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The therapeutic potential of cannabidiol in reducing symptoms of Amiotrophic Lateral Sclerosis: A bibliographic review

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Abstract

Introduction: Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disease that results in the gradual loss of muscle control. There is currently no cure for ALS and treatment aims to alleviate symptoms and improve patients' quality of life. In this context, cannabidiol (CBD), a compound found in the cannabis plant, has been studied as a complementary therapy for ALS.

Objectives: This study consists of a literature review that aims to analyze the scientific evidence available on the use of CBD in the treatment of ALS.

Methodology: This is a bibliographic review based on the PubMed, LILACS, SciELO and Google Scholar platforms. The descriptors used were "treatment" AND "cannabidiol" AND "amyotrophic lateral sclerosis". Studies in Portuguese, Spanish and English were included, from 2000 to 2024.

Results: With progress in neuroscience, cannabidiol emerges as a potential treatment for ALS, presenting anti-inflammatory and neuroprotective effects, in addition to benefits against anxiety and depression.

Conclusion: Therefore, the therapeutic potential of cannabidiol in Amyotrophic Lateral Sclerosis highlights that CBD has promising properties in relieving ALS symptoms and improving patients' quality of life. However, more research is essential to establish it as a standard treatment for ALS, including its interaction with other medications and safety as a therapeutic.

Keywords: *Cannabis sativa*; Neurodegenerative disease; Quality of life; Complementary

1. Introduction

Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease (MND), Lou Gehrig's disease or Charcot's disease, is a disease that affects the central nervous system (CNS) in a progressive and irreversible manner; affecting nerve cells in the brain and spinal cord, resulting in loss of muscle control and then paralysis (Deng *et al.*, 2011). However, the cause is not yet fully understood, as this disease is multifactorial, which makes it difficult to develop therapeutic treatments (Agnello; Ciaccio, 2022).

According to Dr. Acary Bulle, "Sclerosis" is stiffening, "Lateral" is the involvement of the side of the body and amyotrophic is muscle atrophy (Bulle, 2018). In this sense, the main symptoms include: gradual loss of strength and

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muscle coordination; muscle cramps, muscle contractions, inability to perform routine tasks such as climbing stairs, walking and standing up; difficulty breathing and swallowing; choking easily and drooling (Ministry of Health, 2020).

Although the real cause of ALS is unknown, it is known that genetic and environmental factors have a strong relationship. In addition, studies indicate that chronic inflammation may be an important factor in the progression of ALS. The activation of immune cells in the CNS can lead to the death of motor neurons, and modulation of the immune system may be an effective therapeutic strategy (Philips; Rothstein, 2015).

According to Salvioni (2021), it is worth noting that the disease has a global scale, with cases occurring in several countries. In parallel with this issue, classified as rare, the estimated prevalence is two cases for every 100,000 people/year, affecting both men and women. However, there is a discrepancy of cases in men compared to women, being 3:2.

Bule (2018) states that, when it is in an advanced stage, the diagnosis of ALS is made through laboratory tests, magnetic resonance imaging and electroneuromyography, with the latter being performed with priority on the arms, legs, muscles of the face and throat. In addition, the patient's history is also taken into account, as well as previously occurring symptoms.

The treatment of Amyotrophic Lateral Sclerosis is carried out through palliative care, considering that the patient will not be cured. Therefore, the Ministry of Health has programs of Integrative and Complementary Practices for the prevention, promotion and treatment of rare diseases, such as ALS. Therefore, the aim is the well-being of the patient and quality of life.

