AG EDITOR

REVIEW

The use of cannabidiol in epilepsy: therapeutic and legal advances

El uso del cannabidiol en la epilepsia: avances terapéuticos y legales

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ABSTRACT

Epilepsy was defined as a chronic neurological condition characterised by spontaneous and repeated epileptic seizures. Its diagnosis was based on criteria established by the International League Against Epilepsy (ILAE), such as the occurrence of multiple unprovoked seizures or the identification of an epileptic syndrome. The classification of epilepsy allowed treatments to be individualised according to the type of seizure, although a significant percentage of patients presented refractory epilepsy, with no adequate response to conventional medication. Over recent decades, interest in new therapies has increased, including cannabidiol (CBD), a non-psychoactive compound from the Cannabis sativa plant. Preclinical and clinical research has demonstrated its anticonvulsant and neuroprotective potential and its role as a modulator of the endocannabinoid system, especially in severe epileptic syndromes such as Lennox-Gastaut and Dravet. CBD acted without directly binding to the classic receptors of the endocannabinoid system, which broadened its therapeutic potential in other conditions, such as anxiety, chronic pain, inflammatory and neurodegenerative diseases. In Argentina, legal progress was made in the medicinal use of cannabis. Law 27.350 and Decree 883/2020 allowed regulated access to CBD, including self-cultivation for therapeutic purposes. In 2022, Law 27.669 promoted the industrial development of medicinal cannabis, with the creation of the ARICCAME agency. Despite this progress, it was still considered essential to continue researching in order to understand the mechanisms of CBD, define its safe doses and evaluate its long-term effectiveness.

Keywords: Epilepsy; Cannabidiol; Treatment; Legislation; Neuroprotection.

RESUMEN

La epilepsia fue definida como una condición neurológica crónica caracterizada por crisis epilépticas espontáneas y repetidas. Su diagnóstico se basó en criterios establecidos por la Liga Internacional Contra la Epilepsia (ILAE), como la ocurrencia de múltiples crisis no provocadas o la identificación de un síndrome epiléptico. La clasificación de la epilepsia permitió individualizar los tratamientos según el tipo de crisis, aunque un porcentaje significativo de pacientes presentó epilepsia refractaria, sin respuesta adecuada a los medicamentos convencionales. Durante las últimas décadas, se incrementó el interés por nuevas terapias, entre ellas el cannabidiol (CBD), un compuesto no psicoactivo de la planta Cannabis sativa. Investigaciones preclínicas y clínicas demostraron su potencial anticonvulsivante, neuroprotector y modulador del sistema endocannabinoide, especialmente en síndromes epilépticos severos como Lennox-Gastaut y Dravet. El CBD actuó sin unirse directamente a los receptores clásicos del sistema endocannabinoide, lo que amplió su potencial terapéutico en otras condiciones, como ansiedad, dolor crónico, enfermedades inflamatorias y neurodegenerativas. En Argentina, se avanzó legalmente en el uso medicinal del cannabis. La Ley 27.350 y el Decreto 883/2020 permitieron el acceso regulado al CBD, incluyendo el autocultivo con fines terapéuticos. En 2022, la Ley 27.669 impulsó el desarrollo industrial del cannabis medicinal, con la creación de la agencia

ARICCAME. A pesar de estos progresos, aún se consideró esencial continuar investigando para comprender los mecanismos del CBD, definir sus dosis seguras y evaluar su eficacia a largo plazo.

Palabras clave: Epilepsia; Cannabidiol; Tratamiento; Legislación; Neuroprotección.

INTRODUCTION

The occurrence of spontaneous and repeated epileptic seizures characterizes epilepsy. According to the International League Against Epilepsy (ILAE),[1] for a diagnosis of epilepsy, at least one of the following criteria must be met: the occurrence of at least two unprovoked seizures within 24 hours; a single unprovoked seizure and, within a decade after two unprovoked seizures, a risk of at least 60 % of having another similar seizure; or the recognition of an epileptic syndrome.[2]

The categorization of epilepsy is based on three aspects: the nature of the seizure, the type of epilepsy, and the diagnosis of specific epileptic syndromes. Identifying the cause of epilepsy is crucial to defining the most effective treatment. Potential causes are grouped into six categories: structural, genetic, infectious, metabolic, immunological, or unknown, and the condition may be caused by one or more of these causes.[3] The most appropriate treatment or therapy can be selected after determining the cause through tests such as electroencephalogram (EEG), genetic testing, and brain imaging.[3]

Over the past two decades, there has been an increase in the variety of medications available to treat epilepsy. However, even with more medication options, current treatments are still not effective for patients with epilepsy who do not respond to drugs (known as refractory epilepsy), as most work through mechanisms similar to those already in place.[4] It is important to note that treatment may vary throughout the patient's life. Pharmacotherapy is mainly used to reduce or manage the symptoms of epilepsy, not as a cure for the disease.[5]

Therefore, the therapeutic goal of antiepileptic drugs is to reduce the frequency of epileptic seizures while minimizing the adverse effects associated with the use of these drugs, which are generally cognitive.

