Use of *Cannabis sativa L.* for the treatment of Alzheimer's disease

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Graphical Abstract
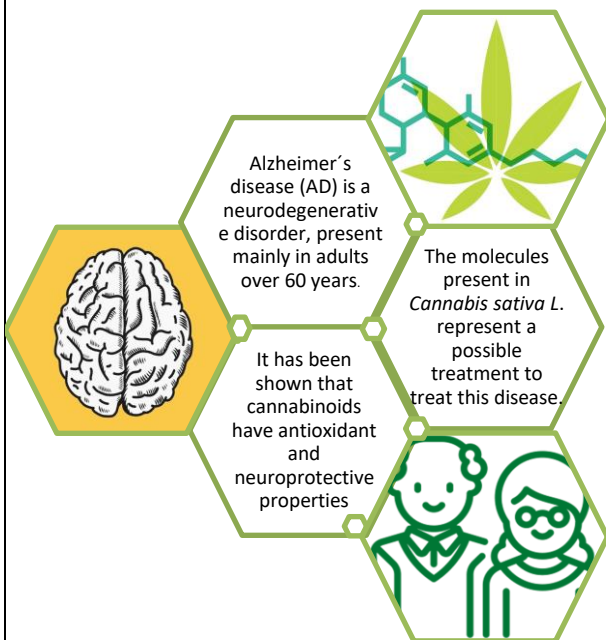
Abstract.

Alzheimer´s Disease (AD) is a neurodegenerative disorder which represents a problem for the public health system because it affects more than 50 million people in the world, currently there is no successful treatment to treat this disease. The most accepted hypothesis regarding the development of this disease is the accumulation of plaques Aβ in the brain, have studied different molecules of natural origin as treatment based on this hypothesis. *Cannabis sativa L.* is a plant that has great potential as a treatment for this disease due to its antioxidant and neuroprotective properties and it has been shown to reduce the accumulation of Aβ plaques.

Keywords: Alzheimer´s disease, Cannabis, Neuroprotection.

Introduction

Alzheimer´s disease (AD) is a neurodegenerative disorder, present mainly in adults over 60 years, studies reveal that it currently affects more than 50 million people in the world and by 2050 it is estimated that the number of patients will triple, within the public health system represents a great threat. This disease is characterized by neuropsychiatric symptoms such a memory loss, symptomatic dementia, psychosis, depression, agitation, irritability and even aggression, these problems affect the patient's daily life as well as their quality of life, once the symptoms are present it is because is a significant an irreversible neuronal damage.

Over the years, studies have been carried out to determine the mechanism of development of AD but it is still not understood. The most accepted hypothesis is related to the accumulation of beta-amyloid plaques (Aβ) and the C-terminal amyloid precursor protein (APP) with the development of AD. Aβ plates also introduce hyperphosphorylation of the protein that forms neurofibrillary tangles that also damage neurons.

Currently there is no cure for this disease. To treat it, different natural alternatives have been sought. It has been reported that small molecules of natural origin that can be used as treatment or to alleviate some symptoms. These can be classified into 4 categories that act with respect to different hypotheses: acetylcholine-related natural products, Aβ and tau protein related natural products, NMDA receptor antagonist and antioxidants, anti-inflammatory. All these molecules represent a potential treatment due to their neuroprotective properties. Most of the existing treatments have been studied based on amyloid hypothesis, but they have not been successful.

Cannabis sativa L. has been little studied by current medicine, but it is a plant with ancestral uses, the cannabis contains more than 500 compounds, of which more than 100 correspond to cannabinoids. The endocannabinoid system is of great importance as it is responsible for carrying out many functions in the body as the response to stress, pain, sleep regulation, food intake and even in neuronal development, which is why it is possible therapeutic objective for the treatment of AD.

There are two types of cannabinoid receptors, cannabinoid 1 (CB1) and cannabinoid 2 (CB2). CB1 are found in neurons, spinal cord and the peripheral nervous system, CB2 are found in immune cells, leukocytes, spleen and tonsils. The neuroprotective characteristics of cannabinoids have been studied through the activation of receptors coupled to the G protein, CB1 and CB2 receptors. Endocannabinoids have been studied for the treatment of neurodegenerative diseases such as AD, they have been shown to be useful when relieving some of the symptoms of this disease such as agitation and aggression and have been shown to be a great alternative treatment to help decrease these symptoms.

It has been shown that Cannabidiol (CBD) decreases the toxicity of beta amyloid peptides that cause the formation of neurofibrillary tangles, this could reduce the rate of disease progression. It has also been shown that by treating mice with delta-9-tetrahydrocannabinol (THC) during the induction of Aβ, the cells do not accumulate the toxic peptide and directly inhibit the Aβ plate aggregation that accumulates in the brain, although this molecule is psychoactive, which is why it is illegal in many countries.

There are other non-psychoactive cannabinoids that have the same ability to eliminate Aβ plate aggregation and protect nerve cells from neurodegenerative diseases, which can be used as therapy for AD. The cannabinoids have antioxidant activities which reduce the rate of radical oxidation, this property is responsible for the neuroprotective effects.

Due to the social rejection and the illegality of this plant there have been few studies for the treatment of AD with the different psychoactive and non-psychoactive molecules it contains, without a doubt it has a great potential as an alternative treatment to treat both the disease and to reduce the symptoms.

Conclusions

The disease of AD is a neurogenerative disease that occurs mainly in adults over 60 years, there is currently no successful treatment to treat this disease, have studied different molecules of natural origin to treat this disease or its symptoms as they have antioxidant properties and neuroprotective. Cannabis sativa L. represents a natural alternative with high potential to treat AD, but for social reasons it has not been widely studied, but within the current studies that have been conducted it has shown successful results to treat both the disease and its symptoms , since it helps reduce the accumulation of Aβ plates, responsible for the development of AD.

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