There is currently no cure for ALS, and treatment is aimed at alleviating symptoms, improving the quality of life of patients (Silva *et al.*, 2014). However, researchers continue to search for new treatments and therapies that can slow or stop the progression of the disease. To date, the most effective and licensed drug is Riluzole, which has anti-glutamatergic effects. However, cannabidiol (CBD) has been studied as a form of treatment because it has anti-inflammatory and analgesic factors, which help both the immune system and pain (Guindon, 2009). Due to technological advances in the Chemistry and Pharmacology sectors, the use of active cannabinoids in Medicine has been permitted, as they have been approved for obtaining them in their pure form, with known constitution, stability and doses. As a result of consensual clinical studies at a scientific level, it has been analyzed that cannabinoids offer benefits to patients with a reduced probability of cure, such as those with neurological diseases such as amyotrophic lateral sclerosis (Ribeiro, 2014). The use of CBD in ALS has been a subject of interest in the scientific community, as it has anti-inflammatory and neuroprotective properties and may have therapeutic potential for the disease (Barbosa *et al.*, 2021). The Cannabis sativa plant, which is part of the Cannabiaceae family and is better known as marijuana, has been used for over 5,000 years for its recreational and therapeutic properties (Alencar *et al.*, 2020).

There are an abundance of compounds originating from the plant, known as cannabinoids, which are classified into three categories: endocannabinoids, synthetic cannabinoids, and phytocannabinoids (FCB). CBD is the best known of the FCB group and has many neuroprotective pharmacological properties, being responsible for regulating neuronal plasticity and, consequently, contributing to the control of ALS symptoms. It is used in various diseases, including neurodegenerative diseases, both in prevention and treatment of diseases (Flores *et al.*, 2017).

In a study conducted by Flores (2017), it was concluded that CBD was tolerated by patients and did not cause significant harm. In addition, there was an improvement in the quality of life of patients, including a decrease in pain, muscle stiffness and spasms.

However, the small number of individuals with ALS who use Cannabis, and the scarce studies conducted on human Amyotrophic Lateral Sclerosis, make it difficult to interpret the results achieved. Furthermore, it is believed that Cannabis and its cannabinoids may be useful in the intervention of ALS (Casimiro, 2019).

Due to the difficulty in finding accessible information and treatments for the pathology of ALS and the global resistance faced regarding CBD therapy, studies that address the effects of cannabidiol on ALS are necessary. Thus, with the expansion of the database, with the enrichment of the available knowledge base and consequent deepening of the understanding about the aforementioned pathology, it will be possible to invest in the relief of ALS symptoms, improving the well-being and quality of life of patients.

2. Methodology

In view of the study proposal and in order to achieve the objective of analyzing the available scientific evidence on the use of CBD in the treatment of ALS, the bibliographic review was used as the method for this investigation.

Regarding the method, the bibliographic review is a process of surveying, analyzing and describing scientific publications in a given area of knowledge. It is also called a literature review, theoretical framework or theoretical foundation. Bibliographic review studies are characterized by the use and analysis of scientific documents, such as books, theses, dissertations and scientific articles; without directly resorting to empirical facts (Oliveira, 2018). In addition to this, it can be seen that bibliographic research uses secondary sources, that is, the contributions of authors on a given topic. Thus, the theoretical and scientific findings made it possible to gather a framework of results for the presentation of this article.

Still on the subject of methodology, in order to prepare a literature review that contributes to the understanding of how the use of CBD can contribute to the relief of ALS symptoms, it is necessary that the steps to be followed are clearly described. The process of preparing the literature review is divided into: identification of the review topic with direct relation to the authors' research topic, reading the main studies on the subject and, subsequently, writing the present work.

The identification of the articles included in this study was done through searches in the following electronic databases: PubMed, LILACS, SciELO and Google Scholar. The descriptors used were “treatment” AND “cannabidiol” AND “amyotrophic lateral sclerosis”.

In order to establish the sample of studies selected for this literature review, the following inclusion criteria were established: original articles, those discussing the impact of CBD on alleviating ALS symptoms, those made available free of charge, systematic reviews and observational studies, those published between 2000 and 2024 and those in the following languages: English, Spanish and Portuguese. Incomplete or duplicate articles and those that did not fit the scope of the study were excluded.

After searching for research, guided by the inclusion and exclusion criteria, the title and abstract of each scientific article were read to verify their suitability for the research theme of this investigation. Data analysis was performed descriptively, emphasizing the impact of CBD as a therapy for improving the quality of life of individuals with ALS.

