World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 5.111
Year - 2025
Volume: 4; Issue: 6
Page: 43-58

THERAPEUTIC POTENTIAL AND PHARMACOLOGICAL INSIGHTS OF CBD GUMMIES: A COMPREHENSIVE REVIEW

Geddada Maheswari*[1], Meka Pooja[2], Chodipilli Revanth Durga[3], Peddireddy Lokesh Babu[4], Khandavalli Sheba[5], Boddani Sunil[6]

[1,2,3,4,5]Department of Pharmacy, Dr. C.S.N Institute of Pharmacy, Bhimavaram, India.
[6]Department of Pharmaceutical Technology, Dr. C.S.N Institute of Pharmacy, Bhimavaram, India.

Article Received: 8 October 2025 | | ***Article Revised: 29 October 2025*** | | ***Article Accepted: 19 November 2025***

***Corresponding Author: Geddada Maheswari**
Department of Pharmacy, Dr. C.S.N Institute of Pharmacy, Bhimavaram, India.
DOI: https://doi.org/10.5281/zenodo.17777402

How to cite this Article: Geddada Maheswari, Meka Pooja, Chodipilli Revanth Durga, Peddireddy Lokesh Babu, Khandavalli Sheba, Boddani Sunil (2025) THERAPEUTIC POTENTIAL AND PHARMACOLOGICAL INSIGHTS OF CBD GUMMIES: A COMPREHENSIVE REVIEW. World Journal of Pharmaceutical Science and Research, 4(6), pg: 43-58. https://doi.org/10.5281/zenodo.17777402

ABSTRACT

Cannabidiol (CBD), a non-psychoactive constituent of *Cannabis sativa*, has gained remarkable scientific and therapeutic attention in recent years. Among its various formulations, CBD gummies have emerged as a popular oral dosage form due to their ease of administration, palatability, and patient compliance. This review aims to provide a comprehensive overview of the pharmacology, mechanism of action, therapeutic potential, and safety profile of CBD gummies. The article highlights the pharmacokinetic behavior of CBD, its interaction with the endocannabinoid system, and its influence on CB1 and CB2 receptors. Furthermore, evidence from preclinical and clinical studies is discussed to emphasize the role of CBD in managing anxiety, epilepsy, chronic pain, and inflammation. The review also explores the formulation aspects, quality control parameters, and legal regulations, particularly within the Indian context. Despite promising outcomes, challenges such as standardization, dosage optimization, and regulatory restrictions remain significant hurdles to clinical application. This paper underscores the need for further research to establish CBD gummies as a scientifically validated, safe, and effective therapeutic option in modern pharmaceutics.

KEYWORDS: Cannabidiol; CBD gummies; Endocannabinoid system; Pharmacology; Therapeutic applications; Formulation.

INTRODUCTION

Cannabidiol (CBD) is a non-psychoactive phytocannabinoid derived from *Cannabis sativa*, distinct from its psychoactive counterpart Δ⁹-tetrahydrocannabinol (THC).[1] Over the past decade, CBD has attracted growing interest due to its diverse pharmacological actions, including anxiolytic, anti-inflammatory, neuroprotective, and anticonvulsant effects.[2,3]. With the global shift toward alternative and natural therapies, the incorporation of CBD into edible dosage forms has become a rapidly expanding trend in both nutraceutical and pharmaceutical markets.[4]

Among these, **CBD gummies** have gained particular attention because of their convenience, improved taste, and Patient acceptability.[5] Gummies offer an easy-to-administer and discreet method for CBD consumption, making them appealing for long-term therapeutic use.[6] They also allow for precise dose adjustment, improved compliance, and potential modifications to enhance bioavailability.[7]

Despite widespread availability, scientific evaluation of CBD gummies as a therapeutic formulation remains limited. Factors such as variable absorption, metabolism, and legal restrictions contribute to the complexity of their regulation and clinical application.[8] This review aims to present a comprehensive overview of the pharmacological and therapeutic insights related to CBD gummies, with emphasis on their mechanism of action, formulation aspects, safety, and regulatory considerations in the Indian and global context.[9]

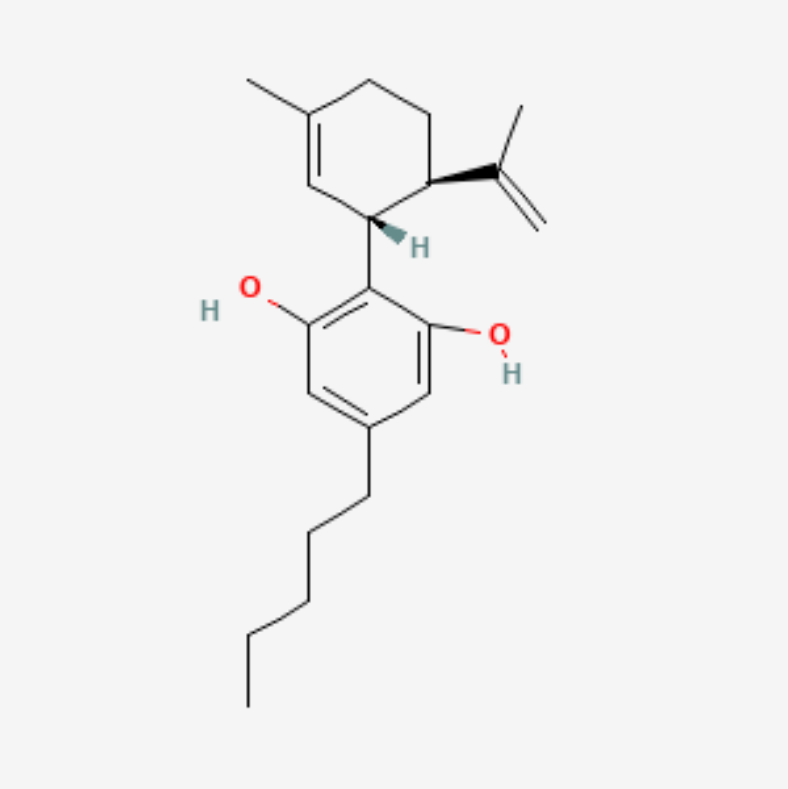

Figure 1: Chemical structure of Cannabidiol (CBD) (Source: PubChem CID 644019, 2025).

HISTORICAL BACKGROUND OF CBD AND EDIBLES

The history of cannabidiol (CBD) is deeply rooted in the evolution of cannabis use across cultures and centuries. Cannabis has been cultivated for medicinal, spiritual, and industrial purposes for over 5,000 years, with its first documented use in ancient China around 2700 BCE, when Emperor Shen Nung described its therapeutic properties in

the *Pen Ts'ao Ching*.[10] Ancient Indian texts such as the *Atharva Veda* also referred to cannabis as one of the five sacred plants, emphasizing its role in traditional healing practices and rituals.[11]

The modern scientific discovery of cannabinoids began in the early 20th century. Cannabidiol (CBD) was first isolated from *Cannabis sativa* in 1940 by Roger Adams and his team at the University of Illinois, marking a milestone in cannabinoid chemistry.[12] However, the structure and full pharmacological properties of CBD were not elucidated until the 1960s, following Raphael Mechoulam's pioneering research in Israel that led to the identification of Δ^9-tetrahydrocannabinol (THC) and the differentiation between psychoactive and non-psychoactive cannabinoids.

