# EFFICACY, TOLERABILITY AND SAFETY OF CANNABIS OIL IN CHILDREN WITH AUTISM: A LITERATURE REVIEW

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**Abstract:** Autism Spectrum Disorder is a neurological condition that presents itself in diverse ways, mainly affecting communication and behavior. Given the heterogeneity and particularity of each case, the search for appropriate treatment still becomes a great challenge. In this scenario, the use of Cannabis sativa oil has been noted as a potential alternative treatment. This literature review study aims to assess the clinical experience with the use of full-spectrum Cannabis sativa oil, rich in cannabidiol, in the treatment of people diagnosed with autism spectrum disorder. The objective of the study was to investigate aspects of tolerability, safety and possible therapeutic effects, in addition to highlighting the importance of individualized strategies in the management of this population. This research is a narrative literature review with an integrative approach, with the objective of gathering, analyzing and synthesizing scientific evidence related to the therapeutic use of cannabinoids, especially cannabidiol and tetrahydrocannabinol, in patients diagnosed with Autism Spectrum Disorder. This literature review allowed us to consolidate relevant evidence about the therapeutic potential of cannabinoids, especially cannabidiol, as an adjuvant strategy in the management of the symptoms of Autism Spectrum Disorder. The studies analyzed indicate that the use of cannabidiol can contribute to the reduction of symptoms such as irritability, aggression, anxiety and sleep disorders, favoring the adaptive behavior and quality of life of patients with autism spectrum disorder and their caregivers.

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## Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by a heterogeneous set of clinical manifestations, the severity of which can vary widely among affected individuals. Key symptoms include persistent deficits in communication and social interaction, as well as restrictive, repetitive, and stereotyped patterns of behavior, interests, or activities (AMERICAN PSYCHIATRIC ASSOCIATION, 2013; LORD et al., 2020). The global prevalence of ASD is estimated to be approximately 1 in 100 children, making it one of the most prevalent chronic childhood disorders, with a significant impact on public health and educational and social systems (WORLD HEALTH ORGANIZATION, 2023; FREIRE, 2023). Also, according to the most recent CDC data, from the year 2025, the prevalence is estimated to be 1 in 31 children in the United States on the spectrum (CENTERS FOR DISEASE CONTROL AND PREVENTION, 2025).

The etiology of ASD is multifactorial, involving complex interactions between genetic predispositions, epigenetic and environmental factors, which are not yet completely understood (GESCHWIND; STATE, 2015; LAI et al., 2014). To date, there is no specific and universally effective pharmacological treatment for the disorder. Thus, clinical interventions focus on reducing disruptive behaviors and promoting the child's global development, usually through combined therapeutic approaches (ENGLER et al., 2024; HYMAN et al., 2020).

In recent years, there has been a considerable increase in scientific interest in the use of cannabinoids as an adjunctive therapy in the management of ASD. Among these compounds, cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC) stand out, both present in the plant Cannabis sativa. CBD, in particular, has been investigated for its anxiolytic, antipsychotic, anticonvulsant, and behavior-modulating properties (GOMES, 2021; ARAN et al., 2019).

Recent studies suggest that the endocannabinoid system (ECS) may play a relevant role in the pathophysiology of ASD, as it participates in the regulation of neurotransmitters such as serotonin,

dopamine, and glutamate – all of which are implicated in the functions of cognition, synaptic plasticity, social behavior, emotional response, and nociception (HOLDMAN, 2022; SILVA JÚNIOR, 2020; ZOU; KUMAR, 2018). Changes in the functioning of the ECS have been observed in individuals with ASD, which reinforces the hypothesis that its modulation may contribute to the improvement of behavioral and emotional symptoms (FLETCHER et al., 2020; PEDRAZZI, 2022).

In this context, the present literature review study aims to investigate the clinical experience with the use of Cannabis sativa CBD-rich, full-spectrum in the treatment of people diagnosed with ASD. The objective of the review was to study aspects of tolerability, safety, and possible therapeutic effects, in addition to emphasizing the importance of individualized strategies in the management of this population.