3. Results and discussion

3.1. Amyotrophic lateral sclerosis

According to Nordon and Espósito (2009), Amyotrophic Lateral Sclerosis is often referred to as “Lou Gehrig’s disease”, in honor of the famous American baseball player who died as a result of the disease. Furthermore, according to Bulle (2018), “sclerosis” is stiffening, “lateral” is the involvement of the side of the body and “amyotrophic” is muscle atrophy.

Calado (2010) states that the disease is a progressive neurodegenerative condition that affects motor neurons in the brain and spinal cord. These neurons are extremely important for voluntary muscle activities, such as speaking, walking and even breathing. The first descriptions of this disease, according to studies by Wijesekera and Leigh (2009), were made in 1824 by scientist Charles Bell, and in 1874, the symptoms were correlated with a neurological disease described by Jean-Martin Charcot in 1869.

According to a study published in the journal Nature and reported by Hardiman *et al.* (2017), ALS results from the death of motor neurons. These cells are responsible for transmitting nerve signals to the muscles and the absence of this action leads to muscle degeneration and gradual weakness, compromising basic motor functions.

The disease is referred to as amyotrophic lateral sclerosis because, according to Cavaco (2016), in this condition, there is hardening and scarring of the lateral portion of the spinal cord, as well as the absence of contraction due to the lack of nerve stimulation.

Oliveira (2006) reports that in 1874, Charcot officially described ALS. However, it was only in 1994, 120 years after the first description of the disease, that Riluzole emerged, a drug capable of modifying the natural progression of the disease,

as it is an antiglutamatergic. This substance, as reported by Soares *et al.* (2021), is responsible for inhibiting the action of glutamate, blocking its receptors or facilitating its reuptake, consequently reducing excitotoxicity.

3.2. Epidemiology, etiology and pathophysiology

In the studies by Bertazzi *et al.* (2017), it is possible to note that ALS is more prevalent in males, although the female population is also affected, but in smaller numbers. Furthermore, Tozani and Siqueira (2023) show that the average survival of patients is around 5 years, usually manifesting around 60 years of age. However, as reported by Silva and Arias (2023), Stephen Hawking, the renowned British physicist (1942-2018), challenged this average, being diagnosed in his youth, at 21 years of age, and living until the age of 76.

The disease is mostly sporadic, with a hereditary variant associated with genetic mutations passed down within families, as patients with familial ALS have a history of the disease, with records in close relatives such as parents or grandparents. While environmental and metabolic factors are considered contributors to the sporadic form, the work of Byrne *et al.* (2011) states that the hereditary form is associated with mutations in specific genes that express toxic enzymes and proteins.

According to Al-Chalabi *et al.* (2017), it was possible to identify mutations in several genes as risk factors for ALS, including SOD1 (encodes the superoxide dismutase 1 protein) and C9orf72 (encodes a protein not yet identified), if they undergo mutations, they may contribute to the progression of the disease. Other research suggests that external factors such as tobacco use, exposure to environmental toxins, physical trauma, and intense physical exercise. The greater the exposure to risk factors, the greater the chances of developing ALS, however, these relationships are still speculative, according to Santos *et al.* (2021). Changes in areas such as the bulbar system and the pyramidal tract, which control voluntary movements, may also be linked to ALS, involving degeneration of the motor system at the bulbar, cervical, thoracic and lumbar levels, as seen by Lima and Gomes (2010).

According to Lima and Gomes (2010), ALS can be caused by a combination of factors: glutamatergic excitotoxicity, oxidative imbalance, protein accumulation and axonal constriction. Glutamatergic excitotoxicity, triggered by the G protein, influences several neurochemical systems, all of which are essential for the proper functioning of the nervous system, according to Valli (2014), allowing the body to respond and adapt to different situations and stimuli. Any dysfunctions in these receptors can contribute to several neurodegenerative diseases, as studied by Silva (2016).