Interest in CBD increased during the late 20th century when clinical observations revealed its potential antiepileptic, anxiolytic, and anti-inflammatory effects, without the intoxicating properties associated with THC. This triggered a global shift in perception of cannabis-derived compounds—from substances of abuse to promising therapeutic agents.
The emergence of *edible formulations*, particularly gummies, can be traced back to the broader development of functional foods and nutraceuticals. The concept of delivering active compounds in palatable forms gained popularity in the early 2000s as consumer demand grew for convenient, discreet, and taste-friendly alternatives to oils or capsules. The legalization of hemp-derived CBD in several countries further accelerated the growth of edible products, transforming CBD gummies into one of the fastest-growing segments in the cannabinoid market.

Thus, the historical trajectory of CBD and its edible forms reflects both scientific innovation and cultural acceptance. What began as traditional herbal medicine has evolved into a sophisticated domain of modern pharmacotherapy and nutraceutical science, bridging ancient wisdom with contemporary technology.[12]

PHARMACOLOGY OF CANNABIDIOL (CBD)

Cannabidiol (CBD) is one of the primary phytocannabinoids isolated from *Cannabis sativa* and *Cannabis indica* species. Unlike Δ9-tetrahydrocannabinol (THC), CBD lacks psychoactive properties and exhibits a broad spectrum of pharmacological actions. Its unique ability to modulate multiple signaling pathways without direct psychotropic effects has made it a compound of immense therapeutic interest.[13]

Mechanism of Action

Cannabidiol (CBD) exerts its pharmacological effects primarily through interaction with the **endocannabinoid system (ECS)**, which plays a vital role in maintaining homeostasis of the nervous, immune, and endocrine systems.[14] Unlike Δ^9-tetrahydrocannabinol (THC), CBD does **not directly activate CB_1 or CB_2 receptors** but acts as a **negative allosteric modulator** of CB_1 receptors, thereby reducing psychoactive effects and modulating neurotransmitter release.[15]

In addition to its indirect cannabinoid receptor activity, CBD influences several **non-cannabinoid signaling pathways**. It interacts with **transient receptor potential (TRP) channels**, particularly TRPV1, TRPA1, and TRPM8, which are involved in pain perception, inflammation, and thermoregulation.[16] CBD also modulates **serotonin 5-HT_1A receptors**, contributing to its anxiolytic and antidepressant effects. Furthermore, CBD affects **adenosine uptake** and **GABAergic transmission**, enhancing inhibitory control in the central nervous system.

This multi-targeted mechanism explains the broad therapeutic potential of CBD, including **neuroprotection, anti-inflammatory activity, and stress regulation**, without producing significant psychoactive effects.

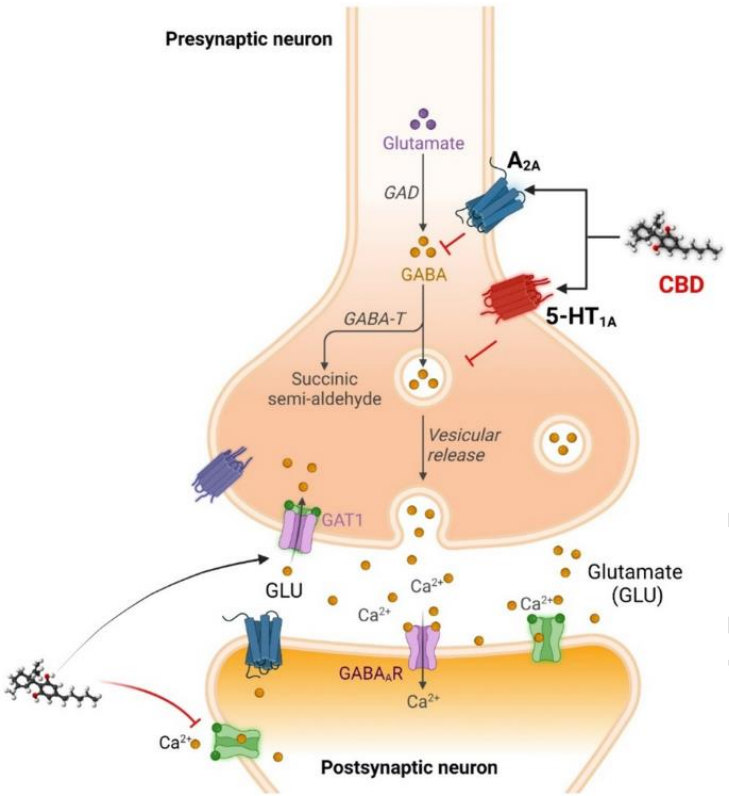

Figure 2: Simplified overview of CBD's mechanism of action showing interaction with ECS, TRPV1, and 5-HT1A receptors (Source: Adapted from Pertwee et al., 2008).

Pharmacokinetics

Following oral administration, CBD undergoes extensive first-pass hepatic metabolism, resulting in an oral bioavailability of approximately 6–19%.[17] It is highly lipophilic and widely distributed in adipose tissues, with plasma protein binding exceeding 95%. CBD is primarily metabolized by the cytochrome P450 enzymes CYP3A4 and CYP2C19, producing hydroxylated metabolites that are subsequently excreted via the biliary route.[18]

Sublingual, inhalational, and transdermal routes bypass first-pass metabolism, improving systemic availability. The elimination half-life of CBD ranges between 18 and 32 hours depending on dose and route of administration.[19]

Pharmacological Effects

Neuroprotective and Anticonvulsant Activity

CBD demonstrates neuroprotective potential through its antioxidant and anti-glutamatergic mechanisms. Studies have shown that CBD attenuates neuronal excitotoxicity by modulating intracellular calcium levels via TRPV1 channels.[20] Its efficacy in treatment-resistant epilepsy, particularly *Dravet syndrome* and *Lennox-Gastaut syndrome*, led to the development of *Epidiolex*, an FDA-approved CBD formulation.[21]

Anti-inflammatory and Analgesic Actions

CBD inhibits pro-inflammatory cytokine release (IL-6, TNF-α) and downregulates NF-κB signaling, reducing both peripheral and central inflammation.[22] In models of neuropathic pain, CBD reduces mechanical allodynia and hyperalgesia by desensitizing TRPV1 channels and enhancing adenosine signaling.[23]

Anxiolytic and Antipsychotic Properties

CBD's anxiolytic action is primarily mediated through *5-HT1A receptor agonism* and modulation of limbic activity.[24] Functional imaging studies reveal that CBD reduces amygdalar hyperactivity and enhances prefrontal-limbic connectivity, mechanisms relevant to anxiety and psychosis.[25] Clinical trials have demonstrated that CBD can reduce anxiety scores in generalized anxiety disorder and exert antipsychotic effects comparable to atypical agents without motor side effects.[26]

