

Chapter 128

Use of cannabidiol as a treatment alternative for alzheimer's: a literature review

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ABSTRACT

Alzheimer's disease is a neurodegenerative disease in which progressive memory loss occurs and presents cognitive symptoms. Currently, the number of studies with Cannabidiol as a treatment alternative for Alzheimer's disease is growing due to its neuroprotective factor. Research indicates that cannabidiol has the ability to control microglial and neuroinflammation function, favoring the survival rate of cells by combining its anti-inflammatory, antioxidant and neuroprotective effects, which act against toxicity caused by the accumulation of beta-amyloid peptides.

Keywords: Cannabidiol; Alzheimer's disease; Neurotoxicology; Neurology; Receivers.

1 INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative disease in which progressive memory loss occurs and presents cognitive - behavioral symptoms (CHUNG; CUMMINGS, 2000). It is one of the most common causes of dementia and has affected more and more individuals, accounting for about 60% to 70% of cases in the adult population (CACACE; Mr SLEEGERS; BROECKHOVEN, 2016).

AD is characterized by the death of neurons caused by the excessive inflammatory response of the central nervous system (CNS) promoted by microglia and neutrophils, occurring the release of substances such as cytokines, thus stimulating the nearest astrocyte-neuron to produce a greater amount of a peptide called β -amyloid 42 ($A\beta$ 42) that form neural plaques in various parts of the brain such as the neocortex, hippocampus, entorhine area, amygdala, anterior thalamus, basal nucleus and monoaminergic nuclei of the brain stem (ORTIZ et al., 2015; KUMAR; SINGH; EKAVALI, 2015).

Cholinergic strategies have long been advised for the treatment of AD, but only with the introduction of cholinesterase inhibitors (IChEs) has their due efficacy been demonstrated since the studies that were initiated. These treatment effects have been demonstrated for the various IChEs, consistently indicating that these drugs are significantly better than placebo. However, the disease progresses despite this treatment. (SUMMERS WK, MAJOWSKI LV, MARSH GM, et al.).

Pharmacological and non-pharmacological options, being pharmacological drugs such as acetylcholinesterase inhibitors, in addition to anxiolytics, antipsychotics or antidepressants. The non-pharmacological options are physical therapy and occupational therapy to stimulate the brain and memory, even in the face of these options it is possible only to delay the disease and not its improvement. Although medications help alleviate some signs and symptoms, such as agitation, anxiety, depression, confusion and insomnia, these medications are only for a limited number of patients and for a short period of time (COSTA et al., 2019; CAZARIM et al., 2016).

Cannabis sativa is a plant popularly known as marijuana, originated from Central Asia and has great adaptability with regard to climate, altitude and soil (COUTINHO; ARAUJO; GONTIÉS, 2004; BRANDÃO, 2014). There are reports of medicinal use in the Chinese pharmacopoeia, where its use is described for the treatment of various diseases, such as: rheumatic pain, intestinal disorders, malaria and problems of the female reproductive system, in addition to treating insomnia, fever and dysentery (RIBEIRO, 2014; CRIPPA; ZUARDI; HALLAK, 2010).

Investigations on the mechanism of action of Tetrahydrocannabinol (THC) generated the discovery of a cannabinoid receptor in the CNS, called cannabinoid receptor 1 (CB1) (DA COSTA et al., 2014). CB1 is mainly found in the CNS and mediates the psychotropic effects of cannabinoids. After molecular identification of this receptor, the first endocannabinoid (endogenous ligand that is able to activate cannabinoid receptors), anandamide (AEA) was discovered. After the discovery of the CB1 receptor in the central nervous system, another receptor was identified and called the cannabinoid receptor 2 (CB2), located mainly in organs and peripheral nervous system. Other endocannabinoids were also found such as 2- arachidonylglycerol (2-AG), virodamine and others (FONSECA et al., 2013).

Current drug therapies for Alzheimer's disease have questionable efficacy, acting only in the relief of symptoms. Treatment does not prevent the progression of the disease, it only offers limited benefits in cognitive function. In addition, they are related to several adverse effects (DE ALMEIDA CAMARGO FILHO et al., 2019; WATT; KARL, 2017).

The therapeutic use of *Cannabis sativa* as a resource for the treatment of AD has resulted in the growth of research on the pharmacological effect of cannabis on the CNS. The derivative of this plant, CBD has been shown to be effective in several pathologies, including neurocognitive disorders. CBD has acetylcholinesterase inhibitory action and butyrylcholinesterases, so they bring a protective action of cells and inhibitor of oxidative stress, in addition to stimulating neurogenesis of the hippocampus. The junction of THC + CBD is much more effective than only the isolated use of these substances (LESZCO, et al, 2021; MOOKO et al. 2021; KIM et al. 2019).

According to the above , this review aims to investigate in the current literature the use of cannabidiol as an alternative in the treatment of Alzheimer's.