Excitotoxicity is a process in which nerve cells are damaged and killed due to excessive stimulation of neurotransmitters. In addition, inflammation triggered by activated immune cells in the CNS can accelerate neuronal death. Mitochondrial dysfunction, which compromises the cell's ability to produce energy efficiently, and defects in axonal transport, which is essential for communication between neurons, are other factors that can contribute to the development of ALS, reported Cavaco (2016).

Although ALS is a pathology that mainly affects the motor system, cognitive and behavioral symptoms can also occur over time. Studies show that some patients with ALS have cognitive deficits, which are characterized by changes in personality, irritability, obsession, difficulty in discernment, and deficits in the executive function of the frontal lobe. According to Linden Júnior *et al.* (2016), these characteristics are similar to the changes observed in frontotemporal dementia, which affect some individuals with ALS, as evidenced by clinical, radiological, and neuropathological studies. Several studies have sought to identify the underlying causes and mechanisms that lead to the development and progression of ALS. Based on the ideas and research of various authors, these causes can be grouped into several categories. Below is a table detailing the different causes of ALS as proposed by different authors.

Table 1 A literature review on possible causes of ALS pathology, described by scholars

Author	Year	Article	Main results
Cerqueira	2007	Consequences of the expression of the enzyme Cu, Zn-superoxide dismutase (SOD1) and its mutant G93a in neuroblastomas. Implications for amyotrophic lateral sclerosis.	The activity of the superoxide dismutase enzyme (SOD1) in the control cell lines remained stable throughout the culture time, while in SH-SY5Y G93A cells there was a significant reduction, with 62 and 54 units/mg of protein after 4 and 8 weeks, respectively. Furthermore, the expression of SOD1 in the transfected neuroblastomas was higher, regardless of the culture time, as confirmed by spectrophotometric and native gel analyses..

Rentzos et al.	2011	Alterations of T cell subsets in ALS: a systemic immune activation?	The main results of the study indicate a significant increase in the number of CD8+ cytotoxic T cells and NKT cells in patients with amyotrophic lateral sclerosis (ALS), compared with the control group (P = 0.02 and P = 0.04, respectively). In addition, a reduction in regulatory T (Treg) cells was observed in ALS patients (P = 0.01), with a negative correlation between Treg cells and disease progression (P = 0.017). These findings suggest systemic immune activation, with the high production of CD8+ T and NKT cells indicating a possible immune reaction to unknown or undetected endogenous proteins or viruses. The study suggests that the immune response may play an important role in the pathogenesis of ALS, with both neurodestructive and neuroprotective functions of Treg cells.
Magrané et al.	2012	Mutant SOD1 in neuronal mitochondria causes toxicity and mitochondrial dynamics abnormalities	The main results of the study demonstrate that the presence of superoxide dismutase 1 (SOD1) mutants significantly compromises mitochondrial function in neurons, with alterations in mitochondrial morphology and dynamics. Mutant SOD1 was observed to form aggregates in the mitochondrial matrix of the brain of mice with ALS, suggesting a toxicity mechanism associated with protein aggregation. Furthermore, the calcium storage capacity of neural mitochondria was impaired before the onset of motor symptoms in G93A mice, indicating that mitochondrial dysfunction may precede the clinical manifestation of the disease. Analysis of neurite length showed that the presence of mutant SOD1 negatively affects neuronal health. Data were analyzed by ANOVA and t-tests, with significant results between the SOD1 wild-type and mutant groups. These findings contribute to the understanding of the pathological mechanisms of ALS, highlighting the role of mitochondrial dysfunction in disease progression.
Oliveira	2015	Familial Amyotrophic Lateral Sclerosis: main associated genes.	The main results of the study on Familial Amyotrophic Lateral Sclerosis (Familial ALS) indicate that the disease can present in two morphological forms: the classic form, similar to sporadic ALS, and a form with spinal involvement, characterized by degeneration of the middle root zones of the posterior column. Typical symptoms include asymmetric weakness, muscle atrophy, paralysis, muscle fasciculations and bulbar effects, such as dysarthria and dysphagia. The study also identified mutations in genes such as SOD1, FUS and TARDBP, with approximately 4% of Familial ALS cases presenting mutations in the FUS gene. The mutations are mostly missense, frameshift or nonsense, with a genotype-phenotype correlation not yet established for many of them. The use of genetic tests, such as PCR and RFLP, has proven crucial to confirm the diagnosis, especially in cases with atypical symptomatic features, and has helped to identify heterozygous mutations in the SOD1 gene in affected individuals. These findings highlight the complexity of familial ALS and the importance of genetic investigation for the diagnosis and understanding of the disease.
Palma	2016	Investigation of the phenotypes and effects of human VAPB	The results of the study show that the expression of the VAPBP56S protein is toxic, leading to the formation of