Antioxidant and Cardioprotective Activity

Beyond its neural effects, CBD acts as a potent antioxidant, preventing lipid peroxidation and oxidative stress-induced cellular damage.[27] In cardiovascular models, CBD reduces ischemia-reperfusion injury and normalizes vascular tone by activating endothelial nitric oxide synthase (eNOS).[28]

Immunomodulatory Role

CBD modulates both innate and adaptive immune responses by suppressing T-cell proliferation and cytokine production. It also promotes macrophage polarization toward an anti-inflammatory M2 phenotype, which may contribute to its therapeutic benefits in autoimmune and inflammatory disorders.[29]

TOXICOLOGY AND SAFETY PROFILE OF CANNABIDIOL (CBD)

CBD has been generally recognized as a compound with a favorable safety profile compared to other cannabinoids. Numerous preclinical and clinical studies have shown that CBD is well tolerated across a wide range of doses without inducing psychotropic or addictive effects.[30]

Acute and Subchronic Toxicity

In animal studies, acute toxicity tests revealed an exceptionally high LD_{50} value, exceeding 200 mg/kg in rodents, indicating low intrinsic toxicity.[31] Subchronic administration of CBD at therapeutic and supratherapeutic doses produced no significant alterations in hematological or biochemical parameters.[32] Mild hepatic enzyme elevations were observed in some cases, which were reversible upon discontinuation.[33]

Clinical Tolerability

Clinical data suggest that CBD is generally safe up to daily doses of 1,500 mg in humans.[34] Reported adverse effects are typically mild to moderate, including fatigue, diarrhea, decreased appetite, and somnolence.[35] However, co-administration with other drugs metabolized by CYP3A4 or CYP2C19 (e.g., clobazam, valproate) can result in pharmacokinetic interactions, requiring careful dose adjustment.[36]

Reproductive and Developmental Toxicity

Preclinical studies in pregnant animals have shown potential fetal growth retardation and skeletal variations at very high doses of CBD.[37] These effects are thought to be related to maternal toxicity rather than direct embryotoxicity. Currently, CBD use during pregnancy and lactation is not recommended due to insufficient human safety data.[38]

Genotoxicity and Carcinogenicity

Long-term studies have shown no evidence of mutagenic or carcinogenic potential.[39] Standard assays such as the Ames test and chromosomal aberration studies confirmed the genetic safety of CBD.[40] Furthermore, its antioxidant properties may actually contribute to the suppression of oxidative DNA damage.[41]

Dependence and Abuse Liability

Unlike THC, CBD does not activate mesolimbic dopaminergic pathways or induce euphoria. Controlled trials by the World Health Organization (WHO) and the U.S. FDA have confirmed the absence of abuse or dependence potential, supporting its classification as a non-psychoactive cannabinoid.[42]

THERAPEUTIC APPLICATIONS OF CBD AND CBD GUMMIES

CBD has gained widespread attention for its broad therapeutic potential, supported by both preclinical and clinical studies. Its ability to modulate multiple biological targets without psychoactive effects makes it suitable for managing several neurological, inflammatory, and metabolic disorders.[43] With the introduction of CBD gummies and other oral edibles, patient compliance and accessibility have improved significantly due to ease of administration and palatable formulations.[44]

1. Neurological Disorders

Epilepsy

The strongest clinical evidence for CBD's efficacy lies in the treatment of refractory epilepsies such as *Dravet syndrome* and *Lennox–Gastaut syndrome*. Controlled clinical trials demonstrated that pharmaceutical-grade CBD (Epidiolex®) significantly reduced seizure frequency in both pediatric and adult populations.[45] The mechanism is attributed to modulation of neuronal excitability through TRPV1 channels and GPR55 receptor inhibition.[46]

Neurodegenerative Diseases

CBD exhibits neuroprotective and anti-inflammatory properties that may benefit conditions such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis[47]. By attenuating oxidative stress and reducing microglial activation, CBD preserves neuronal viability and synaptic integrity.[48] Animal models have shown improvements in memory performance and locomotor function following CBD administration.[49]

2. Anxiety and Psychiatric Disorders

CBD has been recognized for its anxiolytic and antidepressant-like effects through interaction with *5-HT1A receptors* and suppression of amygdalar hyperactivity.[50] Clinical trials involving patients with social anxiety disorder demonstrated significant reduction in anxiety scores following acute oral CBD administration compared to placebo.[51] Furthermore, CBD has been explored as an adjunct in schizophrenia and bipolar disorder management due to its antipsychotic profile without causing extrapyramidal side effects.[52]

3. Pain and Inflammation

CBD exerts analgesic actions by targeting both central and peripheral pain mechanisms. It inhibits inflammatory cytokines such as TNF-α and IL-1β, while modulating nociceptive transmission through TRPV1 and CB2 receptor pathways.[53] In chronic pain models, combination therapies of CBD and low-dose THC have shown synergistic analgesic effects.[54] CBD gummies, with their slow-release characteristics, may offer prolonged pain control and better patient adherence.[55]

4. Cancer and Chemotherapy-Induced Symptoms

Emerging studies suggest CBD possesses antineoplastic properties by inducing apoptosis, inhibiting angiogenesis, and suppressing metastasis in tumor cells.[56] Furthermore, CBD mitigates chemotherapy-induced nausea, vomiting, and

neuropathy through serotonin and vanilloid receptor modulation.[57] In supportive oncology care, CBD gummies are increasingly used to enhance patient comfort and improve appetite.[58]

5. Metabolic and Cardiovascular Health

CBD's antioxidant and anti-inflammatory properties contribute to improved endothelial function and reduced blood pressure.[59] It lowers lipid peroxidation and enhances nitric oxide production, promoting vascular homeostasis.[60] Preclinical models also suggest potential in obesity management and type 2 diabetes by regulating glucose uptake and adipocyte metabolism.[61]

6. Dermatological and Immune Conditions

Topical and oral CBD formulations have shown promise in conditions such as psoriasis, acne, and atopic dermatitis due to their anti-inflammatory and sebostatic effects.[62] Moreover, its immunomodulatory properties make it a potential adjunct in autoimmune disorders like rheumatoid arthritis and inflammatory bowel disease.[63]

FORMULATION AND QUALITY CONTROL OF CBD GUMMIES

CBD gummies are among the most widely accepted oral delivery systems for cannabidiol due to their convenience, stability, and patient-friendly nature. They provide an alternative to traditional oils or capsules, offering precise dosing and better palatability.[64]

1. Formulation Design

The formulation of CBD gummies involves combining *CBD extract or isolate* with gelling agents, sweeteners, and stabilizers. Common gelling agents include gelatin and pectin, while corn syrup, sucrose, or sugar alcohols are used to provide texture and sweetness.[65] To ensure uniform cannabinoid distribution, CBD is typically pre-dissolved in carrier oils such as medium-chain triglycerides (MCT) or hemp seed oil before being blended into the gummy matrix.[66]

