

Review Article

From relief to risks: a comprehensive review of medical cannabis

Nidhi Lokhande¹, Aditya Mokul¹, Namita Deshmukh², Avinash Borkar^{2*}, Suvarna Patil³

¹BKL Walawalkar Rural Medical College, Ratnagiri, Maharashtra, India

²Department of Community Medicine, Dr Rajendra Gode Medical College, Amravati, Maharashtra, India

³Department of General Medicine, BKL Walawalkar Rural Medical College, Ratnagiri, Maharashtra, India

Received: 10 March 2025

Revised: 21 May 2025

Accepted: 22 May 2025

*Correspondence:

Dr. Avinash Borkar,

E-mail: avigod.7@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Cannabis has been used for medicinal purposes for thousands of years, with a resurgence in modern medical applications sparking significant research and regulatory discussions. This review explores the medical benefits, risks, mechanisms of action, and legal considerations of cannabis use. Cannabis-based treatments have shown efficacy in managing multiple conditions, including chronic pain, multiple sclerosis, psychiatric disorders, chemotherapy-induced nausea, epilepsy, and neurodegenerative diseases. Despite its therapeutic potential, cannabis use carries short- and long-term risks, including cognitive impairment, cardiovascular issues, dependency, and adverse mental health effects. The variability in cannabis products, dosing, and regulation raises concerns regarding safety and quality control. Additionally, ethical dilemmas exist in prescribing unstandardized cannabis-based therapies. Legalization trends across various regions continue to shape the accessibility and acceptance of medical cannabis, though significant research gaps remain. Future studies are required to further validate its efficacy, optimize dosing strategies, and mitigate potential health risks. This review provides a comprehensive overview of current evidence, highlighting both the promise and challenges associated with medical cannabis.

Keywords: Clinical research, Health risks, Medical cannabis, Regulation and legalization, Therapeutic benefits

INTRODUCTION

Cannabis has been used in medicine for thousands of years, but its modern resurgence in medical applications has been met with significant research interests and regulatory debates. Proponents of medical cannabis support its use for a highly varied range of medical conditions, most notably in the field of pain management and multiple sclerosis.¹

The current findings from the population based surveys in Canada and the US add to the evidence that cannabis use is more prevalent and frequent among those who experience mental health conditions.² Cannabis is a complex plant with over 400 chemical entities of which more than 60 of them are Cannabinoid compounds, some of them with opposing effects; these are delta-

9-tetrahydrocannabinol, Cannabidiol, tetrahydrocannabinol, endocannabinoids, cannabis, etc.³ Cannabis has been used recreationally for millennia and is the third most commonly used drug after tobacco and alcohol.⁴ There is one direct source of evidence (delta6-tetrahydrocannabinol (delta 6-THC) in ashes) that cannabis was first used medicinally around 400 AD. In the U.S., cannabis was widely utilized as a patent medicine during the 19th and early 20th centuries, described in the United States Pharmacopoeia for the first time in 1850.⁵

The use of cannabis has been reported in India for at least a few thousand years; however, it was only in the 1800 that cannabis cultivation and use expanded rapidly in India and worldwide as nonpsychoactive hemp emerged as a valuable cash crop and thus the British rulers of India

commissioned the mass cultivation of cannabis, which subsequently increased the rates of cannabis use as well.⁶ In 1996, California became the first state to permit legal access to and use of botanical cannabis for medical purposes under physician supervision with the enactment of the compassionate use act.⁵

This review article summarizes the benefits and risks of cannabis use in medicine with a comprehensive format gathering important aspects and evidences of randomized control trials (RCTs). It also includes short term as well as long term side effects along with safety and quality check. It also mentions legal and ethical considerations of medical cannabis.

