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Cannabidiol in Clinical Practice: Scientific Evidence, Therapeutic Applications, and Regulatory Challenges

Cannabidiol In Clinical Practice: Scientific Evidence, Therapeutic Applications And Regulatory Challenges

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Summary

Cannabidiol (CBD), a phytocannabinoid derived from Cannabis sativa, has been attracting increasing interest in contemporary clinical practice. This structured narrative review synthesizes scientific evidence on clinical applications, safety, drug interactions, and Brazilian regulatory aspects.
Robust evidence supports its use in refractory epilepsies, especially in Dravet and Lennox-Gastaut syndromes. In chronic pain, spasticity, and anxiety, the data are heterogeneous. It is concluded that CBD should be used on an individualized basis, with clinical monitoring and scientific justification.

Keywords: cannabidiol; endocannabinoid system; refractory epilepsy; chronic pain; health regulations.

Abstract

Cannabidiol (CBD), a phytocannabinoid derived from Cannabis sativa, has been attracting increasing interest in contemporary clinical practice. This structured narrative review synthesizes scientific evidence on clinical applications, safety, drug interactions, and Brazilian regulatory aspects. Robust evidence supports its use in refractory epilepsies, especially in Dravet and Lennox-Gastaut syndromes. In chronic pain, spasticity, and anxiety, the data is heterogeneous. It is concluded that CBD should be used in an individualized manner, with clinical monitoring and scientific basis.
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1. INTRODUCTION

Scientific interest in cannabidiol has grown exponentially in recent decades1,[2].

Unlike THC, CBD does not exhibit classic psychoactive effects[1]. The identification of

The endocannabinoid system has revealed a complex regulatory mechanism between CB1 and CB2 receptors.

endocannabinoids and manipulation enzymes1,ÿ,ÿ.

Scientific clinical trials have proven the efficacy of CBD in refractory epilepsiesÿÿÿ. Outside

In this context, the evidence remains heterogeneous.10 In Brazil, its use is regulated by RDC No.

327/2019 from ANVISA[11].

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2. THEORETICAL FOUNDATION

2.1 Endocannabinoid System

The endocannabinoid system is composed of CB1 receptors (predominant in the CNS) and CB2 receptors. (primarily in the immune system)1,ÿ. Its main ligands are anandamide and 2-AGÿ.

2.2 Pharmacology of Cannabidiol

CBD has a low outer layer due to CB1 and CB2, acting as an indirect modulator1,ÿ. Interaction with 5-HT1A, TRPV1 and PPAR-ÿÿ receptors,11³.

It is predominantly metabolized via CYP3A4 and CYP2C191ÿ, which implies potential drug interactions.

3. ESTABLISHED CLINICAL APPLICATIONS

3.1 Dravet Syndrome

A randomized study demonstrated a median reduction of 39% in seizures with CBD 20 mg/kg/dayÿ.

3.2 Lennox-Gastaut Syndrome

Reduction of atonic seizures between 37% and 42% compared to placeboÿ,ÿ.

Practical application

- Initial dose: 2.5 mg/kg 2x/day
- Titration up to 10–20 mg/kg/day
- Monitor transaminases

4. OTHER CLINICAL APPLICATIONS

Although the use of cannabidiol is formally established in refractory epilepsies specificÿÿÿ, the expansion of its clinical use has occurred in multiple areas of medicine. In However, the robustness of the evidence varies considerably across the borders, making it essential

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distinguish between biological plausibility, preliminary evidence, and trial-based recommendations.
high-quality methodological clinical practices.

Furthermore, in several clinical conditions, the most significant results were reported.
with combined formulations of CBD and THC, which requires critical analysis regarding the contribution.
specific to each component[1ÿ].

4.1 Chronic Pain

Chronic pain is one of the main medical indications for products derived from...
Cannabis is present in various countries. The endocannabinoid system participates in the modulation of nociception in both
at both peripheral and central levels[1,ÿ]. The activation of CB1 receptors in ascending pain pathways and the
Modulation of inflammatory mediators via CB2 supports the biological rationale for therapeutic use.

A systematic review and meta-analysis conducted by Whiting et al.[1ÿ] demonstrated benefit
Statistically significant effects of cannabinoids in chronic pain, particularly neuropathic pain.
However, most of the studies evaluated used combined formulations containing THC.

4.1.1 Neuropathic Pain

Neuropathic pain, especially associated with diabetic neuropathy, post-herpetic neuralgia and
Central post-stroke pain appears to be the subgroup with the best response. The analgesic effect is probably
This stems from:

- Reduction of neuronal hyperexcitability
- Glutamatergic modulation
- Activation of central CB1 receptors[1,ÿ]
- TRPV1 Desensitization[13]

Isolated CBD exhibits potential anti-inflammatory and ion channel modulating properties, however.
Clinical results are less consistent when compared to combined formulations[10].

4.1.2 Practical Considerations

In patients with refractory neuropathic pain:

- A balanced CBD/THC ratio (e.g., 1:1) can be considered.
- Start with 2.5 mg of THC at night combined with an equivalent dose of CBD.
- Gradually administer the title based on response.
- Monitor for dizziness, drowsiness, and cognitive changes.

