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Review Article

Role of Cannabinoids in Chronic Pain Management: A Pharmacological Review

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Abstract:
Chronic pain is a multifactorial condition with significant physical, emotional, and socioeconomic burdens. Conventional analgesics, including opioids and non-steroidal anti-inflammatory drugs (NSAIDs), often fail to provide sustained relief and are associated with adverse effects, including tolerance, dependence, and gastrointestinal complications. In recent years, cannabinoids—bioactive compounds derived from the Cannabis sativa plant—have emerged as promising alternatives or adjuncts in chronic pain management due to their interaction with the endocannabinoid system (ECS). This system, which plays a crucial role in modulating pain perception, is influenced by both Phyto cannabinoids and synthetic cannabinoids, particularly Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD). This pharmacological review explores the mechanisms through which cannabinoids modulate pain, their pharmacokinetics and pharmacodynamics, clinical efficacy in various chronic pain conditions (neuropathic, inflammatory, cancer-related), and safety profiles. It also examines the legal and regulatory challenges associated with medical cannabis, especially within the Indian context. The report highlights the limitations in existing clinical trials, emphasizing the need for more extensive and standardized studies to support evidence-based use. Moreover, advances in cannabinoid formulation and delivery systems are discussed as they aim to enhance bioavailability and therapeutic outcomes.
The review concludes that while cannabinoids show significant potential in chronic pain management, their clinical application requires a nuanced understanding of their pharmacology, patient variability, and a robust regulatory framework. A multidisciplinary approach incorporating personalized medicine may pave the way for their integration into mainstream pain management strategies.
Keywords: Cannabinoids, Chronic Pain, Endocannabinoid System, Δ9-THC, CBD, Neuropathic Pain, Medical Cannabis, Pharmacological Review, Pain Management, Analgesics.

Chapter 1: Introduction

1.1 Background

Chronic pain affects over 20% of the global population and is recognized as a disease in itself by many health authorities. It not only impairs quality of life but also places a heavy burden on healthcare systems. Traditional pharmacological treatments—such as non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and antidepressants—have limitations, including side effects, tolerance, dependency, and inadequate relief in certain patient populations. As a result, there has been a growing interest in alternative therapeutic strategies, including cannabinoids, for managing persistent pain conditions [1].

Cannabinoids are compounds that act on cannabinoid receptors (CB1 and CB2) in the body and are either derived from the Cannabis sativa plant (Phyto cannabinoids), synthesized chemically (synthetic cannabinoids), or produced endogenously (endocannabinoids). Among them, the most studied are Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD). The therapeutic potential of cannabinoids has been explored in several domains, including neurology, oncology, and pain medicine, with accumulating evidence supporting their use in chronic pain management [2].

1.2 Understanding Chronic Pain

Chronic pain is defined as pain that persists beyond normal tissue healing time, typically lasting more than three to six months. It can result from a variety of etiologies such as injury, infection, inflammation, nerve damage, or underlying diseases like cancer or arthritis. The pain may be classified into three broad categories:

- Nociceptive pain, caused by tissue damage or inflammation.
- Neuropathic pain, arising from nerve injury or dysfunction.
- Mixed pain, which contains elements of both.

Managing chronic pain is complex due to individual variations in perception, psychological status, and response to therapy. Conventional analgesics are often inadequate or result in unwanted adverse effects [3].

1.3 The Endocannabinoid System (ECS) in Pain Regulation

The ECS is a biological system involved in regulating a variety of physiological processes, including mood, appetite, immune response, and pain sensation. It comprises:

- Endocannabinoids (e.g., anandamide and 2-arachidonoylglycerol)
- Cannabinoid receptors (CB1 primarily in the central nervous system and CB2 mainly in peripheral tissues and immune cells)
- Enzymes that synthesize and degrade endocannabinoids

When cannabinoids bind to CB1 receptors in the brain and spinal cord, they inhibit the release of neurotransmitters such as glutamate and substance P, which are associated with pain transmission. CB2 receptor activation reduces inflammation by modulating immune cell activity. These mechanisms form the pharmacological basis of cannabinoid-induced analgesia [4].

