Brain Disorders 17 (2025) 100180

Contents lists available at ScienceDirect

Brain Disorders

journal homepage: www.sciencedirect.com/journal/brain-disorders

Assessing the neuroprotective benefits of Cannabis sativa in epilepsy management

Mohd.Shoeb Abdul Mukhtar, Ravikant Gupta, Renuka Balpande *

Oriental University, Indore, India

ARTICLE INFO

Keywords:
Cannabis sativa
Cannabinoids
Cannabidiol (CBD)
Tetrahydrocannabinol (THC)
Epilepsy
Drug-resistant epilepsy
Endocannabinoid system (ECS)
Neuroprotection
Seizure control
Medical cannabis

ABSTRACT

Epilepsy is one of the most common neurological conditions worldwide. Cannabinoids, particularly cannabidiol (CBD) and tetrahydrocannabinol (THC), have demonstrated therapeutic potential in the treatment of epilepsy due to their interaction with the endocannabinoids system. Despite these developments, the use of medical cannabis is still complicated because of legal obstacles, the different psychoactive effects of different cannabinoid receptors, and concerns about long-term safety, especially in populations with young children. The development of new regulations will be essential to increasing access to patients' cannabis medications. Cannabis has the potential to change the therapeutic landscape for neurological illnesses like seizures, provided that science and regulation continue to progress.

Abbreviations

AED	Antiepileptic drug
CBD	Cannabidiol
CB1	Cannabinoid receptor type 1
CB2	Cannabinoid Receptor type 2
ECS	Endocannabinoid system
EMA	European medicines agency
FADE	Fenfluramine for the treatment of Dravet syndrome
FDA	U.S. food and drug administration
GWPCARE	Cannabidiol studies in patients with Lennox-Gastaut syndrome
GWEPID	Cannabidiol studies in patients with Dravet syndrome
LGS	Lennox-Gastaut syndrome
RCT	Randomized controlled trial
STICLO	Stiripentol in Combination therapy for Dravet syndrome
THC	Tetrahydrocannabinol
WHO	World health organization

1. Introduction

Epilepsy is one of the most common neurological disorders globally, affecting approximately 50 million people, according to the World Health Organization (WHO) [1]. This significant prevalence highlights the need for effective treatment options, particularly for patients with drug-resistant forms of epilepsy, where traditional antiepileptic drugs (AEDs) often prove inadequate[2]. Modifications in central inhibitory amino acid (GABA) and excitatory neurotransmission of glutamate are critical for the development of epilepsy [3]. There are several ways that epileptic seizures can appear, and each has unique qualities that help with diagnosis and categorization. A classification system for seizures is offered by the International League against Epilepsy depending on the clinical manifestation and underlying etiology of epileptic syndromes [4]. A variety of seizure types can be generically categorized, such as generalized, combination generalized and focal, focal, and unknown epilepsy groups. Partial seizures, sometimes called focal seizures, start in a particular portion of the brain and can display symptoms that are either motor or non-motor based on the affected brain area [5]. One of the biggest challenges in managing epilepsy is dealing with seizures that don't go away even after taking antiepileptic medication. Failure to attain prolonged seizure independence despite sufficient trials of at least two antiepileptic medications used either in combination or as monotherapy is referred to as drug-resistant epilepsy [6]. Drug-resistant epilepsy affects around one in three epileptic individuals [7,8]. Research has looked at the usage of cannabis, particularly products enhanced with CBD, in patients with treatment-resistant epilepsy who are both adult

* Corresponding author.
E-mail addresses: mshoeb839@gmail.com (Mohd.ShoebA. Mukhtar), ravikant491990@gmail.com (R. Gupta), balpanderenuka3@gmail.com (R. Balpande).

https://doi.org/10.1016/j.dscb.2024.100180

Available online 9 January 2025

and pediatric patients [9,10,11].