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In elderly patients or patients with psychiatric risk, formulations with a predominance of...
CBD.

4.2 Spasticity in Multiple Sclerosis

Spasticity associated with multiple sclerosis is another area with moderate evidence.
for the use of cannabinoids[1]ÿ. The mechanism involves a reduction in motor excitability via receptors
CB1 in the spinal cord1,ÿ.

Studies with combined extracts have demonstrated subjective improvement in spasticity and
Reduction in the frequency of muscle spasms. However, outcomes are often based on...
in self-reported scales, which can introduce bias.

4.2.1 Clinical Implications

• Primarily indicated for refractory spasticity.
• Start with the nighttime dose
• Monitor for fall risk
• Assess actual functional benefit

4.3 Anxiety Disorders

CBD interacts with 5-HT1A receptorsÿ, a mechanism associated with the modulation of
anxiety. A clinical study demonstrated a significant reduction in anxiety during a public speaking test with
single dose of 600 mg[12].

However, long-term studies with large samples are lacking. Current evidence suggests
It has potential as an anxiolytic, but it does not replace established therapies.

4.3.1 Practical Considerations

• Indicated as an adjunct in refractory anxiety disorders.
• Initial dose between 25–50 mg/day
• Progressive titration up to 150–300 mg/day
• Avoid formulations high in THC.

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4.4 Sleep Disorders

The endocannabinoid system participates in the regulation of the sleep-wake cycle[1]. CBD may Improve sleep secondary to reduced anxiety, while small doses of THC may Reduce sleep latency.

However, high doses of THC can alter the architecture of REM sleep and cause... fragmentation.

The evidence remains limited and based mostly on observational studies.

4.5 Autism Spectrum Disorder (ASD)

Observational studies suggest a reduction in irritability and agitation with extracts rich in CBD containing small amounts of THC. However:

• Lack of standardization of formulations

• Samples are tiny

• Lack of robust randomized trials

Its use should be considered experimental, with detailed informed consent.

5. SECURITY AND INTERACTIONS

Adverse events include drowsiness, fatigue, and gastrointestinal disturbances.7-9 Elevation of Liver enzymes may occur, especially with valproate.7 THC adds risk of side effects. Dose-dependent psychoactive substances. Drug interactions via CYP450 should be considered14.

6. Regulatory Aspects in Brazil

ANVISA's RDC No. 327/201911 regulates the manufacture, prescription, and marketing of [the product]. Products with THC ÿ 0.2% require a type B prescription; above that, type A. Importation is permitted. subject to health authorization11.

7. DISCUSSION

An integrated analysis of the literature shows that cannabidiol occupies a unique position in contemporary therapy. Unlike other historically stigmatized substances, the CBD emerged in the scientific landscape supported by methodologically sound clinical trials in

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field of refractory epilepsiesÿÿÿ.

7.1 Duality Between Robust Evidence and Empirical Expansion

While the epileptic indications show methodological consistency, the expansion of use
The development of knowledge for multiple clinical conditions occurred at a faster rate than scientific production.
corresponding.

Biological plausibility based on the endocannabinoid system1,ÿ supports hypotheses
Broad therapeutic possibilities exist, but the transition from plausibility to clinical recommendation requires trials.
controlled and reproducible.

7.2 Heterogeneity of Formulations

One of the main methodological obstacles lies in the diversity of formulations used.
in studies:

- Purified CBD isolate
- Broad-spectrum extracts
- Combined CBD/THC formulations
- Different routes of administration

This variability compromises comparability between studies and hinders standardization.
therapy.

7.3 Role of THC: Potential and Limitations

The combination with THC appears to enhance efficacy in neuropathic pain and spasticity19.
However, it introduces risks related to:

- Anxiety
- Cognitive changes
- Psychotomimetic symptoms
- Potential risk in vulnerable individuals1,ÿ

The risk-benefit balance becomes central to clinical decision-making.

7.4 Security and Monitoring

Although CBD has a favorable safety profile²,ÿ, it is not a substance free of

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risks. Drug interactions via CYP4501ÿ and liver alterationsÿ reinforce the need for structured monitoring.

Responsible clinical practice requires:

- Individualized assessment
- Laboratory monitoring
- Review of interactions
- Proper documentation

7.5 Social Pressure and Judicialization

The growth of litigation and social demand for prescription can generate distortions in Medical practice. Therapeutic decisions must remain grounded in scientific evidence and analysis. criticism, avoiding both unfounded denialism and uncritical enthusiasm.

7.6 Future Perspectives

Future progress will depend on:

- Multicenter clinical trials
- International standardization of formulations
- Long-term studies
- Evaluation of functional outcomes
- Translational research

Scientific advancements will allow for a more precise definition of the definitive role of Cannabidiol in medical practice.

8. CONCLUSION

Cannabidiol has become established as an evidence-based therapeutic option for epilepsy. refractory. Their use in other conditions should be individualized and monitored. Scientific advancement It will depend on multicenter clinical trials and standardization of formulations.

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