

MEDICINAL USE OF *CANNABIS SATIVA* FOR THE TREATMENT OF AUTISM

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Abstract: *Cannabis Sativa* is a plant with medicinal capacity, its function is to improve patients with different diseases, and is widely used in its oily form to treat fibromyalgia and seizures as the plant has the ability to reduce the number of seizures. Autism is a disorder that has no cure, only treatment, which is medication and not medication, such as therapies. People with ASD, an autism spectrum disorder, can have numerous characteristics such as stereotyping and even seizures.

Cannabidiol is a substance derived from Marijuana that does not have its hallucinogenic principle, which is the active ingredient that causes hallucinations and the effects described when using the drug illegally, this substance is known as CBD and has been studied over the years, one of his studies are applied to the treatment of autism symptoms, in this article we will analyze through a bibliographical review the studies of this case and the effects that Cannabidiol generated in patients with ASD.

Keywords: *Cannabis Sativa*, seizure, autism.

INTRODUCTION

Cannabis sativa, popularly known as marijuana, is a plant used in different ways, mainly for medicinal use, both its oil, smoking or topical use in creams and lotions (Saad, 2019). Over time and different cultural expressions, its consumption, both recreational and medicinal, became prohibited. Even with the controversies surrounding this vegetable, its benefits have not been forgotten and different professionals from different scientific areas have been studying the plant with the aim of discovering more about it, its properties and effects (Saad, 2019).

Given the difficulties related to Autism Spectrum Disorder (ASD), finding alternative treatments that have low side effects on patients has become the current scientific race.

Unlike the neuro-stimulating medications on the market, which cause dozens of side effects, damaging patients' quality of life, the use of oil extracted from *Cannabis sativa sp* has shown promise in this field. This work aims to analyze the influence of *Cannabis sp* oil, with emphasis on patients with ASD and comorbidity in epilepsy and highlight the symptoms of each disorder, as well as how Cannabidiol helps to reduce epilepsies and how the use of this medicine has helped to reduce symptoms and standard behaviors related to this syndrome.

THE USE OF NATURAL PRODUCTS

Numerous plants from Brazilian biodiversity have already been cataloged and studied, however, in the vast national Biomes there are species with extensive potential for study, extraction and commercialization of products that must be explored. Regarding Brazil's biological potential, other countries have managed to take advantage of resources that are still unknown to national researchers. Therefore, it is of crucial importance to unveil the national floristic potential with pharmacological perspectives, seeking to more significantly boost the country's technological and economic development.

Articles 20 and 21 of Law Number 6,360 defend the study of plants and their application, to this end, it is necessary to have their composition known, their application advantageous and present an improvement in the current form or formula from a therapeutic point of view. In other words, even if a plant is traditionally used to treat some illness and/or illness, deeper studies of the substances and their mode of action at the molecular, cellular and tissue level are necessary.

Decree number 2,960 of the National Policy on Medicinal Plants and Phytotherapeutics considered that medicinal herbs are strategic in strengthening employment in family

farming and generating income, in the sustainable use of Brazilian biodiversity, in technological advancement and in improving health care for the population (BRAZIL, 1972). For the success of this inclusion, it is essential that health professionals are aware of the pharmacological activities and toxicity of medicinal plants from Brazilian biomes, as well as their use in accordance with the customs, traditions and socioeconomic status of the population (ARNOUS et al., 2005).

CANNABIS SATIVA IN BRAZIL

Cannabis sativa, also known as marijuana or hemp, is not a plant of Brazilian origin, it is what we call an exotic plant as it was brought around 1500 along with caravels, the plant was used to make candles or its fibers were used on ships, however, it was along with the caravels coming from Africa in the slave trade that the plant was brought and cultivated and its use was quickly disseminated among black slaves and Indians. (SAAD, Luísa 2019)

However, its use was not restricted only to slaves and Indians, its use began to be disseminated among intellectuals and doctors and by the army and this way it began to be seen as a medicine for various diseases, in 1888 the medical form already mentioned the use of marijuana as medicine. (SAAD, Luísa 2019).

“Against chronic bronchitis in children (...) they smoke (Grimault cigarillos) in asthma, laryngeal phthisis, and all. Under its influence, the spirit tends to cheerful ideas. One of its most ordinary effects is to provoke laughter (...), but individuals who continually use haschich live in a state of doldrums and imbecility” (Chernoviz, 1888).