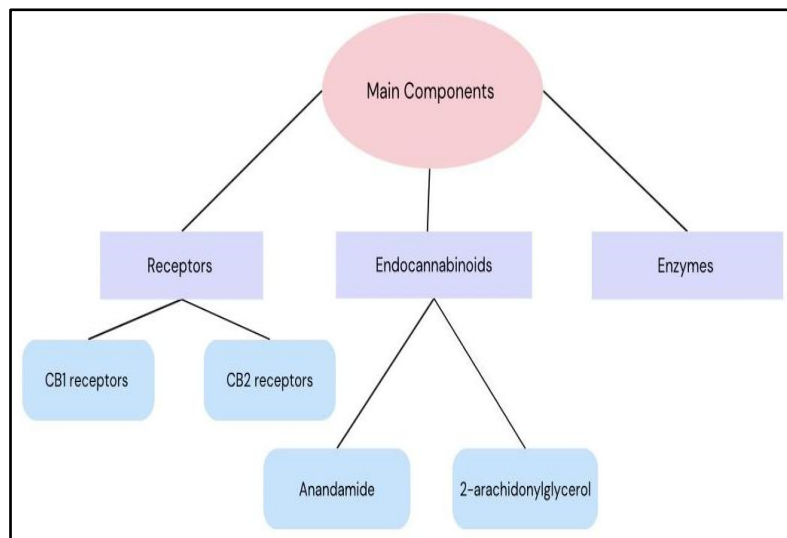


Figure 1: Components of endocannabinoids system.

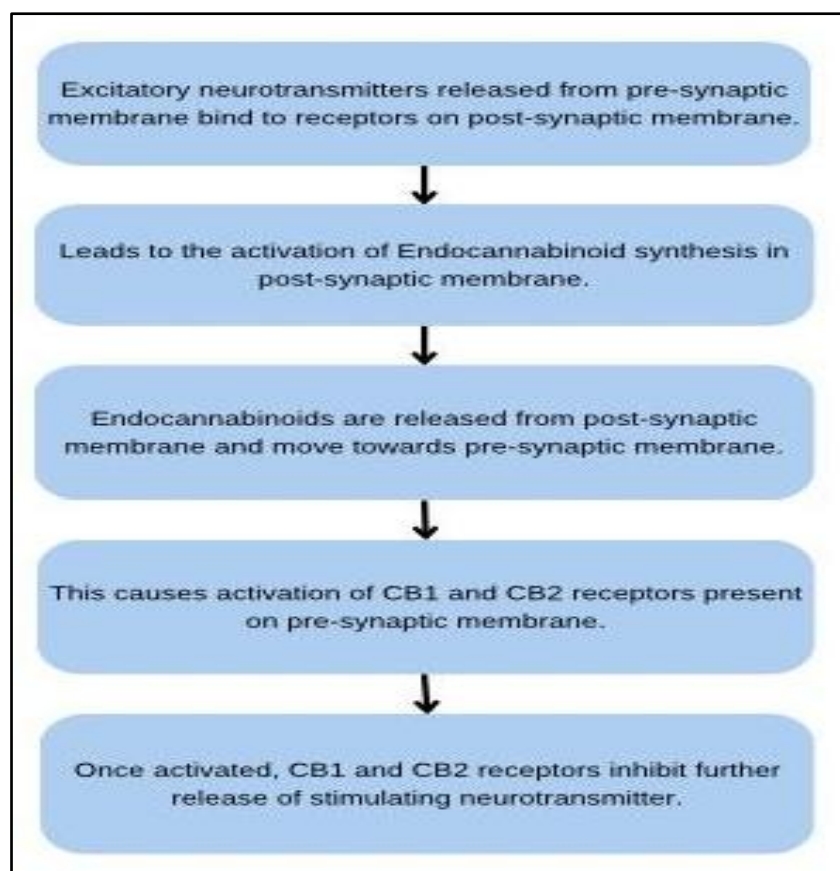


Figure 2: Mechanism of action of endocannabinoid system in response to an excitatory neurotransmitter in the neuronal synapse.

Table 1: Medical uses of cannabis.