The incorporation of emulsifiers like lecithin or polysorbate-80 enhances dispersion of hydrophobic CBD in aqueous systems, improving bioavailability.[67] The final composition may also include flavoring agents, natural colorants, antioxidants (e.g., tocopherol), and preservatives to maintain stability and sensory appeal.[68]

2. Dosage and Bioavailability Enhancement

Oral bioavailability of CBD is relatively low due to first-pass metabolism and poor aqueous solubility. To overcome this limitation, novel formulation strategies such as *nanoemulsions*, *liposomes*, *solid lipid nanoparticles*, and *self-emulsifying drug delivery systems (SEDDS)* are employed.[69] These systems increase surface area and absorption through the intestinal epithelium, resulting in more consistent plasma concentrations.[70]

3. Manufacturing Considerations

The production process requires precise control of temperature and mixing speed to prevent degradation of CBD and preserve consistency. Excessive heating (>70°C) during cooking or gelatinization may cause cannabinoid loss and oxidation.[71] Therefore, encapsulation techniques using spray drying or microencapsulation are often adopted to protect CBD from environmental stress.[72]

Batch-to-batch reproducibility is critical. The use of *Good Manufacturing Practices (GMP)* ensures homogeneity, stability, and purity of the final product.[73] Additionally, maintaining uniform weight and thickness of gummies guarantees accurate dosing per unit.[74]

4. Quality Control Parameters

Quality assessment of CBD gummies includes both physicochemical and microbiological evaluation. Key parameters include weight variation, drug content uniformity, pH, hardness, friability, and disintegration time.[75] Analytical quantification of CBD is typically performed using high-performance liquid chromatography (HPLC) or ultra-performance liquid chromatography (UPLC) coupled with UV or mass spectrometric detection.[76]

Residual solvent testing, heavy metal screening, and microbial load evaluation are conducted in accordance with pharmacopoeial standards to ensure product safety.[77] Stability testing under different environmental conditions (temperature, humidity, and light) determines the shelf-life and degradation kinetics of CBD within the matrix.[78]

5. Labeling and Standardization

Label accuracy is a major concern in commercial CBD gummies. Studies have revealed significant discrepancies between labeled and actual CBD content in marketed products.[79] Therefore, standardization according to validated analytical methods is essential to guarantee consumer trust and regulatory compliance.[80] Clear labeling of CBD concentration, serving size and THC content (if any) must be included in accordance with local and international regulatory frameworks.[81]

LEGAL AND REGULATORY ASPECTS OF CANNABIDIOL (CBD)

The regulatory framework surrounding cannabidiol (CBD) varies widely across countries, reflecting differences in cultural perception, medical use, and legal control of cannabis-derived products.[82] While nations such as the United States and Canada have established guidelines for hemp-derived CBD, India's stance remains complex due to its historical association with the *Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985*.[83]

1. Global Regulatory Overview

In most Western countries, CBD products derived from industrial hemp (containing less than 0.3% THC) are legally permitted under strict quality and labeling standards.[84] The U.S. Food and Drug Administration (FDA) classifies CBD as an investigational compound but allows its use in certain approved formulations such as *Epidiolex*® for rare epileptic disorders.[85] The European Union (EU) permits CBD sale as a "novel food," provided it is derived from authorized hemp varieties and meets safety and purity requirements.[86]

2. Legal Status in India

In India, the cultivation, production, and use of cannabis and its derivatives are governed by the NDPS Act, 1985. Under this act, *cannabis resin* (charas), *flowering tops* (ganja), and *extracts and tinctures* of cannabis are classified as narcotic substances.[87] However, the act excludes *cannabis seeds* and *leaves*, which creates a legal loophole for hemp-derived products such as CBD oils and gummies.[88]

Currently, CBD derived from hemp containing less than 0.3% THC can be marketed under the AYUSH and nutraceutical category, provided it is not advertised as a medical or therapeutic drug.[89] However, any product claiming to treat or prevent disease requires approval from the *Central Drugs Standard Control Organization (CDSCO)* and must adhere to the *Drugs and Cosmetics Act, 1940*.[90]

3. Licensing and Import Regulations

The import and sale of CBD-based formulations for medical use in India require a No Objection Certificate (NOC) from the *Drug Controller General of India (DCGI)*.[91] For industrial or research use, licensing under state excise departments and local drug control authorities is necessary.[92] Furthermore, the Food Safety and Standards Authority of India (FSSAI) has yet to establish definitive guidelines for CBD as a food supplement, creating regulatory ambiguity for manufacturers.[93]

4. Quality and Safety Standards

There is currently no uniform national standard for testing and labeling CBD products in India. However, international standards such as the *U.S. Pharmacopeia (USP)* and *European Pharmacopoeia (Ph. Eur.)* provide guidance for analytical evaluation of cannabinoid content, impurities, and stability.[94] Indian manufacturers are encouraged to follow *Good Manufacturing Practices (GMP)* and maintain documentation as per *Schedule M* of the Drugs and Cosmetics Rules.[95]

The lack of standardization has led to discrepancies in the market, with some CBD gummies containing variable or undeclared THC levels.[96] Implementing a centralized certification system could improve transparency, ensure consumer safety, and promote acceptance of CBD-based products in the pharmaceutical and wellness sectors[97].

5. Ethical and Future Considerations

With growing global evidence supporting CBD's therapeutic potential, India faces both regulatory and ethical challenges. A science-based policy framework recognizing the distinction between psychoactive and non-psychoactive cannabinoids could enable controlled medical use without encouraging recreational misuse.[98]

Collaborative initiatives between AYUSH, CDSCO, and FSSAI could facilitate standardized regulations for CBD products, balancing innovation, patient safety, and societal norms.[99] Establishing national guidelines for testing, labeling, and permissible THC levels would not only enhance credibility but also attract pharmaceutical investment and clinical research in India.[100]

CHALLENGES AND FUTURE PROSPECTS OF CBD GUMMIES

Despite the growing popularity of **CBD gummies** as a therapeutic and lifestyle product, several challenges persist that limit their consistent efficacy, acceptance, and large-scale regulation.[101] One of the most significant issues lies in **bioavailability** — when CBD is administered orally in gummy form, it undergoes **first-pass metabolism** in the liver, which drastically reduces the amount of active compound reaching systemic circulation.[102] This leads to unpredictable absorption rates and inconsistent therapeutic outcomes among users.