1.4 Phyto cannabinoids and Synthetic Cannabinoids

- Phyto cannabinoids: THC and CBD are the most prominent. THC is psychoactive and is primarily responsible for the "high" associated with cannabis, while CBD is non-psychoactive and has anti-inflammatory and analgesic properties.
- Synthetic cannabinoids: These are lab-made compounds that mimic the action of naturally occurring cannabinoids and have been developed to achieve more predictable pharmacokinetic profiles. Examples include nabilone and dronabinol, which are approved in several countries for chemotherapy-induced nausea and pain management [5].

1.5 Rationale for Using Cannabinoids in Chronic Pain

Several factors justify exploring cannabinoids in chronic pain management:

- Novel mechanism of action: Cannabinoids target the ECS, which is distinct from the opioid or NSAID pathways, offering a new avenue for analgesia.
- Multimodal benefits: In addition to pain relief, cannabinoids may reduce anxiety, improve sleep, and attenuate muscle spasticity—symptoms commonly associated with chronic pain syndromes.
- Opioid-sparing effects: Studies suggest that cannabinoids may reduce opioid requirements in some patients, potentially lowering the risk of dependency and overdose [6].

1.6 Historical Perspective and Traditional Use

Cannabis has been used for medicinal purposes for thousands of years. Ancient Ayurvedic texts from India mention its use for pain, sleep, and digestive problems. In the 19th and early 20th centuries, cannabis-based tinctures were commonly prescribed in Western medicine. However, due to regulatory changes and concerns about misuse, its use declined until recent decades saw a resurgence in interest fuelled by scientific validation [7].

1.7 Regulatory Landscape and Legal Challenges

The legal status of medical cannabis varies globally. While countries like Canada, Germany, and Israel have established frameworks for medical cannabis use, others maintain strict prohibitions. In India, cannabis is classified as a narcotic under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985. However, recent advocacy and scientific findings have prompted regulatory agencies to explore legal frameworks for research and clinical applications [8].

1.8 Challenges in Clinical Translation

Despite encouraging preclinical data, the clinical use of cannabinoids is fraught with challenges:

- Variability in formulation and dosing
- Limited high-quality randomized clinical trials
- Potential for psychoactive effects and dependence
- Stigma associated with cannabis use

Healthcare professionals often lack training in cannabinoid pharmacology, and regulatory hurdles further complicate prescribing and monitoring [9].

1.9 Current Trends and Innovations

Recent advancements in cannabinoid research include:

- Nano formulations to improve bioavailability
- Transdermal patches and or mucosal sprays for targeted delivery
- Combination therapies with opioids or antidepressants for synergistic effects

These innovations aim to enhance the safety and efficacy profile of cannabinoids in chronic pain management [10].

1.10 Scope and Objectives of the Report

This project aims to present a comprehensive pharmacological review of cannabinoids in chronic pain management. The objectives include:

- Reviewing the pharmacodynamics and pharmacokinetics of cannabinoids
- Evaluating clinical evidence for their efficacy and safety in chronic pain conditions
- Discussing regulatory challenges and policy implications, particularly in India
- Recommending future directions for research and clinical use

Fig 1. Cannabis leaf

Chapter 2: Pharmacological Profile of Cannabinoids

2.1 Introduction

Understanding the pharmacological properties of cannabinoids is essential for optimizing their clinical use in chronic pain management. This chapter explores the molecular mechanisms, receptor pharmacology, pharmacokinetics, metabolism, and therapeutic potential of major cannabinoids, primarily Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD). It also discusses drug interactions, delivery systems, and formulation advancements aimed at maximizing efficacy while minimizing adverse effects.

2.2 Classification of Cannabinoids

Cannabinoids are classified into three major categories:

- Phyto cannabinoids: Naturally occurring compounds in Cannabis sativa, such as THC, CBD, cannabigerol (CBG), and cannabinol (CBN).
- Endocannabinoids: Endogenously produced compounds like anandamide (AEA) and 2-arachidonoylglycerol (2-AG).
- Synthetic Cannabinoids: Laboratory-synthesized analogs such as nabilone, HU-210, and WIN 55,212-2.

THC is the principal psychoactive component, while CBD is non-psychoactive and exhibits a wide therapeutic index. Their pharmacological behavior is governed by their interaction with the endocannabinoid system (ECS), particularly CB1 and CB2 receptors [23].

