2), novel cannabinoid receptors (GPR), ionotropic receptors (TRPV, TRPA, TRPM), nuclear receptors (PPARγ, PPARα, PPARδ, NF-κB), and various non-cannabinoid targets (5-HT, GlyR, A2A, α2R) [9]. It is estimated that cannabis contains over 500 active compounds, including more than 100 cannabinoids [3, 5]. In this paper, we focus on the two most extensively studied cannabinoids: delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).

Emerging research suggests that a combination of THC and CBD may offer optimal pain management benefits, possibly due to a potentiating syn-

ergy among cannabinoids, terpenes, flavonoids, steroids, pigments, and other compounds in the cannabis plant [5, 10, 11]. Some authors have noted that purified THC or CBD extracts alone appear less beneficial, implying that whole-plant preparations may better reflect the plant's therapeutic potential [12, 13].

Recent studies have highlighted the potential utility of cannabinoids in treating a range of conditions, including neurodegenerative disorders, seizures, nausea and vomiting, insomnia, neuropathic pain, excessive muscle tension, fibromyalgia, osteoarthritis (OA), rheumatoid arthritis (RA), and chronic wounds [9, 11, 14]. According to a recent investigation [15], one year of regular medical cannabis use does not lead to noticeable changes in brain morphology or cognitive functioning. Cannabinoids have demonstrated efficacy exceeding placebo and are often better or comparable to widely used medications for these conditions, typically producing fewer side effects.

Medical cannabis can be administered through inhalation and oral ingestion, as well as via transdermal formulations (lotions, gels), cartridges, concentrates, sublingual drops, and nasal sprays [16].

In 2018, cannabis-based medicinal products were approved in the United Kingdom for prescription to patients with osteoarthritis who did not respond to conventional treatments. Data from the UK Medical Cannabis Registry indicate that these patients reported significant, pain-specific improvements over a one-year period [17].

In 2019, the US Arthritis Foundation surveyed 2,600 patients who had lived with arthritis for over a decade. Arthritis and arthritis-related pain were among the most common reasons given for using cannabidiol (CBD). More than half of the respondents utilized hemp products and CBD topical formulations, with the majority reporting relief from pain and arthritis-related symptoms [18].

Further surveys conducted in the United States [19, 20], Canada [21], and Australia [22] have shown that adults using medical cannabis often report reduced chronic musculoskeletal pain and improved psychological well-being. A decrease in the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids was also observed [5, 23].

Currently, in Poland, one cannabinoid-containing medication—Sativex® (a combination of THC and CBD)—and several types of pharmaceutical cannabis flower (dried raw material) have been approved for treatment. However, none of these medications are specifically approved for musculoskeletal pain management [24].

As patients continue to explore the use of cannabinoids for musculoskeletal pain, there is a growing need for healthcare providers and patients to receive comprehensive education on the current state of evidence, as well as the policy and ethical considerations related to medical cannabis. The increasing popularity of medical cannabis has generated substantial advocacy and interest. Patients frequently inquire about medical cannabis after exposure to its widespread promotion, yet healthcare providers often feel inadequately equipped to provide information due to limited evidence, particularly in orthopedic practice [4, 25, 26].

Aims

The aim of this study was to summarize the current state of knowledge regarding the therapeutic potential of medical cannabis in managing musculoskeletal pain.

Methods

Search strategy

We conducted a systematic search of four electronic databases (PubMed, Medline, Google Scholar, and the PEDro database) and additionally examined gray literature sources. Articles published between January 1, 2014, and July 1, 2024, were identified using the following keywords: "cannabis," "cannabinoids," "medicinal cannabis," "musculoskeletal disorders," "musculoskeletal pain," "topical cannabinoids," and/or "randomized controlled trial.".