		protein expression in Saccharomyces cerevisiae as a model for Amyotrophic Lateral Sclerosis.	dispersed aggregates in cells, while the wild-type protein concentrates in the endoplasmic reticulum and does not significantly affect cell viability. The cell line expressing the mutant protein is more sensitive to oxidative stress, with a lower GSH/GSSG ratio and higher H2O2 production in isolated mitochondria. Proteasome inhibition affects cells with the wild-type protein more, while autophagy inhibition impacts cells with the mutant protein more. The expression of Tsa1, a peroxiredoxin, attenuated the toxicity of VAPBP56S. Furthermore, the expression of the mutant protein altered the levels of endoplasmic reticulum stress markers and UPR. These data suggest that VAPBP56S expression causes alterations in redox metabolism and proteostasis.
Brown e Al-Chalabi	2017	Amyotrophic Lateral Sclerosis	Key findings from the Amyotrophic Lateral Sclerosis (ALS) study include the identification of pathological processes such as oxidative stress, excitotoxicity and mitochondrial dysfunction that contribute to motor neuron degeneration. The research highlights the importance of specific biomarkers to improve diagnosis, disease monitoring and patient selection for clinical trials. In addition, the study emphasizes the need to discover new therapeutic targets and develop combination treatments to address multiple pathogenic mechanisms and slow the progression of ALS. Advances in technologies such as gene editing and advanced neuroimaging are also seen as promising for improving patient quality of life and survival. These results reflect both progress and ongoing challenges in ALS research and treatment.
Diniz et al.	2023	Amyotrophic Lateral Sclerosis (ALS): Mechanisms, diagnosis and possible treatments.	The main results of the study on Amyotrophic Lateral Sclerosis (ALS) highlight advances in the understanding of the mechanisms of the disease, although challenges remain, especially in the identification of biomarkers for diagnosis and monitoring. The research identified the need for new therapeutic targets and combined treatments to address multiple pathogenic mechanisms, aiming to improve the efficacy of therapies and slow the progression of ALS. The work also emphasizes the importance of continued research and the development of new technologies, such as gene editing and advanced neuroimaging, to improve the quality of life and survival of patients. In addition, modulation of the immune response is presented as a promising therapeutic approach. These results reflect the complexity of ALS and the need for a multidisciplinary approach to address its challenges.

Source: Author's own (2024).

3.3. Diagnosis

Currently, there is no specific diagnosis for ALS. There are no specific biomarkers in the blood that can be detected by blood tests, nor can it be diagnosed by a single test alone. Instead, it is a combination of characteristic signs and symptoms, as well as the exclusion of other diseases. Once other diagnoses have been ruled out and the clinical and electrophysiological criteria for ALS are met, the diagnosis can be firmly established. A definitive analysis takes time, and can take around fifteen months, according to Tozani and Siqueira (2023).

The most classic signs and symptoms of ALS are: muscle weakness, spasticity, muscle atrophy, spontaneous and visible contractions, difficulty speaking and swallowing, respiratory problems, difficulty performing daily activities, cognitive-

emotional problems, pain, and difficulty speaking. However, according to Santos *et al.* (2021), the first symptoms of ALS are difficult to identify, due to the different forms of manifestations in each organism.