Another major concern is **quality control and product standardization**. Many commercially available CBD gummies exhibit wide variations in CBD concentration, purity, and labeling accuracy.[103] The absence of strict pharmaceutical-grade manufacturing standards and reliance on dietary supplement regulations further complicates quality assurance. Contamination with heavy metals, residual solvents, and synthetic cannabinoids has also been reported in some unregulated products.[104]

From a **regulatory standpoint**, CBD products still occupy a gray area in several countries, including India, where classification under narcotic or wellness categories remains uncertain.[105] This ambiguity discourages investment,

limits research, and creates barriers for legitimate manufacturers. Additionally, **public perception** remains divided — while some view CBD gummies as safe nutraceuticals, others associate them with cannabis-related stigma, hindering social acceptance.[106]

Looking ahead, the **future prospects** for CBD gummies appear promising. Advancements in **nanotechnology, lipid-based delivery systems, and encapsulation methods** are expected to significantly improve oral bioavailability and consistency of dosing.[107] Furthermore, with increasing clinical validation and evolving regulations, CBD-based edibles may find broader applications in **anxiety, pain, sleep disorders, and neurodegenerative conditions.**[108] Continued collaboration between researchers, regulators, and manufacturers will be crucial to transform CBD gummies from consumer trends into **standardized, evidence-based therapeutic agents.**[109]

CONCLUSION

Cannabidiol (CBD) has evolved from a once-controversial phytochemical to a scientifically recognized compound with wide-ranging therapeutic potential.[110] Among its modern formulations, **CBD gummies** have gained remarkable attention due to their ease of administration, patient compliance, and pleasant sensory profile.[111] Despite these advantages, challenges related to **bioavailability, regulatory clarity, and product standardization** continue to restrict their full potential.[112]

Future research should emphasize **long-term safety studies, optimized formulation techniques, and well-controlled clinical trials** to validate the efficacy of CBD gummies across various medical conditions.[113] Global harmonization of regulatory policies, particularly in emerging markets like India, will also play a key role in shaping the responsible growth of the CBD industry.[114]

In essence, CBD gummies represent a **bridge between natural therapy and modern pharmaceutical innovation** — a symbol of how scientific understanding can transform traditional compounds into reliable and accessible wellness solutions.[115]

REFERENCES

1. Mechoulam R, Parker LA. The endocannabinoid system and the brain. *Annu Rev Psychol*, 2013; 64: 21–47.
2. Devinsky O, Cross JH, Laux L, et al. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. *N Engl J Med*, 2017; 376(21): 2011–2020.
3. Pertwee RG. Pharmacological actions of cannabinoids. *Handb Exp Pharmacol*, 2005; 168: 1–51.
4. Huestis MA. Human cannabinoid pharmacokinetics. *Chem Biodivers*, 2007; 4(8): 1770–1804.
5. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet*, 2003; 42(4): 327–360.
6. Ibeas Bih C, Chen T, Nunn AV, Bazelot M, Dallas M, Whalley BJ. Molecular targets of cannabidiol in neurological disorders. *Neurotherapeutics*, 2015; 12(4): 699–730.
7. Blessing EM, Steenkamp MM, Manzanares J, Marmar CR. Cannabidiol as a potential treatment for anxiety disorders. *Neurotherapeutics*, 2015; 12(4): 825–836.
8. Pisanti S, Malfitano AM, Ciaglia E, Lamberti A, Ranieri R, Cuomo G, et al. Cannabidiol: State of the art and new challenges for therapeutic applications. *Pharmacol Ther*, 2017; 175: 133–150.

9. Hampson AJ, Grimaldi M, Axelrod J, Wink D. Cannabidiol and neuroprotection. *Proc Natl Acad Sci U S A*, 1998; 95(14): 8268–8273.
10. Millar SA, Stone NL, Yates AS, O'Sullivan SE. A systematic review on the pharmacokinetics of cannabidiol in humans. *Front Pharmacol*, 2018; 9: 1365.
11. Izzo AA, Borrelli F, Capasso R, Di Marzo V, Mechoulam R. Non-psychotropic plant cannabinoids: new therapeutic opportunities from an ancient herb. *Trends Pharmacol Sci*, 2009; 30(10): 515–527.
12. Franco V, Perucca E. Pharmacological and therapeutic properties of cannabidiol for epilepsy. *Drugs*, 2019; 79(13): 1435–1454.
13. McPartland JM, Duncan M, Di Marzo V, Pertwee RG. Are cannabidiol and Δ9-tetrahydrocannabivarin negative modulators of the endocannabinoid system? *Br J Pharmacol*, 2015; 172(3): 737–753.
14. Pertwee RG. The diverse CB1 and CB2 receptor pharmacology of three plant cannabinoids: Δ9-tetrahydrocannabinol, cannabidiol and Δ9-tetrahydrocannabivarin. *Br J Pharmacol*, 2008; 153(2): 199–215.
15. Campos AC, Moreira FA, Gomes FV, Del Bel EA, Guimarães FS. Multiple mechanisms involved in the large-spectrum therapeutic potential of cannabidiol in psychiatric disorders. *Philos Trans R Soc Lond B Biol Sci*, 2012; 367(1607): 3364–3378.
16. Zygmunt PM, Andersson DA, Högestätt ED. Cannabinoids and vanilloid receptors: cellular targets for cannabidiol and other plant-derived cannabinoids. *Br J Pharmacol*, 2010; 160(3): 585–590.
17. Devinsky O, Patel AD, Cross JH, Villanueva V, Wirrell EC, Privitera M, et al. Effect of cannabidiol on drop seizures in the Lennox–Gastaut syndrome. *N Engl J Med.*, 2018; 378(20): 1888–1897.
18. Iffland K, Grotenhermen F. An update on safety and side effects of cannabidiol: A review of clinical data and relevant animal studies. *Cannabis Cannabinoid Res.*, 2017; 2(1): 139–154.
19. Bergamaschi MM, Queiroz RH, Zuardi AW, Crippa JA. Safety and side effects of cannabidiol, a Cannabis sativa constituent. *Curr Drug Saf*, 2011; 6(4): 237–249.
20. Shannon S, Lewis N, Lee H, Hughes S. Cannabidiol in anxiety and sleep: a large case series. *Perm J.*, 2019; 23: 18–041.
21. Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br J Pharmacol*, 2011; 163(7): 1344–1364.
22. Silvestro S, Mammana S, Cavalli E, Bramanti P, Mazzon E. Use of cannabidiol in the treatment of epilepsy: Efficacy and security in clinical trials. *Molecules*, 2019; 24(8): 1459.
23. Crippa JA, Guimarães FS, Campos AC, Zuardi AW. Translational investigation of the therapeutic potential of cannabidiol (CBD): toward a new age. *Front Immunol*, 2018; 9: 2009.
24. Pisanti S, Malfitano AM, Ciaglia E, Lamberti A, Ranieri R, Cuomo G, Abate M, Faggiana G, Proto MC, Fiore D, Laezza C, Bifulco M. Cannabidiol: State of the art and new challenges for therapeutic applications. *Pharmacol Ther.*, 2017; 175: 133–150.
25. ElSohly MA, Gul W, Wanas AS, Radwan MM. Synthetic cannabinoids: Analysis and metabolites. *Life Sci.*, 2014; 97(1): 78–90.
26. Devinsky O, Cross JH, Wright S. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. *N Engl J Med.*, 2017; 376: 2011–2020.
27. World Health Organization. Cannabidiol (CBD) Critical Review Report. Geneva: WHO Expert Committee on Drug Dependence, 2018.