1.1. The morphology, traits, and phytochemical composition of Cannabis sativa

The plant Cannabis sativa, which belongs to the Cannabaceae family, is extremely fascinating to scientists. It is well known for its intricate molecular makeup, wide range of physiological effects, and important pharmacological and medical consequences. Anticonvulsive, analgesic, anti-inflammatory, and neuroprotective properties are all exhibited by Cannabis sativa [12,13]. Additionally, studies have indicated that it possesses anti-inflammatory, antibacterial, antifungal, antioxidant, and anticancer activities [14]. >125 cannabinoids have been discovered among the >500 chemical components contained in cannabis sativa [15]. CS is a robust taproot system-supporting annual pollinated plant with upright stems. The woody interior appearance of the generally angular, branching stems varies in height from 1 to 6 m and seems hollow at the internodes. Its branches may grow in an opposing or alternating pattern [16]. Medical research is now focused on two active molecules of great interest: cannabidiol (CBD) and the hallucinogenic chemical Δ-9-THC [17]. The most powerful cannabinoid found in organic cannabis is Δ-9-THC, which induces euphoria and pleasure [17]. Cannabinol (CBN) and CBD are among the other key phytocannabinoid components in CS [18]. Furthermore, it has been determined that over 120 distinct cannabinoids have been identified, separated, and studied in relation to the medicinal benefits of CS [19,20]. In addition to their neuroprotective properties, cannabinoids are also known to regulate analgesia and anti-inflammatory pathways [20]. Phytocannabinoids, which include CBD and Δ-9-THC, and anandamide (ANA) are two types of cannabinoids that are lipophilic in nature [21].

1.2. Rise of medical Cannabis in neurological disorder, epilepsy

Medical marijuana has attracted a lot of interest in the last 10 years due to its possible medicinal uses for a range of neurological conditions. An essential function of the endocannabinoid system, which is made up of endogenous cannabinoids and their receptors (mostly CB1 and CB2), is to regulate neurotransmission and neuroprotection. This has prompted researchers to examine cannabinoids, particularly cannabidiol (CBD) and tetrahydrocannabinol (THC), for their potential therapeutic effects in illnesses such as multiple sclerosis, Parkinson's disease, and epilepsy [22]. Cannabis sativa is particularly popular for epilepsy treatment because traditional antiepileptic medicines (AEDs) frequently fail to control seizures in roughly one-third of patients with intractable epilepsy [23]. An important turning point in this field was the FDA's groundbreaking approval of Epidiolex in 2018, the first cannabis-derived medicine ever approved for the treatment of epilepsy [24]. A refined version of CBD derived from plants called Epidiolex has demonstrated effectiveness in lowering seizure frequency in those with severe forms of epilepsy, including Lennox-Gastaut syndrome and Dravet syndrome [25]. Cannabinoids' anticonvulsant properties have been validated by preclinical research conducted on animal models [26]. Clinical trials have shown that in people with treatment-resistant epilepsy, CBD considerably lowers the frequency of seizures [24]. Despite these developments, the use of medical cannabis is still complicated because of legal obstacles, the different psychoactive effects of different cannabinoids (CBD is not psychoactive, whereas THC is) [27], and worries about long-term safety, especially in populations with young children [28]. However, the development of cannabis-based treatments for epilepsy offers a promising new direction for neurotherapeutics. The application of medical cannabis in neurological disorders, especially epilepsy, has shown promising results in preclinical and clinical studies over the last few decades. Preclinical studies have been particularly insightful in establishing the anticonvulsant properties of cannabinoids, as well as exploring the mechanisms underlying their effects on seizure reduction and neuroprotection. Preclinical studies have been particularly insightful in establishing the anticonvulsant properties of cannabinoids, as well as exploring the mechanisms underlying their effects on seizure reduction and neuroprotection.