Several tests are required for a definitive diagnosis, such as: Computed tomography (CT) and magnetic resonance imaging (MRI) are the most commonly used imaging tests to diagnose neuropathologies. These tests are essential to confirm or rule out a diagnosis, as they allow visualization of the morphology of the nervous tissue and the brain, according to Brito *et al.* (2023).

According to Freitas (2020), Electroneuromyography (ENMG) is a test that allows the identification of variations in neuromuscular units. During the evaluation, the latency and amplitude of the motor potential (CMAP) of the phrenic nerve are observed, in addition to the neurophysiological indexes (INF) and split-hand (ISH). These parameters are used to verify the functionality of the phrenic nerve and the neuronal health of the upper limbs. Lumbar puncture is used to diagnose ALS, which consists of a procedure in which a puncture is performed in the center of the spine, more precisely between the third and fourth vertebrae, to confirm an exact neurological diagnosis, according to Ranzolin Piazzetta *et al.* (2021).

Swallowing tests are widely used, which are performed by videoendoscopy, to evaluate possible swallowing problems, oral and pharyngeal, due to neurological degeneration, as shown by D'Ottaviano *et al.* (2013).

General laboratory tests, to rule out other diseases, such as serology, including infection caused by the human T-lymphotropic virus (HTLV) and dosage of hexosaminidases, uric acid, and specific ones such as creatine phosphokinase (CPK), as highlighted by Pereira (2023), are also used to map ALS. There are also genetic tests, which are performed when there is a family history of ALS, and can be classified according to their purpose: confirmatory diagnosis to diagnose or eliminate a genetic disease; natal or neonatal screening or to detect asymptomatic carriers of genetic pathologies that can be transmitted to other generations, says Oliveira (2015).

The objective of current research is, as stated in the study by Diniz *et al.* (2023), to identify biomarkers and develop advanced imaging techniques to make the diagnosis of the disease easier, more accurate and faster.

3.4. Treatment

Currently, there is no cure for ALS and treatment consists of multidisciplinary care, as seen by Masrori and Van Damme (2020). There are some types of treatments in the testing phase, and one treatment that has already been proven is the drug Riluzole, a drug that inhibits glutamate, extending survival from three to six months, as shown by Nordon and Espósito (2009). It also has pharmacological properties described as analgesic, anti-ischemic, anesthetic and sedative, and in addition to being a glutamatergic antagonist, it is a neuroprotector, according to Lucho (2014). The most common side effects, highlighted by Masrori and Van Damme (2020), are: fatigue, nausea, dizziness, diarrhea, and liver problems. Although it increases survival time and brings benefits to the disease, these benefits may vary depending on the severity of the disease and the time at which treatment is initiated, as indicated by Alencar *et al.* (2020). Another drug that has been studied for the treatment of ALS, according to Sawada (2017), is Edaravone, responsible for increasing the production of prostacyclin and capturing hydroxyl radicals, protecting neurons from damage caused by oxidative stress. Several symptoms of ALS can be alleviated through symptomatic treatments, with pharmacological and non-pharmacological action, such as: spasticity can be treated with cannabinoids, baclofen, tizanidine and muscle stretching and increased saliva with injections of botulinum toxin into the salivary glands and anticholinergic drugs, which are drugs that antagonize acetylcholine Ach, as stated by Michavila *et al.* (2007). The use of CBD in spray or inhalation form can help treat neuropathic pain, as an adjuvant analgesia, improving pain intensity. It can also be beneficial for improving sleep quality and, consequently, greater well-being, as demonstrated in the work of Brucki *et al.* (2015).