2 MATERIAL AND METHODS

This is a narrative-type bibliographic review. The following databases were used: LILACS, PUBMED and SCIELO, with the descriptors cannabidiol; Alzheimer's disease; neurotoxicology; neurology duly validated by the Descriptors in Health Sciences (DeCS) platform.



3 RESULTS AND DISCUSSION

Alzheimer's is the most common cause of dementia that is a group of brain disorders capable of causing the loss of intellectual and social skills. In Alzheimer's disease brain cells degenerate to death causing a constant decrease in memory and mental function (BITTES et al; 2021).

The etiology of this group of pathology is not yet fully recognized, but there is evidence that it is genetically determined. The development of this pathology begins when the processing of certain proteins of the central nervous system begins to develop physiological activities inappropriately. Where it begins to develop, fragments of poorly cut proteins, which are toxic within neurons and between the spaces that exist between them. As a result of toxicity, there is progressive loss of neurons in certain regions of the central nervous system, more specifically in the hippocampus, which controls memory, and the cerebral cortex, essential for language, reasoning, memory, recognition of sensory stimuli and abstract thinking (BARBOSA et al; 2020).

CBD has its ability to reduce reactive gliosis and is further emphasized by inhibition of . A is characterized as an astroglial-derived neutrophine that plays an important role in the pro-inflammatory cytokine cycle and in the promotion of APP for clitoral, also has involvement with catenin-route block, thus inhibiting tau hyperphosphoreinization in healthy nerve cells. Tau protein helps in the formation of microtubules in cylindrical forms, important for communication between neurons. In Alzheimer's, this protein acts inadequately, disorganized and destroying the microtubules, preventing communication between neurons (BARBOSA et al; 2020).S100BS100BA β 41Wnt/ β

CBD activates a broad spectrum of receptors such as serotonin receptors, vanilloid receptors, adenosine receptors, peroxisome proliferator-activated receptors (PPARs), opioid receptors, and dopamine

receptors. Therefore, CBD has an interesting therapeutic potential beyond the presumed action of cannabinoid receptors (Xiong; Lim; 2021). These results implied that Cannabis CBD components may be useful to treat and prevent AD due to suppressing the main causatous factors of AD (Kim et alits components have the ability to ., 2019).

Author/year	Title	Goal	Findings
Barbosa et al (2020)	The use of Cannabidiol compound in the treatment of Alzheimer's disease (literature review)	Take an approach on the use of the compound cannabidiol (in the treatment of Alzheimer's disease.	The results of this study demonstrated that CBD was able to inhibit the expression of mRNA of acid iced fibrillar acid protein (GFAP) and the protein itself. GFAP is the best known marker of activated astrocytes .
Kim et al (2019)	A Review on Studies of Marijuana for Alzheimer's Disease – Focusing on CBD, THC.	Discuss the research trend of treating dementia using cannabis with the aim of providing the basis for cannabis use for medical purposes in the future.	The results of this article imply that cannabis CBD components may be useful to treat and prevent AD because CBD components can suppress the main causatous factors of AD.
Bittes et al (2021)	Use of cannabinoids in the treatment of persons with Alzheimer's/Use of cannabinoids en el tratamiento de personas con Alzheimer's.	Describe the experience of family members/caregivers of people with Alzheimer's who are using Cannabidiol through the ACALME-Association Cannabis Light Medicinal Institute.	The use of cannabidiol provides quality of life for the person with AD, but it is not yet very clarified causing the treatment to become difficult to access in several aspects.
Xiong, Xiong, Lim (2021)	Understanding the Modulatory Effects of Cannabidiol on Alzheimer's Disease.	Recent studies on the effect of CBD, a phytocannabinoid, on Alzheimer's disease and suggest problems to be overcome for the therapeutic use of CBD.	More evidence is needed to illustrate the facticity of CBD-induced autophagic regulation and the mechanism of modulation of AUTOPHAGY by CBD in AD pathology.
Hao; Feng (2020)	Cannabidiol (CBD) enhanced the hippocampal immune response and autophagy of APP/PS1 Alzheimer's mice uncovered by RNAseq.	Therefore, this study aimed to discover the underlying common mechanism in APP/PS1 mice after chronic administration with CBD using RNA-seq	Data from biochemical experiments indicate that CBD can improve immune system response and autophagy pathway in APP/SP1 mice.

Source: prepared by the authors.

4 CONCLUSION

Research indicates that cannabidiol has the ability to control microglial and neuroinflammation function, favoring the survival rate of cells by combining its anti-inflammatory, antioxidant and neuroprotective effects, which act against toxicity caused by the accumulation of beta-amyloid peptides. The articles show the therapeutic potential of the use of Cannabidiol in people with Alzheimer's, but it should be considered that human trials are scarce. Therefore, further studies on the subject are essential to

ensure the efficacy and safety of the use of these substances in humans, thus providing the best possible treatment for Alzheimer's disease.

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