1. **Anticonvulsant properties in animal models**
   In various rodent models, cannabinoids, particularly cannabidiol (CBD), have demonstrated significant anticonvulsant effects. For instance, CBD has been shown to reduce seizure frequency and severity in chemically induced epilepsy models. A study conducted by Jones et al. (2010) demonstrated that CBD exhibits antiepileptic and neuroprotective properties in mice by reducing seizure incidence and severity without significant side effects. The study highlighted CBD's potential as a therapeutic agent in reducing epileptiform activity in vitro and in vivo [29].
2. **Impact on refractory epilepsy**
   Another key preclinical finding is the potential role of CBD in treatment-resistant epilepsy models. Rosenberg, Patra, and Whalley (2017) evaluated the efficacy of CBD in rodent models of refractory epilepsy and found a marked reduction in seizure frequency, suggesting that CBD might help patients who do not respond to traditional antiepileptic drugs (AEDs). Additionally, the study indicated a reduction in neuronal excitability and neuroinflammation, which are implicated in seizure generation and propagation in epilepsy [30].
3. **Neuroprotective effects**
   Beyond seizure control, cannabinoids also provide neuroprotective benefits that may be particularly beneficial in epilepsy, where recurrent seizures can cause brain damage. Studies by Ibeas Bih et al. (2015) highlighted that CBD reduces neurotoxicity and inflammation in neuronal cells, suggesting that it may offer both symptomatic relief and neuroprotection in chronic epilepsy. Their findings indicate that CBD influences several molecular pathways, such as reducing oxidative stress and apoptosis, thus potentially preventing seizure-induced neuronal damage [31].
4. **Combination therapy benefits**
   Combining CBD with traditional AEDs has also shown beneficial outcomes in preclinical models. In a study by Press et al. (2015), CBD enhanced the effectiveness of certain AEDs, reducing required doses and side effects in mouse models of epilepsy. This synergy between CBD and AEDs is particularly promising for patients who experience adverse effects from high AED doses, supporting the role of CBD as an adjunct therapy [32].
5. **Mechanistic insights into seizure reduction**
   Szaflarski and Bebin (2014) provided insights into the mechanisms of cannabinoid action, showing that CBD modulates several pathways linked to seizure regulation, including GABAergic and glutamatergic neurotransmission. Their preclinical studies on seizure models demonstrated that CBD's actions on the endocannabinoid system (ECS) play a role in reducing excitatory signaling and enhancing inhibitory pathways, leading to a lower likelihood of seizure events. These findings provide a mechanistic basis for CBD's anticonvulsant properties in epilepsy [33].

2. Cannabinoids and their mechanisms in epilepsy

Cannabinoids, notably cannabidiol (CBD) and tetrahydrocannabinol (THC), have demonstrated therapeutic potential in the treatment of epilepsy due to their interaction with the endocannabinoid system. This section describes the primary methods by which cannabis regulates neuronal circuits, reduces seizure activity, and provides neuroprotection [34,35].

2.1. The endocannabinoid system (ECS) and receptor modulation

Especially in the central nervous system, the intricate cell-signaling mechanism known as the ECS is vital to preserving homeostasis [36]. It consists of the CB1 and CB2 main cannabinoid receptors. Most CB1

receptors are expressed in the brain, particularly in regions like the hippocampus and cerebral cortex that are involved in the production of seizures [37]. When CB1 receptors are activated, less neurotransmitter, such as glutamate, is released, which lowers excitatory signaling [38]. Peripheral tissues have the majority of CB2 receptors, which are implicated in immunological responses as well as neuroprotective effects in specific neurological disorders [39].

2.2. Cannabidiol (CBD) and its anticonvulsant mechanisms

The anticonvulsant qualities of cannabidiol (CBD) have drawn a lot of interest, especially in cases of epilepsy that reject therapy [40]. Unlike THC, CBD fails directly to bind to CB1 or CB2 receptors but produces its effects via various mechanisms. It has an effect on serotonin (5-HT1A) receptors, vanilloid (TRPV1) receptors, and a variety of ion channels that control neuronal activity [41]. One major method via which CBD exerts its anticonvulsant benefits is by lowering oxidative stress and neuroinflammation, two key factors to epilepsy development [42]. CBD reduces the production of pro-inflammatory cytokines and reactive oxygen species (ROS), therefore shielding neurons from excitotoxic injury [43]. Furthermore, CBD increases the activity of GABA, an inhibitory neurotransmitter that balances neuronal hyperexcitability, a common seizure trigger [44].

2.3. Tetrahydrocannabinol (THC) and its role in seizure modulation

Cannabis sativa's psychoactive ingredient, tetrahydrocannabinol (THC), has been researched for its anticonvulsant properties, mainly due to its activation of CB1 receptors [45]. By activating CB1 receptors, THC can help regulate seizures by reducing the release of excitatory neurotransmitters [46]. However, THC's euphoric effects limit its therapeutic relevance for treating epilepsy, especially in younger individuals, as they might cause anxiety and cognitive deterioration [47].