In addition to the use of drugs to protect nerve cells and antioxidant vitamins, supportive therapies such as physiotherapy, speech therapy, and procedures such as gastronomy and the use of non-invasive ventilators are also important to improve patients' quality of life, according to Oliveira (2019). In line with this perspective, the Federal Council of Biomedicine (CFBM), as determined in resolution no. 365 published on June 23, 2023, allowed biomedical professionals specialized in acupuncture to prescribe CBD-based herbal medicines. This decision has the potential to boost treatments for several diseases, including ALS, especially considering the widespread use of acupuncture in reducing pain, fatigue and improving sleep, significantly improving the quality of life of ALS sufferers, as reported by De Lima (2021).

3.5. Cannabidiol in the treatment of amyotrophic lateral sclerosis

Lima and Neves (2022) report that, although the mechanisms of action of CBD are not fully defined, it interacts with specific receptors and shows a low affinity for CB1 receptors. These mechanisms include: anti-inflammatory, antioxidant, neuroprotective action, glutamate modulation and effects on spasticity and pain, defended by Silva *et al.* (2022), in addition, it also has anxiolytic action, reported by Gregório and Mascarenhas (2022).

In a study, published in the Journal of Neuroimmune Pharmacology and reported by Chiurchiù *et al.* (2015), it was suggested that CBD reduces inflammation and improved the survival of motor neurons in an animal model of ALS. The study concluded that CBD may be a good therapy for ALS, but that more studies in humans are needed to confirm these results. Although studies on CBD have been conducted in Brazil since the 1970s, there is no medication that contains only CBD in its composition, and in order to obtain such a medication, it is necessary to import it, but judicial authorization is required for its release, as reported by Macedo *et al.* (2019).

Recent studies have indicated a possible association between ALS and the loss of small fiber neurons, which may be a contributing factor to neuropathic pruritus. In an article published in 2021 in the journal Palliative Medicine by LOU *et al.* (2021), it was described that CBD provided a significant improvement in this neuropathic pruritus in a patient with ALS. Despite its effectiveness in controlling pruritus, sedation was a notable side effect, to which the patient developed tolerance within a few days after starting treatment. In 2012, the ALSUntangled group published a study suggesting that cannabinoids have the potential to modulate the immune response and inflammation, which may be relevant to ALS. This was confirmed through studies in animals with mutations in the SOD1 gene. In addition, it was described that CBD is more effective in terms of neuroprotection, although THC also reduces glutamate toxicity. CBD stands out because it does not have psychoactive effects, unlike THC (The ALSUntangled group, 2012). Additionally, CBD also contributes to the reduction of symptoms of spasticity, loss of appetite, depression and pain. However, it does not demonstrate efficacy in treating difficulties related to speech, swallowing and sexual dysfunction, according to Amtmann *et al.* (2004). Although there is some resistance to CBD in Brazil and globally, several countries that previously opposed the medicinal use of marijuana and even conducted campaigns against it, now allow its use not only for medicinal purposes, but also recreationally. Although ANVISA has authorized medicinal use in Brazil, the cost is high, making it difficult and even unfeasible for many patients who cannot cover the costs of importing it, according to Gontijo *et al.* (2016). Marijuana is still highly stigmatized in Brazil, considered an illicit drug, even though it has been used medicinally since the 19th century.

4. Conclusion

Therefore, it is clear that, although the mechanisms underlying ALS are still complex and challenging, CBD appears to be a promising therapeutic alternative. The studies reviewed indicate that cannabidiol can contribute to symptom relief, possessing anti-inflammatory and neuroprotective properties that can improve the quality of life of patients.

In addition, it is important to continue investing in rigorous clinical studies to validate the efficacy and safety of CBD, as well as to identify the exact mechanisms by which it acts. The need for new biomarkers and combined therapeutic approaches is evident, and modulation of the immune response emerges as an area of interest that can be explored in future investigations.

Therefore, the integration of CBD in the treatment of ALS should not be seen as an isolated solution, but rather as part of a multidisciplinary approach that includes continuous research, the development of new technologies and collaboration between health professionals. This strategy can not only slow the progression of the disease, but also provide a better quality of life for patients affected by ALS

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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