S. no.	Medical condition	Medical uses	Active forms	Benefit over other drugs
1.	Multiple sclerosis	Reduces chronic pain, Reduces muscle spasticity	Nabiximols (17RCTs)	FDA approved for chronic pain ^{9,10,11,12}
2.	Psychiatric disorders	Reduces anxiety, depression, post-traumatic stress disorders, Psychosis, ADHD	CBD (83 RCTs)	Exclusively used for psychiatric disorders. Better outcome. ^{10,11,13}
3.	Chemotherapy induced- Nausea and Vomiting	reduce symptoms of nausea and vomiting, Placebo	Dronabinol, Nabilone THC (23 RCTs)	In patients who fail to respond with antiemetics. FDA approved. ^{10,14}
4.	Spinal Cord Injury	Reduces muscle spasticity	Nabiximols, Oral THC	FDA approved ^{10,12}
5.	Peripheral Neuropathy	Reduces chronic pain	THC (17 RCTs)	Better than amitriptyline. ^{10,15}
6.	Oncology	Cancer regulation process, antitumor effect, cancer associated anorexia, cachexia syndrome	Dronabinol, THC (60 associations)	Megestrol acetate is superior to dronabinol. ^{10,14}
7.	Irritable Bowel Syndrome	Anti-inflammatory, regulate bowel movements and reduce diarrhoea and constipation, improved appetite	Dronabinol (1 RCT)	lesser side-effects than antispasmodics, anti-depressant and laxatives commonly used ^{10,16}
8.	Parkinson's disease	Symptomatic relief especially dyskinesia	THC, Nabilone (2 RCTs)	Decreases adverse effects of Levodopa ^{10,17}
9.	Epilepsy	Prevent seizures	THC, CBD (4 RCTs)	In addition, with other anti-epileptics. FDA approved. In drug resistant epilepsy like Dravet syndrome and Lennax Gastot syndrome it reduces frequency and severity of seizures. ^{10,18}
10.	Alzheimer's disease	Neuroprotective effects as well as in vascular dementia	Dronabinol THC (2 RCTs) CBD	Use of THC and CBD is more beneficial than individual drugs. Manage symptoms of anxiety, aggression, irritability with lesser sedation or cognitive impairment. ^{10,19}
11.	Amyotrophic lateral sclerosis	symptomatic relief from muscle spasticity, pain, cramping, slows the progression of the disease	Dronabinol (2 RCTs)	Continued. Lesser side-effects, Improved appetite ¹⁰
12.	Glaucoma	Reduces eye pressure	THC Cannabidiol (1 RCTs)	Effect lasts longer and has fewer side effects. ^{10,20}
13.	Huntingtons disease	Improves chorea, Placebo	Nabilone (2 RCTs)	Neuroprotective and lesser side-effects ¹⁰
14.	HIV/ AIDS	reduces anorexia, causes weight gain, Reduces anxiety, depression	Dronabinol (4 RCTs)	FDA approved. ^{10,21}

DISCUSSION

Mechanism of action

The discovery of its compounds has led to the further discovery of an important neurotransmitter system called the Endocannabinoid System. The main components of Endocannabinoid System are the receptors which are G protein coupled receptors (GPCRs), primarily coupling to inhibitory G proteins. CB1 receptors are exclusively found in brain (basal gangli, limbic system, hippocampus, cerebellum, astrocytes) but are also found in thyroid, uterus, testicular tissue, etc. CB2 receptors are found mostly in immune cells, GI system, peripheral nervous system, etc.^{3,8,9}

Risks and side effects

Cannabis use in medicine raises the possible risks and side effects as large doses can increase the risk of significant mental health issues especially psychosis.²² Cannabinoids can have a significant impact on cardiovascular system, respiratory system, nervous system especially in adolescents which could be a future threat. Side effects of Cannabinoids can be grouped into short term and long-term side effects.

Short term side effects

These primarily include intoxication and abuse of large doses of cannabis and early appearance of symptoms lasting for a few hours to weeks in all age groups.