Study selection

Studies were screened based on their titles and abstracts, followed by a full-text review for eligibility. To be included, articles had to meet the following criteria: (1) full-text publications in English, (2) reports of clinical trials or randomized controlled trials in humans, (3) evidence supporting the use of cannabinoids in treating musculoskeletal pain, and (4) inclusion of patient populations with mixed conditions, provided that at least half of the participants used cannabis primarily for musculoskeletal pain management.

Methodological quality

Two independent reviewers assessed the methodological quality of the included studies using the 10-item Physiotherapy Evidence Database (PEDro) scale [27]. Based on the PEDro score, studies were classified as low quality (3–4 points), medium quality (5–7 points), or high quality (8–9 points). Any disagreements were resolved through discussion.

Data extraction

Two authors independently extracted data from the selected studies, focusing on outcomes such as pain reduction, changes in motor function, sleep quality, and overall quality of life in individuals with musculoskeletal pain. Adverse events were also documented. All extracted data were entered into Microsoft Excel 2024 (Microsoft 365 Inc.).

Results

Study selection and characteristics

The initial search yielded 148 articles. Following the screening of titles (n = 128) and article contents (n = 7), 13 studies met the inclusion criteria and were included in the review (**Fig. 1**).

All included articles were full-text, English-language reports that examined various approaches to medical cannabis therapy in humans. These approaches encompassed a range of cannabinoid formulations (e.g., oils, capsules) and administration methods (e.g., inhalation) for the management of musculoskeletal pain. The use of medical cannabis was generally associated with significant pain reduction, decreased muscle tension, improved motor function, enhanced sleep quality, and overall improvements in health-related quality of life (HRQoL). The most commonly reported adverse effects were mild and well-tolerated. A detailed summary of each study's characteristics and findings is presented in **Table 1** [26, 28-39].

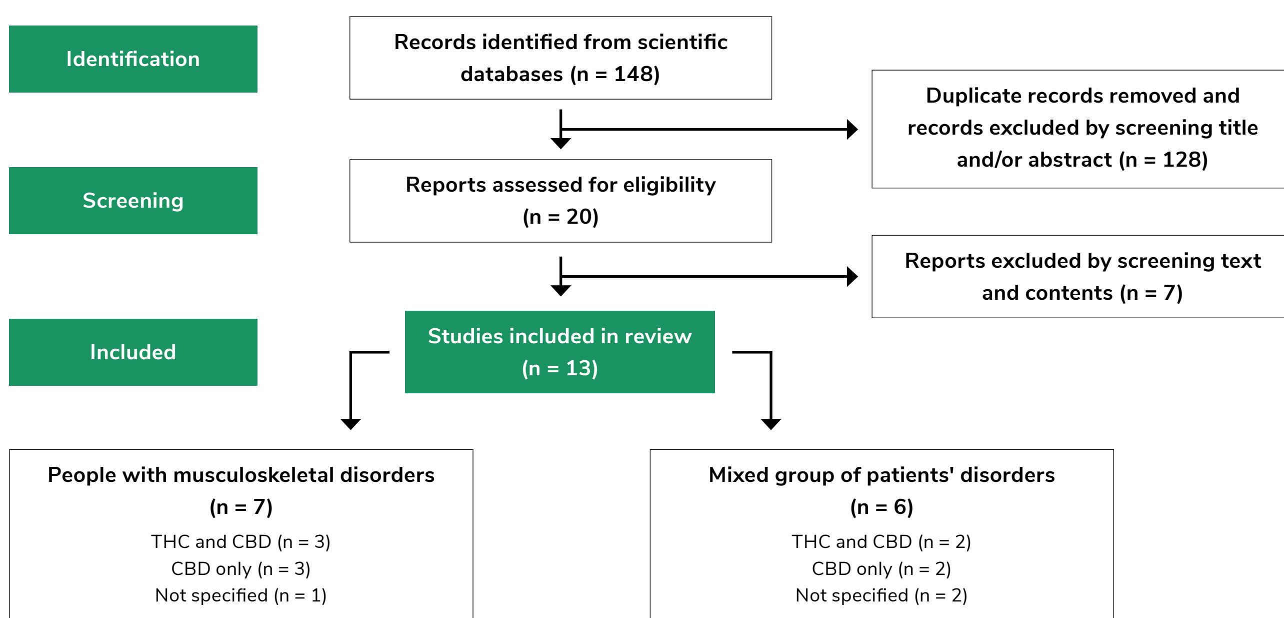

Figure 1. Study flow chart.