A significant obstacle in the management of epilepsy is the difficulty in changing the processes that cause seizures (ictogenesis) and the development of the disease after brain damage (epileptogenesis). Research in rodents has revealed neuroprotective properties of cannabidiol (CBD), suggesting a possible effect on the alteration of the pathology and related comorbidities based on a model of temporal lobe epilepsy.[6]

DEVELOPMENT

Epilepsy is a chronic neurological condition characterized by the recurrence of unprovoked epileptic seizures. According to the International League Against Epilepsy (ILAE), the diagnostic definition is based on specific clinical criteria, including the occurrence of two or more unprovoked seizures more than 24 hours apart or a seizure with a high risk of recurrence, as well as the recognition of an epileptic syndrome.[2]

The ILAE has refined the classification of epilepsy and seizure types,[3] allowing for better individualization of pharmacological treatment. This treatment should aim primarily to reduce seizure frequency without causing significant cognitive adverse effects.[5] However, a large percentage of patients have refractory epilepsy, meaning that they do not respond adequately to conventional treatments.[4]

In this context, there has been growing interest in using cannabidiol (CBD) as a therapeutic alternative. Several preclinical and clinical studies have shown that CBD has anticonvulsant, neuroprotective, and endocannabinoid system-modulating properties, especially in severe epileptic syndromes such as Lennox-Gastaut and Dravet syndromes.[6,7,8]

Medicinal Cannabidiol

Cannabidiol (CBD) is one of the main non-psychoactive compounds in the Cannabis sativa plant. Unlike tetrahydrocannabinol (THC), CBD does not produce psychotropic effects, which has made it a focus of interest for the development of safe and effective medical treatments. This cannabinoid has been the subject of numerous studies due to its potential therapeutic properties in various diseases.[9,10,11]

To understand the medicinal use of CBD, it is necessary to understand the endocannabinoid system, a complex cell signaling system in the human body that participates in functions such as pain, mood, sleep, memory, and immune response.[12,13,14,15]

CB1 and CB2 receptors are distributed mainly in the central nervous and immune systems
- Endocannabinoids: natural substances in the body that bind to these receptors.
- Enzymes: responsible for the synthesis and degradation of endocannabinoids.

CBD modulates this system, although it does not bind directly to CB1 or CB2 receptors. Instead, it interacts with other receptors and ion channels, which explains its diverse therapeutic potential.

CBD has shown potential benefits in the treatment of various medical conditions, including:

- Epilepsy: especially in forms resistant to conventional treatment, such as Dravet syndrome and Lennox-Gastaut syndrome. Epidiolex, a CBD-based drug, has been approved by the FDA for these cases.[16]
- Anxiety and sleep disorders: Studies suggest that CBD may reduce anxiety levels and improve sleep quality without the side effects of traditional anti-anxiety medications.[17]
- Chronic pain and inflammatory diseases: CBD has been found to have analgesic and anti-inflammatory effects and is helpful in arthritis, fibromyalgia, and multiple sclerosis.[18]
- Neurodegenerative disorders: Preliminary research suggests that CBD may have a neuroprotective role in diseases such as Alzheimer's and Parkinson's.[19]
- Cancer: Although still under study, its ability to relieve symptoms related to cancer treatment (nausea, vomiting, pain) and its potential antitumor effect have been explored.[20]

The legal status of medical CBD

The regulation of CBD's medicinal use varies considerably between countries. In some, such as the United States, Canada, Germany, Colombia, and Uruguay, its use is permitted under medical prescription or as a supplement. In Latin America, several countries have begun to regulate access to CBD for patients with chronic or rare diseases.[21]

In Argentina, cannabis legislation has advanced in recent years, especially regarding its medicinal use. Law 27.350 (2017) regulates the medical and scientific use of cannabis.[22]

This law was expanded in 2020 through Decree 883/2020, allowing self-cultivation for therapeutic purposes, both individually and through civil associations (registered with REPROCANN). The Cannabis Program Registry (REPROCANN) allows patients and authorized growers to produce and transport cannabis for medicinal use without penalty.[23]

Using oils, creams, and other derivatives is permitted under medical prescription.[24]

Those who cultivate without registration may face criminal penalties under the Drug Law (23.737).[25]

Possession of cannabis for personal consumption remains illegal, although case law has been changing:

- In 2009, the Supreme Court's "Arriola" ruling declared it unconstitutional to criminalize the possession of small amounts for personal consumption in private settings.[26]
- In 2022, Law 27.669 was passed, creating the legal framework for the development of the medical cannabis and industrial hemp industry.[27]
- ARICCAME (Regulatory Agency for the Hemp and Medical Cannabis Industry) was created to regulate production, marketing, and industrialization.[28]

The medicinal use of CBD represents a transformation in how many diseases are understood and treated. However, more research is still needed to precisely define its indications, dosages, routes of administration, and long-term effects.[29] Advances in scientific evidence and an appropriate legal framework will allow for greater integration of CBD into modern medicine.[30,31]

CONCLUSIONS

Epilepsy continues to be a significant medical challenge, especially in cases where conventional treatments fail to control epileptic seizures effectively. In this context, cannabidiol (CBD) has emerged as a promising therapeutic alternative, supported by growing scientific evidence highlighting its anticonvulsant and neuroprotective properties and its safety profile. In addition, regulatory developments in countries such as Argentina have allowed greater access to CBD for medicinal purposes, marking a paradigm shift in the approach to chronic neurological diseases. Despite these advances, further research is essential to establish its efficacy, mechanisms of action, and potential long-term effects to safely and effectively integrate CBD into current therapeutic regimens.

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CONFLICT OF INTEREST
None.

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