Increased risk of motor-vehicle accidents.²²⁻²⁷ Coronary vasospasm.^{22,23,28} Cannabis Arteritis.^{22,23,28} Increased heart rate, Change in Blood Pressure.^{22,23,25,26} Myocardial Infarction.^{22,26,27} Stroke.^{26,29} Cognitive Impairment.^{5,23,25,26,29} Impairs verbal memory, attention and psychomotor function.^{5,23,26,29} Euphoria, disorientation, sleepiness, dizziness.^{25,29} Hallucinations or delusions.²⁵

Long term side effects

These specifically include symptoms that chronically develop by taking small to large doses over a long period of time usually for months to years in all age groups.

Chronicity of neurocognitive alterations especially in adolescents.^{23-25,29,30} Dependence.^{23-25,28,29} Chronic bronchitis or COPD, asthma, emphysema.^{22,25} Smoking cannabis causes increased risk of lung cancer.²³⁻²⁵ Increased risk of infections (immunosuppressants).²³ Increased risk of cardiovascular diseases.^{23-25,28}

Impact on mental health

Considerable effects have been noted on impacts on mental health as mentioned in the above table by the use of cannabis ranging from potential benefits to risks and dependence. Despite the constant rise of global prevalence rates, many of the current therapeutic options for mental illnesses are far from being ideal in terms of both efficacy and adverse effects.¹³ It can be used in many psychiatric disorders but also has side effects like impairment of memory, psychomotor function and neurocognitive alterations.²²⁻²⁴ It can also lead to intoxication, euphoria, hallucinations and thus should be cautiously evaluated in therapeutic settings.

Safety and quality concerns

The uncertainty surrounding safety and efficacy of exogenous cannabinoids is not a product of lack of research, but rather a product of extreme variability in study methodology and quality.²³ Also, there is insufficient high quality data regarding the efficacy, dose-dependent curve, drug interactions, expected adverse effects and safety of the commercial available medical cannabis products.³¹ When evaluating the safety profile of medicinal cannabis products, it is important to consider the relative THC and CBD content, as CBDs have an excellent safety profile; and thus Therapeutic Goods Administration (TGA) recently approved a legal pathway for low dose formulations to be provided over the counter as Schedule 3 pharmacist-only medications for conditions that do not require medical oversight.³²

Unlike conventional pharmaceuticals, cannabis products often lack consistency and standardization of doses. Additionally, evidence for long term and enduring cognitive and memory dysfunction along with impact on cardiovascular system and dependence is highly

contentious.³² In general, the current evidence suggests that individuals can substantially reduce their risk for adverse health outcomes if they delay the cannabis use until after adolescence, avoid the use of high-potency (THC) cannabis products and high frequency or intensity of its use and refrain from smoking routes of administration.³³ High quality cannabis is defined as not causing excessive intoxication or physical harm.³⁴ This also requires stronger regulatory oversight, standardised production practices and more extensive research to ensure that cannabis can be safely and effectively integrated into medical treatments.

Legal and ethical considerations

Legalization of cannabis use in medicine is taking place rigorously. In 1996, California was the first to legalise and till 2020, 33 states of US and District of Columbia have legalized medical marijuana and 11 states allowed adult recreational use.³⁵ Because specific state laws and regulations may not reflect the current body of evidence, legal and ethical issues of cannabis may at times be a conflict.³⁵

In professional perspective, physicians are expected to prescribe unstandardized agents with no FDA approval, but with potentially unexpected effect and advanced reactions as since medical cannabis dosing and potency is not regulated, there is an unavoidable knowledge gap.³¹

Ethical concerns³⁶

The benefits of medical use of cannabis may exceed its own risks and whether it should be recommended without the usual protections afforded to patients. Concerns of doctor-patient relationship, as major healthcare systems do not allow physicians to recommend drugs which are not FDA approved. Autonomy is an issue, as patient-clinician discussions about the risks, benefits and alternatives to cannabis should include these items. Risk of harm, as non-maleficence imposes an obligation on clinicians to refrain from doing harm and there are several potential harms associated with cannabis. Additional ethical considerations that become salient to cannabis use that are related to social context and lingering misconceptions.³⁵