Table 1. A detailed description of each study qualified in this review.

Reference	Level of evidence	Sample size	Main condition	Type and/or form of cannabis	Length of the study	Pain efficacy conclusion	Other effects
Heineman et al. 2022 [28]	I	18	OA thumb basal joint pain	Transdermal CBD cream	3 weeks	Beneficial (+)	physical function (+) no adverse effects recorded
Nitecka--Buchta et al. 2019 [29]	I	87	Temporomandibular disorder with myofascial pain	Transdermal CBD oil	14 days	Beneficial (+)	physical function (+) myorelaxant (+) no adverse effects recorded
Hunter et al. 2018 [30]	I	320	OA knee pain	Transdermal synthetic CBD gel	12 weeks	Beneficial (+)	physical function (+) application site dryness (-) headache (-)
Capano et al. 2020 [31]	II	97	Chronic pain	Oral CBD capsules	2 months	Beneficial (+)	reduced opioid use (+) sleep quality (+) drowsiness (-) dry mouth (-) nausea (-)
Vigil et al. 2017 [32]	II	37	Chronic back pain	All forms of THC and CBD products sold in state-authorized medical cannabis dispensaries	21 months	Beneficial (+)	quality of life (+) reduced opioid use (+) activity levels and social life (+) concentration (+) no adverse effects recorded
Bawa et al. 2024 [33]	III	15	OA hand pain	Transdermal synthetic CBD gel	4 weeks	Beneficial (+)	physical function (+) anxiety (+) headache (-) sleep quality (-) allergy (-)
Haroutounian et al. 2016 [34]	IV	206	Chronic back pain and musculoskeletal widespread pain	Vaporized and smoked cannabis Edibles and oils	7 months	Beneficial (+)	physical function (+) reduced opioid use (+) sedation (-) heaviness (-) nervousness and difficulty to concentrate (-) elevated liver transaminases (-)

O'Brien et al. 2023 [35]	V	55	Chronic pain	CBD/THC oils THC only oils THC flower vaporized	3 months	Beneficial (+)	physical function (+) quality of life (+) general health (+) mood/depres-sion and sleep (+) dry eyes (-)
Poisblaud et al. 2023 [26]	V	27	Chronic musculoskeletal pain	Vaporized and smoked cannabis Edibles	Single interview	Beneficial (+)	physical function (+) quality of life (+) cough after smoking (-) anxiety (-) too short-effect on pain (-)
Mangual--Pérez et al. 2022 [36]	V	184	Musculoskeletal pain and related musculoskeletal disorders with muscle spasms	Vaporized cannabis Edibles Topical gels and lotions	2 months	Beneficial (+)	reduced opioid use (+)
Holt et al. 2024 [37]	V	5391	Chronic musculoskeletal pain	THC THC/CBD CBD/ route of administration not specified/	Medical records from 2018 to 2021	Beneficial (+)	arrhythmia (-) most pronoun-ced in the 180 days following the initiation of treatment
Sakafish et al. 2020 [38]	V	751	Chronic musculoskeletal pain	THC and/or CBD dry flower or oil	12 months	Beneficial (+)	physical function (+) quality of life (+) reduced opioid use (+) dry mouth (-) increased appetite (-) drowsiness (-) impaired memory (-)
Bellnier et al. 2018 [39]	V	29	Chronic non-cancer pain	Oral THC/CBD capsules Vaporized THC	3 months	Beneficial (+)	quality of life (+) reduced opioid use (+) cost savings (+) dry mouth (-) dizziness (-) increased appetite (-)