However, over the decades, the use of marijuana came to be repressed. The 2nd opium conference was the starting point for the beginning of criminalization, but it was only in 1920 that the police began to effectively

persecute it. (SAAD, Luísa 2019)

Criminalization and prejudice against marijuana began to be disseminated through socio-cultural means, as tobacco is an exotic drug and was used for years by black and indigenous people. The view attributed to the drug was that it threatened religious institutions, families and policies; Another point worth highlighting is that cannabis has come to be overlooked in a drug classification as it is considered “less sophisticated” than drugs such as cocaine and opium. (SAAD, Luísa 2019)

USE OF MEDICAL MARIJUANA

The medical use of marijuana gained voice in Brazil in 2014 in the Anny Fisher case, where a 5-year-old girl who suffered from seizures, her parents had their first contact with cannabis oil clandestinely and soon realized its benefit in well-being. daughter, they soon sought support from the judiciary where the importation of *Cannabis oil* for the family was approved,

“At this moment, given the progress that the author has shown with the use of the substance, with a significant improvement in her quality of life, it would be absolutely inhumane to deny her the requested protection. [...] I anticipate the effects of the guardianship to order Anvisa to refrain from preventing the import, by the author, of the substance Cannabidiol (CBD), whenever there is a medical request. [...] The substance proved to be effective in mitigating or blocking seizures and, in the author’s particular case, fundamental in eliminating the recurrent crises produced by the disease she is suffering from, giving her a quality of life never before experienced. [...]. There is no way to make the author wait indefinitely until the completion of these studies without this causing irreversible damage [...]” (GONÇALVES, Lucas,2020)

This case gained great visibility, which encouraged other families to seek help from

Cannabidiol, which generates fewer side effects than controlled medicines popularly known as "black stripe", in addition to seizures, the use of Cannabis sativa has been studied for chronic diseases such as sclerosis multiple and neuropathic pain. (GONÇALVES, Lucas,2020)

Since then, its use has become more widespread, but bureaucracy is still an impediment for many doctors as doctors were not given the right to free prescriptions, so all those who prescribe must be subjected to a public trial that will determine the release for importation. and use of the medicine beyond the doctor, not being supported in any way and completely assuming the risk for its prescription and being able to be punished by their respective regional councils. (GONÇALVES, Lucas,2020)

Marijuana used for medicinal use is known as industrial hemp because it does not contain the psychoactive substance of marijuana, THC. In this species, which is devoid of this substance, we can only find Cannabidiol or CBD and also Cannabinoid.

Cannabidiol acts on our endocannabinoid system, it activates cannabidioid receptors such as CB1 and CB2, this entire system regulates various physiological functions in our body, which is why it has proven to be efficient for the treatment of many pathologies, as mentioned.

"The main endogenous cannabinoids are Anandamide (AEA) and 2-Arachidonylglycerol (2-AG). As for exogenous cannabinoids, the main ones are Δ -9-tetrahydrocannabinol (Δ -9-THC), cannabidiol (CBD), Δ -8-tetrahydrocannabinol (Δ -8-THC), cannabinol (CNB), dronabinol, nabilone and rimonabant." (Silva,2020)

The reason why Cannabidiol is used to combat epilepsies is due to the vanilloid receptor, which acts on the release and subsequent reuptake of glutamate and adenosine neurotransmitters, in addition to

stimulating neuroprotection by producing antioxidant and anti-inflammatory substances together. A medicine released for children over 2 years old that has Cannabidiol as its active ingredient and is approved by the European Medicines Agency (EMA) is Epidiolex®, it is prescribed for Dravet syndrome and Lennox-Gastaut syndrome. (Silva,2020)

AUTISM SPECTRUM DISORDER

Autism spectrum disorder (ASD) is a developmental neurological disorder that presents difficulties in communication and social interaction as well as restricted, repetitive and stereotyped interest. It was first cited in medical literature in 1911 by Eugen Bleuler and later by Leo Kanner (1943) and Hewitte (2006) to diagnose children with these characteristics.

The word autistic comes from "autos" which means own and "ism" which symbolizes a state, that is, it shows a person closed in on themselves, that is, autism is a condition where the person is reclusive in themselves, the term of ASD has changed over the years but has currently stabilized in Autism Spectrum Disorder according to the Diagnostic and Statistical Manual of mental disorders (DMS-V), however the diagnosis is very difficult as it is not very palpable and as there are no means that can test it because there is no biological marker that identifies the disorder, when parents notice their child's dystonia, other children have hyperactive behaviors, refuse to socialize with other children, walk in circles or aimlessly, they look for a neurologist who will forward it to therapists to analyze themselves and check whether or not the diagnosis of ASD will be finalized, this moment is extremely important and for this reason professionals must always maintain an ethical and respectful attitude so that this process is not traumatic for parents and not for the child and that they can work

together to clarify their children's condition so that they can help effectively. (BOSA; SEMENSATO, 2013).