28. Pamplona FA, Ferreira J, Menezes de Lima O Jr, Duarte FS, Bento AF, Forner S, Pereira LM, Mazzuco TL, Souza GE, Sachs D, Cunha FQ. Anti-inflammatory properties of cannabidiol in experimental models of various diseases. *Eur J Pharmacol*, 2018; 833: 112–128.
29. Atalay S, Jarocka-Karpowicz I, Skrzydlewska E. Antioxidative and anti-inflammatory properties of cannabidiol. *Antioxidants (Basel)*, 2019; 9(1): 21.
30. Perucca E. Cannabinoids in the treatment of epilepsy: Hard evidence at last? *J Epilepsy Res.*, 2017; 7(2): 61–76.
31. Millar SA, Stone NL, Yates AS, O'Sullivan SE. A systematic review on the pharmacokinetics of cannabidiol in humans. *Front Pharmacol*, 2018; 9: 1365.
32. Schier AR, Ribeiro NP, Silva AC, Hallak JE, Crippa JA, Nardi AE, Zuardi AW. Cannabidiol, a Cannabis sativa constituent, as an anxiolytic drug. *Rev Bras Psiquiatr*, 2012; 34(Suppl 1): S104–S110.
33. Taylor L, Gidal B, Blakey G, Tayo B, Morrison G. A phase I, randomized, double-blind, placebo-controlled, single ascending dose, multiple dose, and food effect trial of the safety, tolerability, and pharmacokinetics of highly purified cannabidiol in healthy subjects. *CNS Drugs*, 2018; 32(11): 1053–1067.
34. Shannon S, Lewis N, Lee H, Hughes S. Cannabidiol in anxiety and sleep: A large case series. *Perm J*, 2019; 23: 18–041.
35. Crippa JA, Zuardi AW, Garrido GE, Wichert-Ana L, Guarnieri R, Ferrari L, Azevedo-Marques PM, Hallak JE, McGuire PK, Busatto GF. Effects of cannabidiol (CBD) on regional cerebral blood flow. *Neuropsychopharmacology*, 2004; 29(2): 417–426.
36. Hurd YL, Yoon M, Manini AF, Hernandez S, Olmedo R, Ostman M, Jutras-Aswad D. Early phase in the development of cannabidiol as a treatment for addiction: Opioid relapse takes initial center stage. *Neurotherapeutics*, 2015; 12(4): 807–815.
37. Pavlovic R, Nenna G, Calvi L, Panseri S, Borgonovo G, Giupponi L, Cannazza G, Giorgi A. Quality traits of "CBD oils": Cannabinoids content, terpene fingerprint and oxidation stability of European commercially available preparations. *Molecules*, 2018; 23(5): 1230.
38. United Nations Office on Drugs and Crime (UNODC). The International Drug Control Conventions: Schedules of Controlled Substances. Vienna: UNODC, 2020.
39. Ministry of AYUSH, Government of India. Guidelines for the use of Cannabis and its products for medical and scientific purposes. New Delhi: Ministry of AYUSH, 2023.
40. Russo EB. The case for the entourage effect and conventional breeding of clinical cannabis: No "strain," no gain. *Front Plant Sci.*, 2019; 9: 1969.
41. Ujváry I, Hanuš L. Human metabolites of cannabidiol: A review on their formation, biological activity, and relevance in therapy. *Cannabis Cannabinoid Res*, 2016; 1(1): 90–101.
42. Lachenmeier DW, Rajcic de Rezende T, Nagy C, Walch SG. Curbing the CBD craze: Review of potential harms and regulatory approaches. *Int J Legal Med*, 2022; 136(3): 803–810.
43. European Medicines Agency (EMA). CBD-containing medicinal products: Guidance on development and approval. Amsterdam: EMA, 2022.
44. McGregor IS, Cairns EA, Abelev S, Cohen R, Henderson M, Couch D, Arnold JC. Access to cannabidiol without a prescription: A cross-country comparison and analysis. *Front Psychiatry*, 2020; 11: 611.
45. Blessing EM, Steenkamp MM, Manzanares J, Marmar CR. Cannabidiol as a potential treatment for anxiety disorders. *Neurotherapeutics*, 2015; 12(4): 825–836.

46. Capano A, Weaver R, Burkman E. Evaluation of the effects of cannabidiol hemp extract on opioid use and quality of life indicators in chronic pain patients: A prospective cohort study. *Postgrad Med*, 2020; 132(1): 56–61.
47. White CM. A review of human studies assessing cannabidiol's (CBD) therapeutic actions and potential. *J Clin Pharmacol*, 2019; 59(7): 923–934.
48. Devinsky O, Patel AD, Cross JH, Villanueva V, Wirrell EC, Privitera M, Greenwood S, Roberts C, Checketts D, VanLandingham KE, Zuberi SM. Effect of cannabidiol on drop seizures in the Lennox–Gastaut syndrome. *N Engl J Med*, 2018; 378(20): 1888–1897.
49. Crippa JA, Derenusson GN, Ferrari TB, Wichert-Ana L, Duran FL, Martin-Santos R, Simões MV, Bhattacharyya S, Fusar-Poli P, Atakan Z, Santos Filho A. Neural basis of anxiolytic effects of cannabidiol (CBD) in generalized social anxiety disorder: A preliminary report. *J Psychopharmacol*, 2011; 25(1): 121–130.
50. Stinchcomb AL, Valiveti S, Hammell DC, Ramsey DR. Human skin permeation of Δ^8-tetrahydrocannabinol, cannabidiol and cannabinol. *J Pharm Pharmacol*, 2004; 56(3): 291–297.
51. Bonn-Miller MO, Loflin MJE, Thomas BF, Marcu JP, Hyke T, Vandrey R. Labeling accuracy of cannabidiol extracts sold online. *JAMA*, 2017; 318(17): 1708–1709.
52. U.S. Food and Drug Administration (FDA). Warning letters and test results for cannabidiol-related products. Silver Spring, MD: U.S. FDA, 2021.
53. Vandrey R, Raber JC, Raber ME, Douglass B, Miller C, Bonn-Miller MO. Cannabinoid dose and label accuracy in edible medical cannabis products. *JAMA*, 2015; 313(24): 2491–2493.
54. Hazekamp A. The trouble with CBD oil. *Med Cannabis Cannabinoids*, 2018; 1(1): 65–72.
55. Gurley BJ, Murphy TP, Gul W, Walker LA, ElSohly MA. Content versus label claims in cannabidiol (CBD)-containing products obtained from commercial outlets in the state of Mississippi. *J Diet Suppl.*, 2020; 17(5): 599–607.
56. United States Pharmacopeia (USP). Cannabis and cannabis-derived compounds: Quality considerations for clinical research. Rockville, MD: USP, 2022.
57. European Commission. Novel Food Catalogue: Cannabidiol and hemp extracts. Brussels: European Commission; 2023.
58. Lachenmeier DW, Habel S, Fischer B, Herbi F, Walch SG, Schönfeld N. Are cannabidiol (CBD) products safe for human consumption? Regulatory challenges and safety aspects. *Toxics*, 2022; 10(1): 34.
59. Izzo AA, Borrelli F, Capasso R, Di Marzo V, Mechoulam R. Non-psychotropic plant cannabinoids: New therapeutic opportunities from an ancient herb. *Trends Pharmacol Sci.*, 2009; 30(10): 515–527.
60. Carcieri C, Tomasello C, Simiele M, De Nicolò A, Avataneo V, Canzoneri L, Cusato J, Di Perri G, D'Avolio A. Cannabinoids concentration variability in cannabis oils: Clinical and forensic toxicological implications. *Forensic Sci Int.*, 2018; 289: 222–230.
61. Jiang R, Yamaori S, Takeda S, Yamamoto I, Watanabe K. Identification of cytochrome P450 enzymes responsible for metabolism of cannabidiol by human liver microsomes. *Life Sci.*, 2011; 89(5–6): 165–170.
62. Lucas CJ, Galettis P, Schneider J. The pharmacokinetics and pharmacodynamics of cannabinoids. *Br J Clin Pharmacol*, 2018; 84(11): 2477–2482.
63. Fasinu PS, Phillips S, ElSohly MA, Walker LA. Current status and prospects for cannabidiol preparations as new therapeutic agents. *Pharmacotherapy*, 2016; 36(7): 781–796.