Notes: **Level I (randomized controlled trial), Level II (cohort study), Level III (case control study and single-centre study), Level IV (case series/case report), Level V (opinion/survey/qualitative study).*

Abbreviations: *(+) – beneficial effect, (-) – non-beneficial or adverse effect; CBD – cannabidiol; HRQoL – health-related quality of life; OA – osteoarthritis; THC – tetrahydrocannabinol.*

Quality assessment

Based on the PEDro scale assessment, 10 trials were deemed low quality, while three trials were classified as high quality (**Table 2**). Overall, the average PEDro score across the included trials was low.

Table 2a. PEDro scores for qualified studies in this review.

Author / PEDro Scale Item	Bawa et al. 2024 [33]	Bellnier et al. 2018 [39]	Capano et al. 2020 [31]	Haroutounian et al. 2016 [34]	Heineman et al. 20222 [28]	Holt et al. 2024 [37]
Eligibility criteria	YES	YES	YES	YES	YES	YES
Random of allocation	NO	NO	NO	NO	YES	NO
Concealed allocation	NO	NO	NO	NO	YES	NO
Group similarity at baseline	NO	NO	NO	NO	YES	YES
Blinding of all subjects	NO	NO	NO	NO	YES	NO
Blinding of all therapists	NO	NO	NO	NO	YES	NO
Blinding of all assessors	NO	NO	NO	NO	NO	NO
Measures of at least one key outcome from more than 85% of the subjects	YES	YES	YES	YES	YES	YES
Treatment or control condition as allocated or ITT analysis	YES	NO	NO	YES	YES	NO
Between group statistical comparisons	NO	YES	YES	NO	YES	NO
Total score*	**3**	**3**	**3**	**3**	**9**	**3**

Notes: **3 to 4 points = low quality; 5 to 7 points = medium quality; 8 to 9 points = high quality.*

Table 2b. PEDro scores for qualified studies in this review.

AUTHOR / PEDro Scale Item	Hunter et al. 2018 [30]	Mangual-Pérez et al. 2022 [36]	Nitecka-Buchta et al. 2019 [29]	O'Brien et al. 2023 [35]	Poisblaud et al. 2023 [26]	Sakafish et al. 2020 [38]	Vigil et al. 2017 [32]
Eligibility criteria	YES	YES	YES	YES	YES	YES	YES
Random of allocation	YES	NO	YES	NO	NO	NO	NO
Concealed allocation	YES	NO	YES	NO	NO	NO	NO
Group similarity at baseline	YES	YES	YES	NO	NO	NO	YES
Blinding of all subjects	YES	NO	YES	NO	NO	NO	NO
Blinding of all therapists	NO	NO	YES	NO	NO	NO	NO
Blinding of all assessors	NO	NO	YES	NO	NO	NO	NO
Measures of at least one key outcome from more than 85% of the subjects	YES	YES	YES	YES	YES	YES	YES
Treatment or control condition as allocated or ITT analysis	YES	NO	YES	NO	NO	NO	NO
Between group statistical comparisons	YES	YES	YES	YES	YES	YES	YES
Total score*	**8**	**4**	**10**	**3**	**3**	**3**	**4**

Notes: ** 3 to 4 points = low quality; 5 to 7 points = medium quality; 8 to 9 points = high quality.*

Discussion

Although the evolutionary basis of the endocannabinoid system is well-documented, reliable information regarding this system is scarce in most Polish medical textbooks [40]. While cannabinoids are being approved for pain management worldwide, controversies and uncertainties persist regarding their benefits and risks [41]. A lack of robust scientific research [42] and limited knowledge on the clinical use of medical cannabis contribute to confusion, fear, and misunderstanding among both patients and healthcare professionals [10].