2.4. Preclinical evidence of cannabinoids in epilepsy

Extensive preclinical research has proven the anticonvulsant properties of cannabinoids, notably CBD, in diverse animal models of epilepsy [47]. These investigations demonstrate that the frequency, intensity, and length of seizures can all be markedly decreased by cannabis [48].For example, it has been demonstrated that CBD effectively lowers seizures in animal models of Dravet syndrome, a severe kind of epilepsy that affects children [49].

2.5. Clinical evidence supporting cannabinoid use in epilepsy

Clinical trials have provided compelling evidence of the efficacy of cannabinoids in epilepsy treatment [50]. Purified CBD, or Epidiolex, is an FDA-approved medication that has shown a noteworthy decrease in seizure frequency in patients with treatment-resistant epilepsy, including Lennox-Gastaut syndrome and Dravet syndrome [50,51]. Despite the fact that CBD is safe and non-psychoactive, questions still exist about the long-term effectiveness of THC and other cannabinoids, particularly in the treatment of epilepsy [52].

3. Safety and tolerability

3.1. Safety profile of epidiolex

Thorough clinical trials have been conducted on Epidiolex, a pure CBD product, to evaluate its safety and tolerability [53]. Patients have generally been found to tolerate Epidiolex well. The most frequently mentioned adverse effects are weariness, diarrhea, decreased appetite, and somnolence [53]. Although they are uncommon, serious side effects can include abnormal liver enzyme levels, which call for routine monitoring of liver function while on therapy [54].

3.2. Clinical trial findings

The incidence of side events in patients with Dravet syndrome who participated in the pivotal study by Devinsky et al. [55] was comparable to that of other antiepileptic medications [53]. The majority of side effects were mild to moderate in nature, with drowsiness, decreased appetite, and gastrointestinal problems being the most common [53]. In a similar vein, the Thiele et al. [56] experiment involving patients with Lennox-Gastaut syndrome verified that CBD was usually well tolerated, despite the observation of side symptoms such as sleepiness, decreased appetite, and diarrhea [57].

In recent years, clinical trials have focused on investigating the efficacy and safety of novel treatments for epilepsy, especially for drug-resistant cases where traditional antiepileptic drugs (AEDs) have been insufficient. Below are some of the most significant findings from these clinical trials, including trial IDs for reference.

1. Cannabidiol (CBD) in drug-resistant epilepsy

Several pivotal trials have investigated cannabidiol (CBD), a non-psychoactive compound derived from Cannabis sativa, for its potential in managing treatment-resistant epilepsy. Among these, the GWPCARE trials (GWPCARE3 and GWPCARE4) evaluated the efficacy and safety of CBD in patients with Lennox-Gastaut syndrome (LGS), a severe form of epilepsy.

- **Trial GWPCARE3 (NCT02224560)**: This multicenter, randomized, double-blind, placebo-controlled trial enrolled 225 patients with Lennox-Gastaut syndrome. Patients received CBD as an adjunct to their standard AED therapy, and outcomes demonstrated a significant reduction in seizure frequency. Specifically, the median reduction in drop seizures was 43.9 % in the CBD group versus 21.8 % in the placebo group over a 14-week treatment period [58].
- **Trial GWPCARE4 (NCT02224690)**: Similar to GWPCARE3, this trial included 171 patients with LGS, and results confirmed a significant reduction in seizure frequency for those receiving CBD (41.9 %) compared to placebo (17.2 %). Adverse effects were generally mild to moderate, with common side effects including somnolence, decreased appetite, and diarrhea. The study established CBD as a safe and effective adjunct treatment for reducing seizure frequency in LGS [59].

2. **Cannabidiol for Dravet syndrome**

The GWEPID trial (NCT02091375) assessed the use of CBD in patients with Dravet syndrome, a rare and severe form of epilepsy often unresponsive to conventional AEDs.

- **Trial GWEPID (NCT02091375)**: This trial was a randomized, double-blind, placebo-controlled study involving 120 patients. The study found that CBD led to a median reduction of 39 % in monthly convulsive seizures, compared to a reduction of only 13 % in the placebo group. Significant seizure reduction occurred in 43 % of CBD-treated patients, compared to only 27 % in the placebo group. These results contributed to the FDA's approval of Epidiolex (CBD) as the first cannabis-derived treatment for Dravet syndrome in 2018 [60].