2.3 Endocannabinoid System (ECS) and Pain Modulation

The ECS consists of:

- Cannabinoid Receptors: CB1 and CB2
- Endogenous Ligands: AEA and 2-AG
- Metabolic Enzymes: Fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL)

CB1 receptors are abundant in the brain, spinal cord, and peripheral nerves, where they inhibit neurotransmitter release, thereby dampening nociceptive signalling. CB2 receptors are primarily located in immune cells and modulate inflammatory responses, making them particularly relevant in inflammatory and cancer-related pain [24].

CBD has low affinity for CB1/CB2 but indirectly influences ECS by inhibiting FAAH, enhancing anandamide availability, and modulating TRPV1, 5-HT1A, and PPARγ receptors—all of which contribute to its analgesic and anti-inflammatory properties [25].

2.4 Pharmacodynamics of THC and CBD

- THC: Acts as a partial agonist at CB1 and CB2 receptors. It reduces neurotransmitter release (e.g., glutamate, GABA), modulates pain thresholds, and produces psychoactive effects.
- CBD: Exhibits multiple mechanisms including modulation of ion channels, serotonin receptors, and enzyme inhibition. It may counteract THC's psychoactive effects and provides anti-inflammatory, anxiolytic, and anticonvulsant actions [26].

Studies show that the synergistic effect of THC and CBD (the "entourage effect") enhances therapeutic efficacy while minimizing adverse effects, making combination therapies (e.g., nabiximols) more clinically viable [27].

2.5 Pharmacokinetics

The pharmacokinetics of cannabinoids varies significantly based on the route of administration, formulation, and patient-specific factors.

2.5.1 Absorption

- Inhalation (smoking/vaporizing): Rapid absorption; peak plasma concentrations reached within minutes.
- Oral ingestion: Slower onset (30–90 minutes); affected by first-pass metabolism in the liver.
- Sublingual/buccal: Bypasses first-pass effect; provides intermediate onset and duration.

2.5.2 Distribution

Cannabinoids are lipophilic and rapidly distributed to highly perfused tissues (brain, liver, adipose tissue). THC binds extensively to plasma proteins (~97–99%) and accumulates in fat tissue, resulting in prolonged effects [28].

2.5.3 Metabolism

Cannabinoids undergo extensive hepatic metabolism:

- THC: Metabolized by CYP2C9 and CYP3A4 to 11-OH-THC (active) and then to inactive THC-COOH.
- CBD: Metabolized primarily by CYP3A4 and CYP2C19 into hydroxylated metabolites.

Both compounds are subject to drug–drug interactions due to their influence on cytochrome P450 enzymes [29].

2.5.4 Elimination

Cannabinoids are excreted via feces (major) and urine (minor). THC can be detected in the body for days to weeks due to its storage in fat and slow release into the bloodstream [30].

2.6 Drug Interactions and Contraindications

- Opioids: Cannabinoids may enhance analgesic effects and reduce opioid requirements, but combined CNS depression is a concern.
- Antidepressants and antiepileptics: CYP450-mediated interactions may occur.
- Warfarin: CBD may increase INR by inhibiting CYP2C9, requiring dose adjustments.

Cannabinoids are contraindicated in individuals with psychiatric disorders (e.g., schizophrenia), unstable cardiovascular conditions, or a history of substance abuse [31].

2.7 Tolerance, Dependence, and Safety

Tolerance to THC may develop with chronic use, especially at high doses. However, dependence is less severe compared to opioids. Withdrawal symptoms are generally mild and include irritability, sleep disturbances, and appetite changes [32].

CBD has a favourable safety profile, with rare instances of hepatic enzyme elevation and gastrointestinal discomfort. The World Health Organization (WHO) has classified CBD as generally well-tolerated with no risk of abuse or dependence [33].

2.8 Formulations and Delivery Systems

Modern pharmaceutical technology has enabled the development of standardized and patient-friendly cannabinoid formulations:

- Oral capsules/tablets: Standardized dosing, e.g., nabilone.
- Oro mucosal sprays: Nabiximols (Sativex) – enables rapid absorption and dose titration.
- Transdermal patches: Provide sustained release with minimal systemic side effects.
- Nano formulations: Enhance solubility and bioavailability (e.g., CBD nanoparticles) [34].