Adopting a biopsychosocial-spiritual model of pain has enabled many healthcare providers, particularly in North America, to acknowledge the consequences of inadequately treated pain as well as the dangers associated with excessive opioid use [7, 10]. In response, efforts have been undertaken to educate patients, alleviate their pain, and improve overall quality of life through the development of novel, safe, and targeted cannabinoid formulations [5].

In Poland, however, the medical community often does not recognize cannabis as a legitimate therapeutic agent. Contributing factors may include non-standardized products, misinformation, and low-quality studies. Simultaneously, numerous cannabinoid-based products—often not scientifically tested and lacking proven efficacy—are readily available. These include products labeled as CBD, or CBD with small amounts of THC (usually <0.3%), marketed as edibles, dietary supplements, hemp oils, dried flowers, and cosmetic additives. Such unregulated products may present serious health hazards [43].

Cannabidiol (CBD), frequently sold as oils, creams, and gels, is commonly marketed as an alternative or adjunct for managing chronic musculoskeletal pain. This marketing can create the false impression that CBD is entirely devoid of significant side effects and safe for unrestricted use [40]. In one survey of 100 cannabis users in San Francisco with chronic osteoarthritis, participants perceived medical marijuana as more effective and causing fewer severe side effects than other treatments. However, inconsistencies in reporting potential adverse effects led the authors to conclude that cannabis users may be unaware of certain side effects, underscoring the need for more rigorous monitoring [20].

Physical therapists may play a crucial role in integrating emerging research findings and patient education on the safety and utility of medical cannabis for musculoskeletal pain management. Given the growing popularity of cannabis-based medicines in Poland and the increasing volume of scientific evidence supporting their beneficial pharmacological effects in musculoskeletal disorders, greater emphasis on educating healthcare personnel and patients is warranted to ensure the most effective and safest possible therapy [44].

This review provides detailed evidence regarding the use of medical cannabis in treating musculoskeletal pain. Cannabis use has demonstrated positive effects in pain reduction, improved patient well-being, and potentially enhanced quality of life. These improvements were observed in adult orthopedic patients who used medical cannabis and cannabinoids as an alternative or adjunct to opioids for various pain conditions. Notably, adverse effects were generally mild and well-tolerated. Similar findings have been reported for CBD-only formulations [45] and other cannabis variants, including in older adult populations [14, 46-48].

Overall, the evidence suggests that medical cannabis may represent a promising therapeutic option for individuals suffering from musculoskeletal pain, contributing to substantial improvements in quality of life and well-being. Such benefits are particularly salient given the risk of addiction and complications related to long-term opioid use.

Study limitations

One of the primary limitations of this review was the lack of blinding among the working group. Many of the included studies were of low-quality evidence, limited by small sample sizes and the absence of extended follow-up periods. Moreover, the diverse routes of cannabinoid administration and varying formulations made direct comparisons challenging. Without statistical analysis, the findings of this review should be considered primarily informative rather than conclusive.

Conclusions

Early clinical evidence indicates that medical cannabis can effectively reduce musculoskeletal pain, with most findings pertaining to patients with osteoarthritis and back pain. Nevertheless, these studies often lack robust methodological quality and involve small patient cohorts. Future research should focus on identifying effective and safe dosage regimens, optimizing administration routes, and conducting more rigorous, high-quality studies to clarify the benefits and potential risks of medical cannabis therapy for musculoskeletal pain disorders.

Declarations

Ethical Considerations: Ethical considerations are not required for this manuscript due to its review nature. This paper is based on a review of existing literature and does not involve new research on human or animal subjects; therefore, ethical approval is not applicable in light of the COPE (Committee on Publication Ethics) guidelines.

Clinical Trials: This study was not registered as a clinical trial as it did not involve investigational products or interventions that would classify it under clinical trial regulations.

Conflict of Interest: The authors declare no conflict of interest. The study was conducted independently and without any influence from external organizations or entities.

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