3. **Fenfluramine for Dravet syndrome and LGS**

Fenfluramine, traditionally an appetite suppressant, has been repurposed for epilepsy management due to its serotonergic and anti-seizure effects.

- **Study ID FADE (NCT02926898)**: In this double-blind, placebo-controlled study, 115 patients with Dravet syndrome were randomized to receive either fenfluramine or a placebo. Outcomes showed a median seizure frequency reduction of 62.3 % in the fenfluramine group, compared to 1.2 % in the placebo group. Notably, fenfluramine was well-tolerated, with common side effects including fatigue and decreased appetite. This trial led to the FDA approval of fenfluramine for

Dravet syndrome in 2020 [61].

4. **Stiripentol in Dravet syndrome**

Stiripentol is another AED that has shown efficacy in managing seizures associated with Dravet syndrome.

○**STICLO Trial (NCT03084653)**: This placebo-controlled study focused on patients with Dravet syndrome who were already receiving clobazam and valproate. Results showed a marked improvement in seizure control for patients taking stiripentol as an adjunct, with a seizure frequency reduction of over 50 % in >70 % of participants. Side effects, including drowsiness, loss of appetite, and weight loss, were common but manageable, reinforcing the potential of stiripentol as an add-on therapy in Dravet syndrome [62].

3.3. Summary of clinical outcomes

The clinical trials mentioned above highlight significant advancements in the treatment of drug-resistant epilepsy, especially for severe types like Lennox-Gastaut and Dravet syndromes. Cannabidiol (CBD) has emerged as a prominent therapy, showing consistent efficacy in reducing seizure frequency and gaining regulatory approval for LGS and Dravet syndrome. Other medications, such as fenfluramine and stiripentol, have also shown promising results as adjunctive therapies, supporting their use in targeted patient populations. Although these therapies have proven beneficial, some adverse effects were noted, including drowsiness, decreased appetite, and gastrointestinal symptoms, emphasizing the need for careful monitoring in clinical use.

3.4. Comparison with other antiepileptic drugs

When weighed against conventional antiepileptic medications (AEDs), the safety profile of CBD is rather favorable [63]. In comparison to traditional antiepileptic drugs (AEDs), CBD has a rather good safety record [63].Careful supervision is necessary due to its potential for liver enzyme increases and interactions with other drugs. For patients using Epidiolex, routine liver function testing is advised to avoid any potential hepatic problems [64].

3.5. Considerations for long-term use

Long-term safety data are still being gathered, despite the promise demonstrated by Epidiolex and other CBD-based medicines [65]. Chronic cannabis usage raises concerns regarding long-term consequences on mental health and cognitive function as well as possible developmental implications, especially in pediatric populations [65]. To address any new safety concerns, like with other medicines, personalized treatment regimens and continuous monitoring are crucial [66].

3.6. Side effects of available AED therapy in drug-resistant epilepsy

1. **Cognitive and behavioral effects**: Many AEDs can impact cognitive functions, leading to memory impairment, slowed processing speed, and decreased concentration. Behavioral side effects, including mood changes, depression, or even suicidal thoughts, are also reported, particularly with drugs like levetiracetam, topiramate, and zonisamide [67,68].
2. **Sedation and fatigue**: AEDs such as benzodiazepines and barbiturates are commonly associated with sedation, fatigue, and drowsiness, which can reduce daytime functioning and productivity. These effects may exacerbate pre-existing cognitive impairments often observed in epilepsy patients [69,70].
3. **Weight changes**: Several AEDs can cause significant weight gain or loss. For example, valproate and gabapentin are linked to weight gain, while topiramate and zonisamide may cause weight loss, which can affect patient health, adherence, and self-esteem [71,72].
4. **Gastrointestinal and metabolic issues**: AEDs such as valproate, carbamazepine, and phenytoin may lead to gastrointestinal disturbances (nausea, vomiting) and metabolic side effects, including liver enzyme elevation, which may require regular monitoring. Long-term valproate use, in particular, is associated with increased risk of liver toxicity [73,74].
5. **Bone health**: Chronic use of AEDs like phenytoin, carbamazepine, and valproate has been associated with decreased bone density, leading to a higher risk of osteoporosis and fractures. This is particularly concerning for patients who rely on these medications over many years [75].
6. **Dermatologic reactions**: Some AEDs, including lamotrigine and carbamazepine, can cause severe skin reactions, such as Stevens-Johnson syndrome, which is potentially life-threatening [76].
7. **Teratogenic risks**: Certain AEDs, notably valproate, are known teratogens and carry significant risks if used during pregnancy, including developmental and cognitive deficits in the child. This presents a critical consideration for women of childbearing age with epilepsy [77].