Innovative delivery systems are being developed to address limitations like poor oral bioavailability and variable absorption.

2.9 Therapeutic Window and Dosing Strategies

Cannabinoids exhibit a narrow therapeutic window, particularly THC. Initiating treatment with low doses and gradual titration (the "start low, go slow" approach) is widely recommended. For example:

- THC: Start at 1–2.5 mg/day
- CBD: 5–10 mg/day, titrated based on response and tolerance

Combination products typically contain a 1:1 or 1:2 THC:CBD ratio, optimized for efficacy with minimal psychotropic effects [35].

2.10 Personalized Medicine and Pharmacogenomics

Genetic polymorphisms in CYP450 enzymes (e.g., CYP2C9*3) and cannabinoid receptors (CNR1, CNR2) influence individual responses to cannabinoids. Pharmacogenomic profiling may soon guide cannabinoid selection and dosing in chronic pain management.

Ongoing research is exploring biomarkers to predict therapeutic response, minimizing trial-and-error approaches in cannabinoid prescribing [36].

Chapter 3: Clinical Challenges and Recommendations

3.1 Introduction

Despite mounting scientific evidence supporting the use of cannabinoids in chronic pain, widespread clinical integration remains limited. Challenges range from regulatory ambiguity and

lack of prescriber education to variability in product quality and ethical dilemmas. This chapter critically examines these barriers and provides practical, policy, and clinical recommendations to facilitate evidence-based use of cannabinoids in chronic pain management, especially in the Indian context.

3.2 Regulatory and Legal Barriers

3.2.1 Global Legal Disparities

The legal status of medical cannabis varies globally. While countries like Canada, Germany, and Israel have well-regulated frameworks for cannabinoid-based therapeutics, others continue to classify cannabis as a controlled substance. This legal fragmentation hinders cross-border research collaborations, consistent prescribing guidelines, and international standardization [37].

3.2.2 Indian Legal Framework

In India, cannabis is regulated under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985, which prohibits cultivation, possession, and use of cannabis resin and flowers but permits the use of leaves and seeds for medicinal purposes. The Ministry of AYUSH has acknowledged the therapeutic potential of cannabis, particularly in Ayurvedic formulations. However, there is a lack of clarity on prescription-based usage and limited scope for RCTs due to regulatory bottlenecks [38].

Recommendation: A clear regulatory framework for medical cannabis use in India is essential, including licensing for cultivation, clinical trials, and pharmacy-based dispensation.

3.3 Lack of Clinical Guidelines and Standardized Protocols

There is an absence of universally accepted treatment protocols for prescribing cannabinoids in chronic pain. Most clinicians rely on trial-and-error dosing due to inadequate clinical trial data and lack of experience.

Several expert panels, including the International Association for the Study of Pain (IASP), have hesitated to endorse cannabinoids due to variability in outcomes and concerns about long-term safety [39].

Recommendation: National pain societies and pharmacological bodies should develop India-specific clinical guidelines incorporating dose titration protocols, monitoring tools, and adverse effect management.

3.4 Product Quality and Variability

Cannabinoid products vary widely in composition, potency, and purity, especially in unregulated markets. The lack of Good Manufacturing Practice (GMP) compliance in some preparations leads to contamination with heavy metals, pesticides, or solvents.

A study by Bonn-Miller et al. (2017) showed that only 31% of commercially available CBD products in the US were accurately labeled regarding cannabinoid concentration [40].

Recommendation: Implementation of mandatory quality control standards, including batch-wise cannabinoid profiling, stability testing, and safety certification by independent laboratories.

3.5 Adverse Effects and Psychoactive Concerns

While generally well-tolerated, cannabinoids—especially THC-rich formulations—can cause adverse effects such as:

- Cognitive impairment
- Anxiety or paranoia
- Sedation
- Psychosis (in predisposed individuals)

Long-term use may lead to Cannabis Use Disorder (CUD), particularly in adolescents and patients with psychiatric comorbidities [41].

Recommendation: Preference should be given to high-CBD, low-THC formulations. Patients must be screened for psychiatric illness, and risk–benefit analysis must guide therapy.