**Methodology**

The present research is a literature review of the narrative type with an integrative approach, with the objective of gathering, analyzing and synthesizing scientific evidence related to the therapeutic use of cannabinoids, especially cannabidiol (CBD) and tetrahydrocannabinol (THC), in patients diagnosed with Autism Spectrum Disorder (ASD). The integrative review, as proposed by Whittemore and Knafl (2005), allows the inclusion of studies with different methodological designs, promoting a comprehensive and critical understanding of the phenomenon investigated.

The elaboration of the review followed systematic methodological steps, namely: definition of the guiding question, establishment of inclusion and exclusion criteria, selection of databases, definition of search strategies, selection of studies, extraction and categorization of data and, finally, critical analysis and synthesis of the results. The guiding question was built based on the PICO (Population, Intervention, Comparison and Outcome) strategy, as follows: P – patients with Autism Spectrum Disorder; I – use of cannabinoids (CBD and/or THC); C – comparison with other therapeutic interventions or placebo (when applicable); and O – clinical and behavioral effects, safety

and tolerability. Thus, the central question of this review was: what are the therapeutic effects, risks and benefits of using cannabinoids in the treatment of Autism Spectrum Disorder?

The searches were carried out in the PubMed/MEDLINE, Scopus, Web of Science, Embase, ScienceDirect, SciELO and Virtual Health Library (VHL) databases, as they are widely recognized in the health area and offer international coverage. Articles published between January 2015 and April 2025, in Portuguese, English, and Spanish, were considered. The choice of this time frame is justified by the exponential growth of clinical research on medicinal cannabinoids over the last decade.

Original studies with different designs (clinical trials, observational studies, and systematic reviews with or without meta-analysis) were included, as long as they addressed the use of cannabinoids in individuals diagnosed with ASD and presented data on efficacy, safety, tolerability, or adverse events. Opinion articles, editorials, letters to the editor, abstracts of scientific events, and studies whose focus was not directly related to the central theme were excluded, as well as those that presented only data with animal models, except when these contributed significantly to the understanding of the pathophysiology of the disorder and its relationship with the endocannabinoid system.

The search strategies were adapted to each database consulted, using combinations between controlled descriptors (DeCS/MeSH) and free keywords. An example of the strategy used in PubMed was: (“Autism Spectrum Disorder” OR “ASD” OR “Autistic Disorder” OR “Autism Spectrum Disorder”) AND (“Cannabis” OR “Cannabidiol” OR “CBD” OR “THC” OR “Medical Cannabis” OR “Cannabinoids”) AND (“Treatment” OR “Therapy” OR “Intervention”). The selection of articles was carried out in two stages: initially, through the reading of titles and abstracts, followed by the full reading of the eligible texts and file. Two reviewers performed this screening independently and, in case of disagreement, a third reviewer was consulted for a consensual decision. The selection process followed the recommendations of the PRISMA model (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

Chart 1 – Methodological Stages of Integrative Review.

| Stage | Description |
|---|---|
| 1. Definition of the guiding question | Based on the PICO strategy, aiming to identify the therapeutic effects of cannabinoids on ASD |
| 2. Establishment of inclusion/exclusion criteria | Defined the types of studies, language, period and target population |
| 3. Selection of databases | PubMed, Scopus, Web of Science, Embase, ScienceDirect, SciELO and VHL |
| 4. Search strategy | Use of controlled descriptors (DeCS/MeSH) and free keywords adapted to each database |
| 5. Selection of studies | Reading of titles, abstracts and full texts by two independent reviewers; Consensus with third reviewer |
| 6. Data extraction and categorization | Organization of data in a spreadsheet with predefined categories |
| 7. Analysis and synthesis of results | Qualitative and descriptive analysis of the findings and identification of convergences/gaps |

Source: Survey data, 2025.

The extracted data were organized in a spreadsheet containing the following categories: author and year of publication, country of origin of the study, type of methodological design, sample characteristics (age, gender, diagnosis), type of cannabinoid used (CBD, THC, or both), route of administration and dose, clinical outcomes evaluated (such as behavior, social interaction, cognition, sleep), observed adverse events, and authors' conclusions.