CONCLUSION

Advancements in the cannabinoid research would not stop even if there are considerable barriers.⁷ Research Gaps do exist concerning the effectiveness of cannabidiol or cannabidiol-enriched cannabis in treating the following:¹⁰

Oncology, epilepsy, irritable bowel syndrome, spasticity due to paraplegia from spinal cord injury, huntington's disease, psychiatric disorders, amyotrophic lateral sclerosis, etc. Impact of Phyto cannabinoids as therapy to restore the function of MGBA in TBI patients. Further

research for an in-depth investigation into signaling pathways and its activation. Impact of Cannabinoids on adhesion molecules, co-stimulation, and chemotaxis.¹¹ Approach to cannabis as a legitimate therapeutic agent.²³ Impact of marijuana in pregnant women.²⁴ Finding relevance in cannabis use associated with fatal motor-vehicle accidents.²⁴

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

- Pratt M, Stevens A, Thuku M, Butler C, Skidmore B, Wieland LS, et al. Benefits and harms of medical cannabis: a scoping review of systematic reviews. *Syst Rev*. 2019;8(1):320.
- Rup J, Freeman TP, Perlman C, Hammond D. Cannabis and mental health: Prevalence of use and modes of cannabis administration by mental health status. *Addict Behav*. 2021;121:106991.
- Atakan Z. Cannabis, a complex plant: different compounds and different effects on individuals. *Ther Adv Psychopharmacol*. 2012;2(6):241-54.
- Baker D, Pryce G, Giovannoni G, Thompson AJ. The therapeutic potential of cannabis. *Lancet Neurol*. 2003;2(5):291-8.
- Bridgeman MB, Abazia DT. Medicinal Cannabis: History, Pharmacology, And Implications for the Acute Care Setting. *P T*. 2017;42(3):180-8.
- Karki P, Rangaswamy M. A review of historical context and current research on cannabis use in India. *Indian J Psychol Med*. 2023;45(2):105-16.
- Hill KP, Gold MS, Nemeroff CB, McDonald W, Grzenda A, Widge AS, et al. Risks and benefits of cannabis and cannabinoids in psychiatry. *Am J Psychiatry*. 2022;179(2):98-109.
- Lu HC, Mackie K. Review of the Endocannabinoid System. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2021;6(6):607-15.
- Webb CW, Webb SM. Therapeutic benefits of cannabis: a patient survey. *Hawaii J Med Public Health*. 2014;73(4):109-11.
- National Academies of Sciences, Medicine, Medicine Division, Board on Population Health, Public Health Practice, Committee on the Health Effects of Marijuana, An Evidence Review, Research Agenda. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. Available at: <https://www.ncbi.nlm.nih.gov>. Accessed on 21 January 2025.
- Leinen ZJ, Mohan R, Premadasa LS, Acharya A, Mohan M, Byrareddy SN. Therapeutic potential of cannabis: a comprehensive review of current and future applications. *Biomed*. 2023;11(10):2630.
- Malfitano AM, Proto MC, Bifulco M. Cannabinoids in the management of spasticity associated with multiple sclerosis. *Neuropsychiatr Dis Treat*. 2008;4(5):847-53.
- Scherma M, Muntoni AL, Riedel G, Fratta W, Fadda P. Cannabinoids and their therapeutic applications in mental disorders. *Dialogues Clin Neurosci*. 2020;22(3):271-9.
- Bodine M, Kemp AK. Medical cannabis uses in oncology. 2024. Available at: <https://www.ncbi.nlm.nih.gov>. Accessed on 21 November 2024.
- Bennici A, Mannucci C, Calapai F, Cardia L, Ammendolia I, Gangemi S, et al. Safety of medical cannabis in neuropathic chronic pain management. *Molecules*. 2021;26(20):6257.
- Desai P, Mbachi C, Vohra I, Salazar M, Mathew M, Randhawa T, et al. Association between cannabis use and healthcare utilization in patients with irritable bowel syndrome: a retrospective cohort study. *Cureus*. 2020;12(5):8008.
- Patel RS, Kamil S, Shah MR, Bhimanadham NN, Imran S. Pros and Cons of Marijuana in Treatment of Parkinson's Disease. *Cureus*. 2019;3;11(6):e4813.
- Zaheer S, Kumar D, Khan MT, Giyanwani PR, Kiran F. Epilepsy and cannabis: a literature review. *Cureus*. 2018;10(9):3278.
- Kim SH, Yang JW, Kim KH, Kim JU, Yook TH. A Review on Studies of Marijuana for Alzheimer's Disease - Focusing on CBD, THC. *J Pharmacopuncture*. 2019;22(4):225-230.
- Lopez MJ, Nataneli N. Cannabis use for glaucoma and associated pain. Available at: <https://www.ncbi.nlm.nih.gov>. Accessed on 22 December 2024.
- Woolridge E, Barton S, Samuel J, Osorio J, Dougherty A, Holdcroft A. Cannabis use in HIV for pain and other medical symptoms. *J Pain Symptom Manage*. 2005;29(4):358-67.
- McMahon I, Harris-Lane LM, Donnan J, Bishop L, Harris N. Emerging adult perceptions of higher-risk cannabis consumption behaviours. *Harm Red J*. 2023;20(1):127.
- Sachs J, McGlade E, Yurgelun-Todd D. Safety and Toxicology of Cannabinoids. *Neurotherapeutics*. 2015;12(4):735-46.
- Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. *N Engl J Med*. 2014;370(23):2219-27.
- Begum J. Medical marijuana benefits and side effects. WebMD Editorial Contributors. 20224. Available at: <https://www.webmd.com>. Accessed on 21 November 2024.
- Hoch E, Volkow ND, Friemel CM. Cannabis, cannabinoids and health: a review of evidence on risks and medical benefits. *Eur Arch Psychiatry Clin Neurosci*. 2024;3:56.
- MacCallum CA, Lo LA, Boivin M. "Is medical cannabis safe for my patients?" A practical review of cannabis safety considerations. *Eur J Intern Med*. 2021;89:10-8.