3.6 Inadequate Training Among Healthcare Providers

Most healthcare professionals receive little or no formal training in cannabinoid pharmacology. A survey conducted in the U.S. found that fewer than 10% of medical schools included cannabis education in their curriculum [42].

In India, allopathic practitioners are further constrained by the lack of official endorsement, while practitioners of AYUSH may have limited exposure to modern pharmacology.

Recommendation: Incorporate cannabinoid modules in medical, pharmacy, and nursing curricula. Conduct CME (Continuing Medical

Education) programs and certification workshops.

3.7 Ethical and Social Concerns

3.7.1 Stigma

Cannabinoids continue to be associated with recreational drug use and addiction, creating stigma among patients and practitioners alike. This often deters open dialogue, leading to underutilization of potentially beneficial therapy.

3.7.2 Vulnerable Populations

Ethical concerns arise when prescribing cannabinoids to elderly patients, adolescents, or those with mental illness. Balancing autonomy with non-maleficence remains a challenge.

Recommendation: Public health campaigns and community engagement are needed to shift the narrative toward medical utility. Clinical ethics committees should be involved in complex cases.

3.8 Research Limitations

3.8.1 Methodological Weaknesses

Many studies have small sample sizes, short durations, and lack standardization in cannabinoid formulations, making it difficult to draw robust conclusions.

3.8.2 Limited Indian Data

There is a dearth of Indian clinical trials despite the country's deep historical and cultural association with cannabis. Without local data, regulators and clinicians remain skeptical.

Recommendation: Government bodies like the Indian Council of Medical Research (ICMR) and CDSCO should prioritize funding for cannabinoid research. Multicenter RCTs on chronic pain conditions prevalent in India (e.g., cancer, arthritis, fibromyalgia) are urgently needed [43].

3.9 Reimbursement and Cost-Effectiveness

Most cannabinoid-based treatments are not covered under insurance schemes, leading to high out-of-pocket expenses. In a low-income setting like India, affordability becomes a significant barrier.

Recommendation: Cost-effectiveness analyses should be conducted to inform pricing policies. States with pilot programs can consider subsidizing cannabinoid therapy for eligible patients, especially those with refractory pain.

3.10 Drug Interactions and Monitoring

Due to hepatic metabolism via CYP450 enzymes, cannabinoids may interact with drugs like warfarin, clobazam, SSRIs, and antiepileptics. However, drug monitoring tools for cannabinoids are lacking in clinical practice.

Recommendation: Implement therapeutic drug monitoring (TDM) programs and develop clinical decision-support systems to guide safe polypharmacy.

3.11 Integration with Conventional Pain Management

Rather than replacing existing treatments, cannabinoids should be viewed as adjuvants. Their role lies in multimodal pain strategies that also include physical therapy, counseling, NSAIDs, antidepressants, and in some cases, opioids.

Recommendation: Develop integrated care models that allow for combination therapies, with regular outcome tracking to assess functional and psychological improvement.

3.12 Future Policy Recommendations

Policy Area	Recommendation
Legal Reforms	Amend NDPS Act to allow controlled clinical use
Research	Government-funded, multicentric Indian RCTs
Education	Introduce cannabinoid medicine in UG/PG programs
Safety	Implement GMP and mandatory quality checks
Clinical Tools	Develop treatment algorithms and monitoring protocols
Affordability	Include cannabinoid formulations in national drug list