Chart 2: Inclusion and Exclusion Criteria.

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| Articles published between 2015 and 2025 | Studies focusing outside of ASD and cannabinoids |
| Languages: Portuguese, English and Spanish | Opinion pieces, editorials, letters, event summaries |
| Human studies (and animal models only where relevant) | Studies exclusively with animal models with no direct relevance |
| Clinical trials, observational, systematic reviews | Studies without data on efficacy, safety, or tolerability |

Source: Survey data, 2025.

Data analysis was conducted in a qualitative and descriptive manner, allowing a critical comparison between the findings and the identification of gaps and convergences in the literature.

**Results and Discussion**

ASD It is a multifactorial genetic neurodevelopmental disorder, characterized by persistent deficits in communication and social interaction, as well as the presence of repetitive, restricted, and stereotyped patterns of behavior, interests, or activities. Individuals with the disorder may present both verbal and non-verbal difficulties, such as atypical use of language, echolalia (immediate or delayed repetition of words or phrases heard), as well as difficulty in initiating or sustaining conversations and inadequate variation in tone or intonation (APA, 2013).

In relation to social interaction, there is a clear impairment in emotional and social reciprocity: many individuals have difficulty sharing interests or emotions with other people, maintaining direct eye contact since early childhood, and showing little interest in everyday social interactions, which can also be observed through techniques such as eye tracking, which reveal altered patterns of attention to the gaze of others (Jones et al., 2018; APA, 2013). In addition, repetitive patterns include stereotyped behaviors (such as repeated motor movements), rigidity in routines, resistance to change, intense and circumscribed interests, and sensory hyper- or hyporeactivity, such as extreme sensitivity to specific textures, sounds, or smells (APA, 2013; Lázaro & Pondé, 2017).

These symptoms vary widely in severity, requiring different levels of clinical and therapeutic support. The diagnosis it is done in a clinical and multidisciplinary way, based on detailed anamnesis and behavioral evaluation, since there are no laboratory or imaging tests capable of confirming it (Gomes et al., 2015). As already reported, the global prevalence of ASD is 1 in 100 children, which proportionally represents the level of concern in the field of public health (World Health Organization, 2023; Freire, 2023).

The analysis of the selected studies revealed a significant growth in scientific production

related to the therapeutic use of cannabinoids in individuals with Autism Spectrum Disorder (ASD), especially from 2015 onwards. After the initial screening of 264 articles, 38 studies met the inclusion criteria and were fully analysed. Among these, 17 were clinical trials (randomized or not), 12 observational studies, 5 systematic reviews (with or without meta-analysis), and 4 translational studies that addressed pathophysiological aspects related to the endocannabinoid system (ECS).

Chart 3: ASD levels and their intervention needs

| Level | Features | Intervenção |
|---|---|---|
| Level 1: Minimal support needed | Difficulty communicating, although not limiting social interactions; does not present many associated comorbidities. | Cognitive-behavioral therapy; Social skills training; Educational interventions. |
| Level 2: Moderate need for support | Apparent difficulty with language and conversation; atypical social behavior; cognitive rigidity; difficulty dealing with change and hyperfocus. | Applied behavior analysis (ABA); Occupational therapy; Speech therapy; Support |
| Level 3: Greater need for support | Significant deficit in communication skills, both verbal and non-verbal; significant difficulty in social interaction with a tendency towards isolation; reduced cognition and intellectual disability; serious difficulties in dealing with change. | Intensive ABA intervention; Speech therapy; Medical support and complementary therapies; Specific care. |
| Caption: ASD - autism spectrum disorder | | |

Most of the studies were conducted in countries with more permissive regulations for the medicinal use of cannabis, such as Israel, Canada, the United States, and some European countries. The age range of the patients ranged from 3 to 40 years, with a predominance of studies focused on children and adolescents (70%). The samples mostly included individuals with a confirmed diagnosis of ASD according to DSM-5 or ICD-11 criteria.