28. Subramaniam VN, Menezes AR, DeSchutter A, Lavie CJ. The Cardiovascular Effects of Marijuana: Are the Potential Adverse Effects Worth the High. *Mo Med*. 2019;116(2):146-53.
29. Archie SR, Cucullo L. Harmful effects of smoking cannabis: a cerebrovascular and neurological perspective. *Front Pharmacol*. 2019;10:1481.
30. Jacobus J, Tapert SF. Effects of cannabis on the adolescent brain. *Curr Pharm Des*. 2014;20(13):2186-93.
31. Sagy I, Peleg-Sagy T, Barski L, Zeller L, Jotkowitz A. Ethical issues in medical cannabis use. *Eur J Intern Med*. 2018;49:20-2.
32. Arnold JC. A primer on medicinal cannabis safety and potential adverse effects. *Aust J Gen Pract*. 2021;50(6):345-50.
33. Fischer B, Robinson T, Bullen C, Curran V, Jutras-Aswad D, Medina-Mora ME, et al. Lower-Risk Cannabis Use Guidelines (LRCUG) for reducing health harms from non-medical cannabis use: A comprehensive evidence and recommendations update. *Int J Drug Policy*. 2022;99:103381.
34. Belackova V. "The Good, the Bad, and the Ugly Weed": How Consumers in Four Different Policy Settings Define the Quality of Illicit Cannabis. *Contemporary Drug Problems*. 2020;47(1):43-62.
35. Glickman A, Sisti D. Prescribing medical cannabis: ethical considerations for primary care providers. *J Med Ethics*. 2020;46(4):227-30.
36. Cornella FA. Medical Marijuana and Professional Ethics. *Mo Med*. 2020;117(6):532.

Cite this article as: Lokhande N, Mokal A, Deshmukh N, Borkar A, Patil S. From relief to risks: a comprehensive review of medical cannabis. *Int J Community Med Public Health* 2025;12:2894-9.