There is no cure for ASD, but there are drug and non-drug treatments to help sufferers. Non-drug treatments include psychotherapy, the most recommended being cognitive behavioral therapy (CBT) and even music therapy is used.

Drug treatment aims to control behaviors caused by the syndrome, such as aggressiveness and stereotypical behaviors, and thus facilitate more sociable behavior and help control so that other therapies can take effect more effectively. It is estimated that 55% of patients use antipsychotics such as Risperidone, Olanzapine; psychostimulants such as Ritalin and the other 7% of the pharmacological classes used are selective serotonin reuptake inhibitors (Fluoxetine and Sertraline), mood stabilizers (Divalproex Sodium) and benzodiazepines (Clonazepam). Risperidone is highly recommended for controlling aggression, irritability and stress. Ritalin will act on hyperactivity, impulsivity and inattention.

The Brazilian government emphasizes specific measures for autism because in 2013 the Brazilian Ministry of Health, in partnership with the Unified Health System (SUS), developed a booklet entitled "Guidelines for Attention to the Rehabilitation of People with Autism Spectrum Disorders (ASD)." these guidelines have the role of guiding the multidisciplinary professionals involved in the treatment of the individual with the disease and their family. The sooner the family begins investigations and treatments the better for the child with ASD as they have brain plasticity which makes it easier for them to be taught.

EPILEPSY SEIZURES

Epilepsy is a condition of brain disorder and is divided into types, being generalized epilepsy that affects the entire brain, partial when restricted to just one area, simple which has less risk of unconsciousness and is focused, while complex is characterized by a disorder of consciousness and epileptic discharge. Crises affect the central nervous system, which causes dysfunction in neurons, chemical signals in the brain and brain activity and electrical impulses become abnormal. These changes can happen to any individual of any age group, ethnicity or social group, having considering that depending on the degree of epilepsy, more specialized intervention will be required.

Epilepsies can cause complications in memory, social interaction, perception, communication and language. Its diagnosis can be made through magnetic resonance imaging, electrophoresis, and an assessment that takes place while the person is experiencing a crisis that can be kept in analysis for five to thirty minutes without finding neurological damage to the person. Its cause can be diverse, including genetics, neurological diseases, head trauma, low sugar levels, high fever, prenatal injuries, infectious diseases and patients with Autism spectrum disorder may present comorbidity.

Approximately 80% of patients who present this condition need medication intervention with anticonvulsants, which help control seizures and prevent them from happening. There are currently several medications on the market developed for this with a small number of side effects, such as Carbamazepine, Phenobarbital, Phenobarbital. However, there are lines of research that study the effects of Cannabidiol in people who have this epileptic condition and have observed a great improvement in the condition, thus the effects of CBD.

USE OF CANNABIS FOR AUTISM

Once the patient is diagnosed, the doctor begins drug treatment to contain the crises that are part of the syndrome. Treatment with *Cannabis* can be a new alternative within these medicinal treatments that deviates from the traditional medicines used. The main symptoms that parents begin to notice in their children are difficulty developing verbalization, motor development, impaired sleep and restrictive eating.

Its administration is done gradually so that the body gradually gets used to it. Patients with ASD may experience epilepsy and Cannabis can be introduced to reduce these seizures, in addition it can be used to reduce behavioral and psychological crises and regulate social responses, pleasure, cognition, concentration, body movement, gastrointestinal function, pain and the five senses; A recent study also highlighted that the use of marijuana could also be related to the patient's immune system, which provides a better quality of life as sufferers have a deficit in this area.