64. Jones É, Vlachou S. A critical review of the role of the cannabinoid receptor CB1 in the rewarding effects of Δ⁹-tetrahydrocannabinol and other cannabinoids. *Behav Pharmacol,* 2020; 31(8): 710–724.
65. Pertwee RG. The diverse CB_1 and CB_2 receptor pharmacology of three plant cannabinoids: Δ⁹-tetrahydrocannabinol, cannabidiol and Δ⁹-tetrahydrocannabivarin. *Br J Pharmacol,* 2008; 153(2): 199–215.
66. Silvestro S, Mammana S, Cavalli E, Bramanti P, Mazzon E. Use of cannabidiol in the treatment of epilepsy: Efficacy and security in clinical trials. *Molecules,* 2019; 24(8): 1459.
67. Esposito G, Scuderi C, Savani C, Steardo L Jr, De Filippis D, Cottone P, Iuvone T, Cuomo V, Steardo L. Cannabidiol in inflammatory bowel diseases: A brief overview. *Phytother Res.,* 2013; 27(5): 633–636.
68. Millar SA, Stone NL, Yates AS, O'Sullivan SE. A systematic review on the pharmacokinetics of cannabidiol in humans. *Front Pharmacol,* 2018; 9: 1365.
69. Martin BR, Mechoulam R, Razdan RK. Discovery and characterization of endogenous cannabinoids. *Life Sci.,* 1999; 65(6–7): 573–595.
70. Atalay S, Jarocka-Karpowicz I, Skrzydlewska E. Antioxidative and anti-inflammatory properties of cannabidiol. *Antioxidants (Basel),* 2019; 9(1): 21.
71. Nichols JM, Kaplan BLF. Immune responses regulated by cannabidiol. *Cannabis Cannabinoid Res.,* 2020; 5(1): 12–31.
72. Zuardi AW. History of cannabis as a medicine: A review. *Rev Bras Psiquiatr,* 2006; 28(2): 153–157.
73. Baswan SM, Klosner AE, Glynn K, Rajgopal A, Malik K, Yim S, Stern N. Therapeutic potential of cannabidiol (CBD) for skin health and disorders. *Clin Cosmet Investig Dermatol,* 2020; 13: 927–942.
74. McPartland JM, Duncan M, Di Marzo V, Pertwee RG. Are cannabidiol and Δ⁹-tetrahydrocannabivarin negative modulators of the endocannabinoid system? A systematic review. *Br J Pharmacol,* 2015; 172(3): 737–753.
75. Zhornitsky S, Potvin S. Cannabidiol in humans—the quest for therapeutic targets. *Pharmacol Ther,* 2012; 133(1): 35–54.
76. Rudroff T, Sosnoff JJ. Cannabidiol to improve mobility in people with multiple sclerosis. *Front Neurol,* 2018; 9: 183.
77. Brierley DI, Samuels J, Duncan M, Whalley BJ, Williams CM. Neuromodulatory effects of cannabidiol on acetylcholine release in the hippocampus: A role for GPR55. *J Neurochem,* 2016; 136(4): 768–778.
78. Scuderi C, Filippis DD, Iuvone T, Blasio A, Steardo A, Esposito G. Cannabidiol in medicine: A review of its therapeutic potential in CNS disorders. *Phytother Res,* 2009; 23(5): 597–602.
79. García-Gutiérrez MS, Navarrete F, Gasparyan A, Austrich-Olivares A, Manzanares J. Cannabidiol: A potential new alternative for the treatment of anxiety, depression, and psychotic disorders. *Biomolecules,* 2020; 10(11): 1575.
80. Shannon S, Lewis N, Lee H, Hughes S. Cannabidiol in anxiety and sleep: A large case series. *Perm J.,* 2019; 23: 18–041.
81. Moltke J, Hindocha C. Reasons for cannabidiol use: A cross-sectional study of CBD users, focusing on self-perceived stress, anxiety, and sleep problems. *J Cannabis Res.,* 2021; 3(1): 5.
82. Fattore L, Fratta W. Beyond THC: The new generation of cannabinoid designer drugs. *Front Behav Neurosci,* 2011; 5: 60.
83. Hložek T, Uttl L, Kadeřábek L, Balíková M, Lhotková E, Horsley RR, Nováková P, Šulcová A, Šlamberová R. Pharmacokinetic and behavioural profile of cannabidiol in rats and mice. *Front Pharmacol,* 2017; 8: 140.