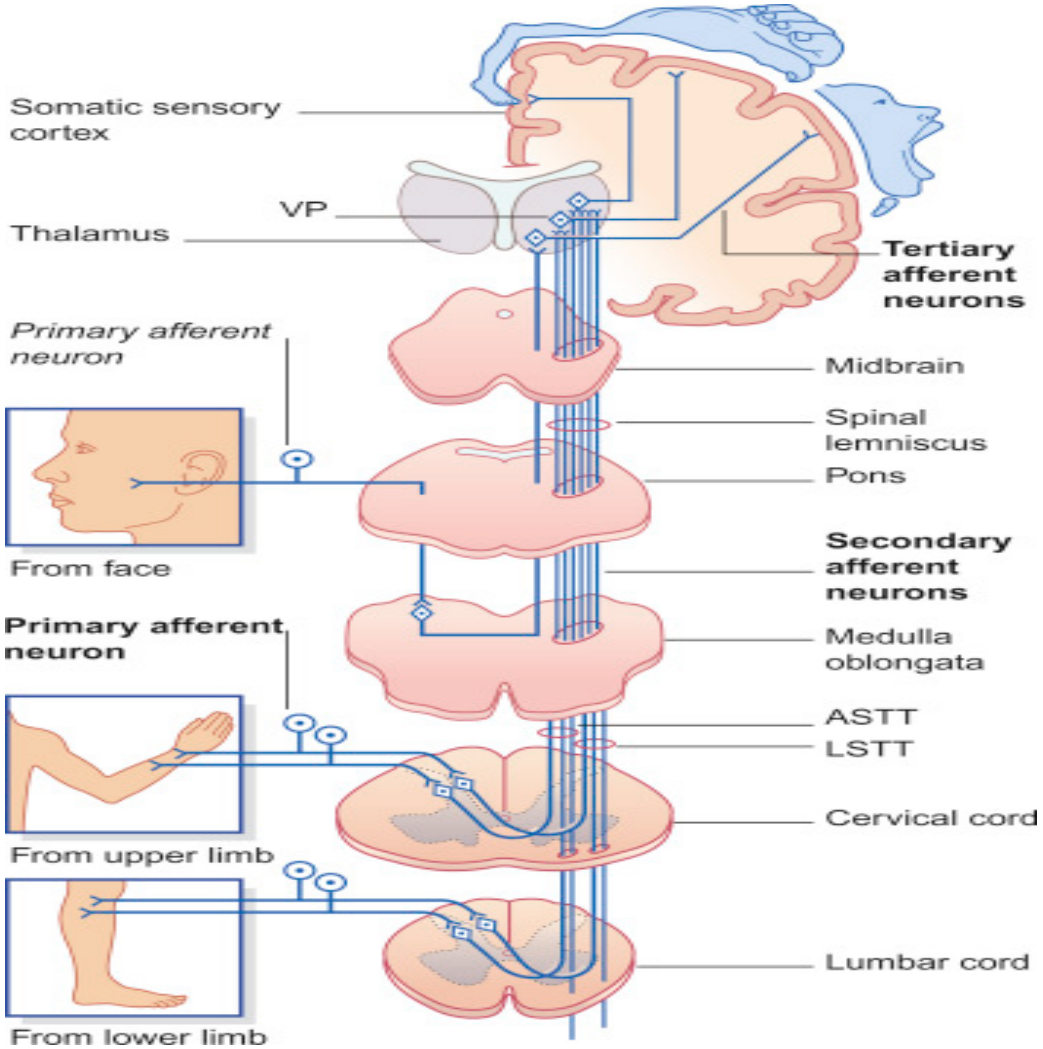

Fig 2. Pain Pathway

Chapter 4: Conclusion and Future Outlook

4.1 Introduction

Chronic pain remains a formidable challenge for healthcare providers and patients alike. Conventional analgesics such as opioids, NSAIDs, and antidepressants, although widely used, are often insufficient for long-term pain relief and carry considerable risks, including dependence, tolerance, and systemic side effects. Against this backdrop, cannabinoids have emerged as promising therapeutic agents, capable of addressing not only nociceptive but also neuropathic and inflammatory pain through a distinct mechanism involving the endocannabinoid system (ECS).

This chapter synthesizes the pharmacological, clinical, and regulatory aspects discussed in earlier chapters and outlines a forward-looking perspective for the safe and effective integration of cannabinoids into chronic pain management—especially within the Indian healthcare framework.

4.2 Key Findings

4.2.1 Cannabinoid Mechanisms and Pharmacology

Cannabinoids exert their analgesic effects through interaction with CB1 and CB2 receptors, modulation of neurotransmitter release, and influence over inflammatory mediators. While THC contributes to central pain inhibition, CBD offers anti-inflammatory and anxiolytic benefits without psychoactivity. Together, they create a balanced therapeutic effect known as the "entourage effect" [44].