The fact that autistic people have a basal neuronal state of hyperexcitability makes the herb a determining factor in the study of autism, which is why its use has been studied so much, being manipulated in a ratio equivalent to 20:1 of CBD: THC (Castro; Albino; Lima, 2021)

``play a role by inhibiting the metabolic degradation of anandamide, because CBD inhibits the enzyme Fatty Acid Amid Hydrolase (FAAH) responsible for degrading this endogenous cannabinoid, leading to its accumulation. This effect will reduce autistic deficits related to neural hyperexcitability, as they have little anandamide stimulating synaptic modulation. `` (Castro; Albino; Lima, 2021)

In addition to the anxiolytic effects and improvement in aggressive behaviors, cannabidiol has been widely used to treat convulsive crises that may be associated with

the disorder. As we saw previously, it was a case of epilepsy in Brazil that gained visibility for the use of this medication for this purpose. (Castro; Albino; Lima, 2021)

The use of *Cannabis* provided behavioral improvements in aggression, self-mutilation and temper tantrums, better interaction at school, quality of sleep, anxiety and repetitive behaviors, which provides a satisfactory quality of life, however, when it comes to improvements in the cognitive aspect, *Cannabis* did not present satisfactory results and patients with ASD with comorbidity in ADHD do not have good response results in this area, therefore it is necessary that, in addition to cannabidiol, other medications such as Ritalin be used. (Aragão,2021)

A study carried out over 9 months analyzed what effects *Cannabis* would have on patients and reported that 60% of individuals completely stopped or significantly reduced their symptoms with these types of medications, once they started using *Cannabis extracts.* `` (Aragão,2021)

It was believed that cannabidioid can improve four functions of the autism phenotype, namely social reward responsiveness, symptoms linked to anxiety, neural development, circadian rhythm which is basically through hormones such as melatonin and cortisol, in addition to the stimuli that the body receives during The day is responsible for regulating metabolism and sleep, thus the scientific community gains four different areas for study to better assist and stimulate patients with this syndrome. (Almeida,2021)

A research carried out, as mentioned by De Souza, (2019) ``analyzed the effects of cannabidiol in 53 patients with an average age of 11 years (85% male and 15% female), followed for a minimum period of 30 days after the start of treatment (average duration of 66 days). Using the cannabinoid oil solution

at a concentration of 30% and a CBD/THC ratio of 1/20, there was an improvement of: 68.4% in the symptom of hyperactivity; 67.6% in self-injurious behavior; 71.4% in sleep problems; finally, 47.1% in signs of anxiety. In all categories of signs, there was no inferiority of CBD in relation to conventional treatments. Considering the general change in signs associated with ASD, there was an improvement in 74.5%, no change in 21.6% and worsening in 3.9%. Side effects were reported to be transient and without repercussions''

Even though there is no medicine on the market capable of comprehensively remedying all the needs of autism spectrum disorder, Cannabis is the one that has brought the most promising results because, unlike other medicines, which act to remedy specific parts of the problem and cause different effects. side effects that harm the sufferer so much that some medications have their use discontinued. Cannabis is an unconventional and very promising medication as its side effects are mild or transient, such as loss of appetite and drowsiness. When starting treatment with the herb and the first results begin to appear, the patient and family benefit, parents of patients with ASD try to spend a lot with their children on psychological treatments, ABA therapies, speech therapists to provide a better quality of life to their children, this together with medications that come at a high cost and unfortunately they live in a reality where they see their children go through all the side effects of the medications and do not develop as well in therapy as the medication cannot do much more than that and are limited and unable to progress in an effective quality of life, Cannabidiol offers an alternative for this advancement where, as mentioned, many patients showed significant improvements and in this context, the patient and the family benefit from this aspect. (Almeida,2021)

FINAL CONSIDERATIONS

We can observe that industrial hemp really presents a significant improvement in the patient's quality of life as there are behavioral improvements in patients who begin to find it easier to use non-drug treatments, as the therapies improve social interaction. We can link this because once behavioral difficulties are mitigated, it facilitates internal intervention for a better approach. Furthermore, the patient's well-being is promoted by providing quality of life as sufferers are often harmed by their repetitive or aggressive behaviors where they can be injured in these situations and with the use of Cannabis we already have a significant reduction in these acts.

Some autistic people have seizures and suffer even more in the process of developing in therapies because not only is their disorder a delaying factor in their neurological and behavioral development, with each seizure they lose the progression they had in therapies because of this. It is extremely important to find a medication that can mitigate this condition so that the child with ASD can suffer fewer brain changes throughout their development, the situation in itself of a child with ASD is already challenging for the family and multidisciplinary professionals. which is part of the routine development and symptoms of the syndrome. Another benefit of introducing Cannabis is that, unlike traditional medicines, it is a natural alternative and has fewer so-called "black stripe" side effects.

From the study texts we can infer that Cannabis Sativa is a new alternative and that it needs more in-depth studies on its long-term effects, especially in pediatric use, thus including children and adolescents who are in the growth phase and thus the effect of marijuana over time is still very uncertain in its neurological development.

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