84. González-Cuevas G, Martin-Fardon R, Kerr TM, Stouffer DG, Parsons LH, Hammell DC, Banks SL, Stinchcomb AL, Weiss F. Unique treatment potential of cannabidiol for the prevention of relapse to drug use: Preclinical proof of principle. *Neuropsychopharmacology*, 2018; 43(10): 2036–2045.
85. Silvestri C, Di Marzo V. The endocannabinoid system in energy homeostasis and the etiopathology of metabolic disorders. *Cell Metab*, 2013; 17(4): 475–490.
86. Rossi F, Siniscalco D, Luongo L, De Petrocellis L, Bellini G, Petrosino S, Torella M, Santoro C, Nobili B, Perrotta S, Di Marzo V, Maione S. The endocannabinoid system in human osteoblasts: Regulation of cell growth and differentiation. *J Biol Chem*, 2009; 284(20): 13533–13543.
87. Adams R, Hunt M, Clark JH. Structure of cannabidiol, a product isolated from the marihuana extract of Minnesota wild hemp. *J Am Chem Soc.*, 1940; 62(1): 196–200.
88. Pisanti S, Malfitano AM, Ciaglia E, Lamberti A, Ranieri R, Cuomo G, Abate M, Faggiana G, Proto MC, Fiore D, Laezza C, Bifulco M. Cannabidiol: State of the art and new challenges for therapeutic applications. *Pharmacol Ther*, 2017; 175: 133–150.
89. Leas EC, Nobles AL, Caputi TL, Dredze M, Smith DM, Ayers JW. Trends in Internet searches for cannabidiol (CBD) in the United States. *JAMA Netw Open*, 2019; 2(10): e1913853.
90. World Health Organization (WHO). *Cannabidiol (CBD) Critical Review Report.* Geneva: WHO Expert Committee on Drug Dependence, 2018.
91. Franco V, Perucca E. Pharmacological and therapeutic properties of cannabidiol for epilepsy. *Drugs*, 2019; 79(13): 1435–1454.
92. Crippa JA, Nogueira Derenusson G, Borduqui Ferrari TB, Wichert-Ana L, Duran FL, Martin-Santos R, Simões MV, Bhattacharyya S, Fusar-Poli P, Atakan Z, Santos Filho A, Freitas-Ferrari MC, McGuire PK, Zuardi AW, Hallak JEC. Neural basis of anxiolytic effects of cannabidiol (CBD) in generalized social anxiety disorder: A preliminary report. *J Psychopharmacol*, 2011; 25(1): 121–130.
93. Blessing EM, Steenkamp MM, Manzanares J, Marmar CR. Cannabidiol as a potential treatment for anxiety disorders. *Neurotherapeutics*, 2015; 12(4): 825–836.
94. Bergamaschi MM, Queiroz RHC, Chagas MHN, de Oliveira DCG, De Martinis BS, Kapczinski F, Quevedo J, Roesler R, Schröder N, Nardi AE, Martín-Santos R, Hallak JEC, Zuardi AW, Crippa JAS. Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients. *Neuropsychopharmacology*, 2011; 36(6): 1219–1226.
95. Bitencourt RM, Takahashi RN. Cannabidiol as a therapeutic alternative for post-traumatic stress disorder: From bench research to confirmation in human trials. *Front Neurosci*, 2018; 12: 502.
96. Xu DH, Cullen BD, Tang M, Fang Y. The effectiveness of topical cannabidiol oil in symptomatic relief of peripheral neuropathy of the lower extremities. *Curr Pharm Biotechnol*, 2019; 20(1): 1–5.
97. Philpott HT, O'Brien M, McDougall JJ. Attenuation of early phase inflammation by cannabidiol prevents pain and nerve damage in rat osteoarthritis. *Pain*, 2017; 158(12): 2442–2451.
98. Iffland K, Grotenhermen F. An update on safety and side effects of cannabidiol: A review of clinical data and relevant animal studies. *Cannabis Cannabinoid Res.*, 2017; 2(1): 139–154.
99. Silvestro S, Mammana S, Cavalli E, Bramanti P, Mazzon E. Use of cannabidiol in the treatment of epilepsy: Efficacy and security in clinical trials. *Molecules*, 2019; 24(8): 1459.

100. Russo EB. Taming THC: Potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br J Pharmacol*, 2011; 163(7): 1344–1364.
101. Pavlovic R, Nenna G, Calvi L, Panseri S, Borgonovo G, Giupponi L, Cannazza G, Giorgi A. Quality traits of "Cannabidiol oils": Cannabinoids content, terpene fingerprint and oxidation stability of European commercially available preparations. *Molecules*, 2018; 23(5): 1230.
102. Upton R, Craker L, ElSohly M, Romm A, Russo E, Sexton M. *Cannabis Inflorescence: Standards of Identity, Analysis, and Quality Control.* American Herbal Pharmacopoeia, 2014.
103. Huestis MA. Human cannabinoid pharmacokinetics. *Chem Biodivers*, 2007; 4(8): 1770–1804.
104. Hložek T, Lhotková E, Horsley RR, Balíková M, Uttl L, Šlamberová R. Comparative pharmacokinetics of cannabidiol in rats and humans. *Front Pharmacol*, 2017; 8: 140.
105. Deiana S, Watanabe A, Yamasaki Y, Amada N, Arthur M, Fleming S, Woodcock H, Dorward P, Pigliacampo B, Close S, Platt B, Riedel G. Plasma and brain pharmacokinetic profile of cannabidiol (CBD), cannabidivarine (CBDV) and cannabigerol (CBG) in rats and mice following oral and intraperitoneal administration and CBD action on obsessive–compulsive behaviour. *Psychopharmacology (Berl)*, 2012; 219(3): 859–873.
106. Zuardi AW, Crippa JA, Hallak JEC, Bhattacharyya S, Atakan Z, Martin-Santos R, McGuire PK, Guimarães FS. A critical review of the antipsychotic effects of cannabidiol: 30 years of a translational investigation. *Curr Pharm Des.*, 2012; 18(32): 5131–5140.
107. Madras BK. Update of cannabis and its medical use. *World Health Organization Drug Dependence Committee Report*, 2015.
108. Taylor L, Gidal B, Blakey G, Tayo B, Morrison G. A phase I, randomized, double-blind, placebo-controlled, single ascending dose, multiple dose, and food effect trial of the safety, tolerability, and pharmacokinetics of highly purified cannabidiol in healthy subjects. *CNS Drugs*, 2018; 32(11): 1053–1067.
109. Chesney E, Oliver D, Green A, Sovi S, Wilson J, Englund A, Freeman TP, McGuire P. Adverse effects of cannabidiol: A systematic review and meta-analysis of randomized clinical trials. *Neuropsychopharmacology*, 2020; 45(11): 1799–1806.
110. Leweke FM, Piomelli D, Pahlisch F, Muhl D, Gerth CW, Hoyer C, Klosterkötter J, Hellmich M, Koethe D. Cannabidiol enhances anandamide signaling and alleviates psychotic symptoms of schizophrenia. *Transl Psychiatry*, 2012; 2: e94.
111. Borgelt LM, Franson KL, Nussbaum AM, Wang GS. The pharmacologic and clinical effects of medical cannabis. *Pharmacotherapy*, 2013; 33(2): 195–209.
112. Zuardi AW, Hallak JEC, Crippa JAS. Interaction between cannabidiol (CBD) and Δ⁹-tetrahydrocannabinol (THC): Influence of administration order and dose ratio on human performance. *Psychopharmacology (Berl)*, 2017; 234(17): 2685–2696.
113. Food and Drug Administration (FDA). *FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD).* Silver Spring, MD: U.S. Food & Drug Administration, 2023.
114. Pertwee RG. The diverse CB_1 and CB_2 receptor pharmacology of three plant cannabinoids: Δ⁹-tetrahydrocannabinol, cannabidiol, and Δ⁹-tetrahydrocannabivarin. *Br J Pharmacol*, 2008; 153(2): 199–215.
115. European Medicines Agency (EMA). *Guideline on Quality of Herbal Medicinal Products Containing Cannabis and Cannabinoids.* Amsterdam: EMA, 2024.