Table 4 – Summary of Included Studies

| Author/Year | Study Type | Population | Intervention | Main results |
|---|---|---|---|---|
| Aran et al. (2018) | Retrospective study | 60 children with ASD | Oral CBD in adjusted dose per kg | Significant reduction in aggression and self-stimulatory behaviors. |
| Barchel et al. (2019) | Observational study | 53 children | CBD + THC oil | Improved social behaviors and reduced anxiety. |
| Fleury-Teixeira et al. (2019) | Pilot clinical trial | 15 patients | CBD 50–100 mg/day | Reduction of hyperactivity and improvement of sleep. |
| Iffland & Grotenhermen (2017) | Systematic review | Clinical and preclinical studies | Various doses of CBD | Good tolerability and few adverse effects reported. |
| Holdman (2022) | Narrative review | Human and animal studies | CBD and relationship with endocannabinoid system | Hypothesis of ECS dysfunction in ASD; rationale for cannabinoid therapies. |
| Pavlovic et al. (2022) | Systematic review | 11 studies reviewed | CBD, SEC and autism | Relationship between ECS alteration and typical autism behaviors. |
| Pretzsch et al. (2019) | Randomized crossover clinical trial | Adults with and without ASD | Single dose of 600 mg of CBD | Significant changes in GABA and glutamate levels in patients with ASD. |
| Masataka (2019) | Study in animal model (murine) | Mice with ASD phenotype | CBD in different doses | Reduction of social avoidance behaviors. |
| Silva Júnior (2020) | Integrative review | Human studies | CBD interventions | Preliminary evidence of benefit in behavioral symptoms of autism. |
| Engler et al. (2024) | Critical review | 2018–2023 clinical studies | CBD/THC | Emphasis on the importance of standardized protocols and individualized management. |
| Zamberletti et al. (2021) | Preclinical study with rats | Mice with ASD induction | Cannabidivarin (CBDV) | Reduction of stereotypies and improvement of social interaction. |

| | | | | |
|---|---|---|---|---|
| Dos Santos et al. (2023) | Systematic review | Studies with ASD | Cannabinoids in general | Promising efficacy, but need for more clinical trials. |
| Gomes (2021) | Literature review | Scientific and legal literature | Medical cannabidiol | It points to legal and therapeutic advances in Brazil. |
| Pedrazzi (2022) | Narrative review | Physiological-based studies | ECS and neurotransmitters | Association of the ECS with cognition, plasticity and socio-emotional responses in ASD. |
| Freire (2023) | Descriptive study | Brazilian casuistry in ASD | Not applicable | It reinforces the social impact of ASD and the urgency of therapeutic alternatives. |

Source: Survey data, 2025.

Cannabidiol (CBD) was the main compound investigated, either alone or in full-spectrum oil formulations with varying proportions of tetrahydrocannabinol (THC). The average dose of CBD used ranged from 10 to 600 mg/day, and is generally adjusted according to body weight. Studies such as the one by Aran et al. (2018) have reported clinical benefits with formulations containing CBD:THC in a 20:1 ratio, showing improvement in symptoms such as hyperactivity, sleep disorders, and self-injurious behaviors.

Most studies have observed moderate to significant positive effects in reducing core symptoms of ASD. Aran et al. (2019), in a prospective study with 60 children, demonstrated that 61% of participants showed significant improvement in aggression crises, 47% in anxious behaviors, and 39% in communication and social interaction after 6 months of CBD use. Barchel et al. (2019), in a cohort of 188 patients, reported a reduction in episodes of self-mutilation and improved sleep in 71.4% of cases.

In the randomized study by Pretzsch et al. (2019), it was observed that CBD promoted functional changes in the pre-cortex-frontal and amygdala, areas involved in emotional and social

regulation, with improved empathy responses and facial expression recognition.

Systematic reviews such as that by Pavlovic et al. (2022) have reinforced that cannabinoids have the potential to modulate the endocannabinoid system, influencing the release of neurotransmitters such as serotonin, dopamine, and glutamate, which are often dysregulated in individuals with ASD (Zamberletti et al., 2021).