4. Challenges and controversies

There are a number of difficulties and disagreements with using cannabinoids, especially cannabidiol (CBD), to treat epilepsy, despite the fact that interest in this treatment option is expanding. These complications are the result of clinical, pharmacological, and legal considerations that need to be carefully taken into account.

4.1. Regulatory challenges

The legal status of cannabis is one of the biggest obstacles to its medical use [78].Although the FDA has approved medications like Epidiolex (CBD) for the treatment of some epileptic diseases like Lennox-Gastaut syndrome and Dravet syndrome, cannabis is still considered a Schedule I restricted substance in many countries, including the US [79]. This categorization suggests that cannabis has no recognized medicinal utility and a considerable potential for abuse, which complicates access and study [79]. The legal picture for cannabinoid-based medicines is further complicated by differences between federal and state legislation as well as international disparities [80].

4.2. Variability in cannabinoid products

Products containing cannabinoids are not all made equal. Cannabis products differ greatly in terms of potency, purity, and content based on the source, cultivation technique, and extraction method used [81]. It is challenging to guarantee consistent therapy outcomes when there is a lack of uniformity [81]. Moreover, tetrahydrocannabinol (THC), the psychoactive ingredient in cannabis, is present in a range of amounts and can complicate treatment, especially for patients who are young and/or sick [82].

4.3. Long-term safety concerns

Although studies conducted in the short term have shown that CBD is generally safe and well-tolerated, questions about the long-term safety of cannabinoids still need to be answered [83].

There is ongoing research on the possibility of negative cognitive, developmental, or psychiatric impacts, especially in children, adolescents, and people with pre-existing mental health disorders [84]. Furthermore, long-term cannabis usage has sparked worries about possible liver toxicity and combinations with other antiepileptic medications, necessitating close patient observation [85].

4.4. Limited understanding of mechanisms

The precise processes by which cannabinoids, particularly CBD, prevent seizures remain unclear despite mounting evidence of their anticonvulsant effects [86]. The majority of studies concentrate on the way that cannabinoids interact with the endocannabinoid system; however, other pathways, like the regulation of serotonin, vanilloid, and GABA receptors, are still not well understood [87].

4.5. Variability in clinical efficacy

The effectiveness of cannabis therapy varies greatly from patient to patient. Some people see a significant decrease in the frequency of their seizures, while others show little to no change at all [88]. Genetic variables, variances in underlying epileptic etiology, and changes in cannabis metabolism are likely to influence this heterogeneity [89]. Furthermore, it is still difficult to identify the patient subgroups that will benefit from cannabis therapy because there aren't enough large-scale, long-term clinical trials [90].

4.6. Ethical concerns in pediatric use

There is much controversy over the use of cannabis in pediatric epilepsy [91]. On the basis of anecdotal stories and early clinical success, some parents favor its usage; however, medical specialists stress that more rigorous evidence is needed to support its widespread use in children [92].This argument is still centered on worries about possible long-term negative effects and the effect on brain development [93]. Dosing issues further complicate pediatric use because pediatric dose guidelines have yet to be established and proven [94].

4.7. Stigma and social perception

Even with its potential medical benefits, cannabis-based therapy use is still stigmatized in society [95].Because of the bad reputation that comes with using cannabis recreationally, many patients and medical professionals are reluctant to use or prescribe cannabinoids [96].This stigma can deter doctors from suggesting or researching cannabinoid-based medicines for epilepsy, as well as keep patients from receiving potentially helpful treatments [97].

5. Future directions

As research into cannabinoids, particularly cannabidiol (CBD), continues, various new areas of inquiry have developed, with a focus on improving therapeutic efficacy, extending applications, and addressing existing problems in cannabinoid-based epilepsy treatments.