Cannabinoids exhibit complex pharmacokinetics, including high lipophilicity,

first-pass hepatic metabolism, and variable bioavailability depending on the delivery route. Advances in nanoformulations and transdermal systems are addressing many of these limitations.

4.2.2 Clinical Evidence

A growing body of evidence supports the use of cannabinoids in various types of chronic pain, including:

- Neuropathic pain (e.g., HIV, multiple sclerosis)
- Cancer-related pain, particularly in opioid-tolerant patients
- Inflammatory and rheumatic conditions (e.g., arthritis)
- Fibromyalgia and central sensitivity syndromes

However, the evidence is often limited by small sample sizes, short follow-up periods, and heterogeneity in cannabinoid formulations and dosing strategies.

4.2.3 Safety and Tolerability

Cannabinoids are generally well tolerated when used responsibly. Common side effects include dizziness, dry mouth, and mild cognitive impairment. Serious adverse events are rare and usually associated with high doses of THC. CBD has a more favorable safety profile and is not associated with addiction or psychoactive effects [45].

Long-term use may result in tolerance and mild withdrawal symptoms but poses far less risk compared to opioid dependency.

4.2.4 Regulatory and Social Barriers

The legal status of cannabinoids remains a significant hurdle, especially in India where outdated drug policies have hindered research and access. Stigma associated with cannabis also deters patients and prescribers, despite its historical and Ayurvedic significance.

Educational gaps, lack of clinical guidelines, and unregulated product quality further impede clinical adoption. Insurance exclusion and cost-related issues continue to restrict access in low-income populations.

4.3 Future Outlook

4.3.1 Research and Evidence Generation

There is an urgent need for high-quality, large-scale randomized controlled trials (RCTs) to validate the efficacy and safety of cannabinoids in chronic pain, particularly within the Indian demographic context.

Key areas for future research:

- Comparative studies between THC, CBD, and combination therapies
- Long-term safety and dependency analysis
- Pharmacogenomic profiling for individualized therapy
- Real-world observational studies across diverse patient populations

Establishing robust research frameworks through national bodies such as ICMR, CSIR, and AYUSH will help generate India-specific evidence that can influence policy and clinical guidelines.

4.3.2 Integration into Mainstream Medicine

As the medical cannabis field matures, it is essential that cannabinoids are integrated into multimodal pain management approaches. These should include physiotherapy, behavioral therapy, NSAIDs, antidepressants, and, when necessary, low-dose opioids.

Creating clinical algorithms and care pathways will allow physicians to initiate, monitor, and discontinue cannabinoid therapy safely and effectively.

4.3.3 Regulatory Reform in India

India stands at a unique crossroads—armed with a rich tradition of cannabis use in Ayurvedic medicine and a modern pharmaceutical infrastructure. Reforming the NDPS Act, establishing GMP-compliant cannabis cultivation, and promoting licensed dispensaries and prescription-based access will be essential for unlocking the potential of medical cannabis.

4.3.4 Educational and Ethical Considerations

Developing educational modules for undergraduate and postgraduate healthcare training is imperative. Ethics committees and legal advisory boards must be involved in shaping responsible and equitable cannabinoid use, especially among vulnerable populations.

Creating public awareness campaigns to destigmatize medical cannabis is also a crucial step in transforming public perception.

4.3.5 Economic and Policy Implications

A well-regulated medical cannabis sector can:

- Reduce the economic burden of chronic pain
- Create employment and revenue through regulated cannabis industries
- Lower dependence on opioids, which are costlier and more dangerous
- Provide accessible care options to rural and underserved populations

Inclusion of cannabinoids in essential medicine lists, insurance coverage, and public health programs will enhance affordability and equity in pain care.

4.4 Conclusion

Cannabinoids offer a paradigm shift in chronic pain management. Their multifaceted pharmacology, efficacy in difficult-to-treat pain types, and relatively benign safety profile position them as valuable components in the pain management toolbox. Yet, several challenges must be addressed to realize their full potential—especially within India's socio-legal and healthcare context.

By embracing a multidisciplinary, evidence-based, and ethically grounded approach, cannabinoids can be safely and effectively incorporated into mainstream medicine. Regulatory reform, clinical education, and localized research are key to establishing cannabis-based therapeutics as both scientifically valid and socially acceptable options for managing chronic pain.

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