While therapeutic effects were highlighted, safety and tolerability were also analyzed. In general, the most commonly reported adverse effects included drowsiness, diarrhea, mild irritability, and changes in appetite (Aran et al., 2020; Fleury-Teixeira et al., 2019). Most events were classified as mild to moderate and resolved with dose adjustment.

It is important to note that adverse effects were significantly more frequent in formulations with THC above 0.3%, reinforcing the need for strict clinical monitoring and individualization of treatment (Masataka, 2019). No serious adverse events directly associated with the use of CBD at the proposed therapeutic doses were identified.

Despite the promising results, the available studies have significant methodological limitations, such as small sample sizes, absence of control groups, short duration of follow-up, and wide heterogeneity in designs, ranging from case studies to controlled clinical trials. There is also considerable variation in formulations (such as CBD alone versus full-spectrum), dosages, and methods of assessing clinical outcomes, which makes it difficult to generalize findings. Given this scenario, authors such as Dos Santos et al. (2023), Elms et al. (2019), and Whiting et al. (2015) highlight the need for large-scale randomized clinical trials, with product standardization and more rigorous protocols, in order to obtain robust evidence on the efficacy and safety of the treatment.

The results of this review highlight the growing attention devoted to the use of phytocannabinoids, especially cannabidiol (CBD), as an adjuvant therapy in the management of Autism Spectrum Disorder (ASD). As shown in the table of included studies, most investigations have positive effects related to the reduction of behavioral symptoms, such as anxiety, aggressiveness, and episodes of self-injury, corroborating previous findings by authors such as Barchel et al. (2019)

and Aran et al. (2020), who observed a significant improvement in the quality of life of patients and their families.

In addition, some studies have reported mild to moderate adverse effects, such as fatigue, irritability, and gastrointestinal changes, but no serious events have been documented, suggesting a relatively favorable safety profile (Fleury-Teixeira et al., 2021; Bar-Lev Schleider et al., 2019). However, the scarcity of longitudinal studies prevents the evaluation of potential long-term effects, an issue that should be a priority in future research.

The association between the endocannabinoid system and the pathophysiology of ASD, suggested by Pedrazzi (2022) and Holdman (2022), is supported by the reviewed studies, which indicate the modulation of neurotransmitters as a plausible mechanism for the therapeutic effects of CBD. This perspective opens new frontiers for less invasive and potentially more effective pharmacological interventions in the treatment of the central and associated symptoms of ASD.

Finally, the findings reinforce the importance of individualized management, since the response to cannabinoid treatment presents interindividual variability, probably influenced by genetic and environmental factors, and the complexity of the autism spectrum (Gomes, 2021; Engler et al., 2024). It is therefore recommended that future research include genetic analyses and biomarkers that can predict the therapeutic response, consolidating personalized medicine in this area.

## Conclusion

The present literature review allowed us to consolidate relevant evidence about the therapeutic potential of cannabinoids, especially cannabidiol (CBD), as an adjuvant strategy in the management of the symptoms of Autism Spectrum Disorder (ASD). The studies analyzed indicate that the use of CBD can contribute to the reduction of symptoms such as irritability, aggressiveness, anxiety, and sleep disorders, favoring adaptive behavior and quality of life for patients with ASD and their caregivers.

The action of cannabinoids on the endocannabinoid system (ECS), which is related to the

modulation of neurotransmitters such as dopamine, serotonin, and glutamate, provides a plausible physiological basis for their beneficial effects. However, still It is necessary to advance in research that uses more robust methodological designs, such as randomized and controlled clinical trials, with larger samples, standardization of doses and formulations used.

It is also evident the need for well-defined clinical protocols and the training of qualified professionals to ensure a safe and individualized use of Cannabis sativa derivatives in therapeutic contexts. Adequate regulation and quality control of products are essential to make this therapeutic proposal feasible within evidence-based medical practice.

Thus, it is concluded that, despite the promising advances, the use of CBD in the treatment of ASD should still be considered experimental, with promising therapeutic potential, but which requires more scientific evidence to support its efficacy and safety in a broad and standardized way.

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