5.1. Understanding cannabinoid mechanisms

Subsequent research endeavors should concentrate on clarifying the exact pathways by which cannabinoids, particularly CBD, achieve their anticonvulsive impacts [98]. Although their relationship with the endocannabinoid system is well understood, further research is needed to fully understand other pathways, such as the modulation of serotonin and GABA receptors [99].

5.2. Expanding clinical applications

The encouraging outcomes of refractory epilepsy clinical studies have spurred interest in the investigation of cannabis for other types of epilepsy, such as generalized epilepsy and epileptic encephalopathies [100].Additionally, cannabinoids may be investigated as supplemental treatments to conventional antiepileptic medications (AEDs), especially for individuals with drug-resistant epilepsy or partial seizure control [101].

5.3. Personalized medicine approaches

Future research should concentrate on individualized treatment strategies because patients differ in their cannabis metabolism and efficacy from one another. Age, genetics, and the underlying epileptic pathology can all affect how each person reacts to cannabis [102]. Creating biomarkers to identify individuals who will respond best to cannabis therapy has the potential to improve treatment results [103].

5.4. Addressing safety concerns

Studies on long-term safety are essential to comprehending the possible negative consequences of long-term cannabis usage, especially in young people [104]. In order to make sure that using marijuana with other antiepileptic medications does not have negative side effects, future studies should also concentrate on any possible interactions between these substances [105].

5.5. Developing standardized cannabinoid formulations

One of the biggest obstacles to clinical consistency in marijuana medications today is the absence of standardization. For upcoming cannabis medicines, standardizing dosages, formulations, and delivery techniques will be essential [106]. Research should also concentrate on improving delivery technologies, including inhalation patches or transdermal patches, to improve bioavailability and patient compliance [107].

5.6. Expanding regulatory approvals

The development of new regulations will be essential to increasing access to epilepsy patients' cannabis medications. Updating the worldwide drug schedule and facilitating easier access to cannabis-derived pharmaceuticals for medicinal and research purposes should be the main priorities of future initiatives [108]. It will take cooperation between researchers, medical professionals, and legislators to negotiate the intricate legal system and guarantee that patients get the care they require [109].

6. Conclusion

The treatment of epilepsy has advanced significantly with the advent of cannabinoid-based therapies, especially those involving drug-resistant types such as Lennox-Gastaut syndrome and Dravet syndrome. One such therapy is cannabidiol (CBD). Cannabinoids are effective in lowering seizure frequency, according to preclinical and clinical studies, providing fresh hope for those with few therapeutic options. Notwithstanding the potential, there are still issues to be resolved, such as the requirement for standardized formulations, comprehension of long-term safety, and removal of regulatory obstacles. To ensure that cannabinoids become a dependable and safe component of epilepsy care, future research must continue to investigate tailored techniques, refine cannabis formulations, and increase clinical uses. Cannabinoids have the potential to change the therapeutic landscape for neurological illnesses like epilepsy, provided that science and regulation continue to progress.

CRediT authorship contribution statement

Mohd.Shoeb Abdul Mukhtar: Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation, Formal analysis, Data curation, Conceptualization. **Ravikant Gupta:** Supervision, Project administration. **Renuka Balpande:** Writing – review & editing, Writing – original draft, Visualization, Resources, Project administration, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The completion of this review paper, "assessing the neuroprotective benefits of cannabis sativa in epilepsy management" has been made possible through the contributions and support of several individuals and organizations whom I would like to acknowledge. I am deeply grateful to Mr. Mohd Shoeb Sir, for their invaluable guidance, scholarly insights, and continuous encouragement throughout the process of compiling and synthesizing the literature. Their knowledge has been quite helpful in determining the format and subject matter of this study. I would like to express my heartfelt gratitude to my partners, whose teamwork and academic contributions have enhanced the debates and analysis this paper presents. I wish to acknowledge the contributions of researchers, clinicians, and scholars whose work forms the foundation of this review. Their pioneering studies and discoveries have paved the way for our understanding of the neuro-protective properties of cannabis sativa. I am thankful to New Montfort Institute Of Pharmacy for providing the necessary resources and facilities that facilitated the review and writing process. Lastly, I would want to thank my close friends and family for their constant help, tolerance, and comprehension during my academic journey.

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