Alzheimer's Disease

Alzheimer's disease (AD) is a neurological disorder of unknown origin that is characterized by a progressive loss of memory and learned behavior. Patients with Alzheimer's are also likely to experience depression, agitation, and appetite loss, among other symptoms. Over 4.5 million Americans are estimated to be afflicted with the disease. No approved treatments or medications are available to modulate the progression of AD, and few pharmaceuticals effectively treat symptoms of the disease.

Preclinical data shows the potential of cannabinoids to moderate the progression of AD while clinical data demonstrates that these compounds can provide symptom relief.

Writing in the *Journal of Neuroscience*, investigators at Madrid's Complutense University and the Cajal Institute in Spain reported that the intracerebroventricular administration of the synthetic cannabinoid WIN 55,212-2 prevented cognitive impairment and decreased neurotoxicity in rats injected with amyloid-beta peptide (a protein believed to induce Alzheimer's). Additional synthetic cannabinoids were also found to reduce the inflammation associated with Alzheimer's disease in human brain tissue in culture. "Our results indicate that cannabinoids succeed in preventing the neurodegenerative process occurring in the disease," investigators concluded. Further studies by investigators demonstrated that the administration of the nonpsychotropic plant cannabinoid cannabidiol also mitigated memory loss in a mouse model of the disease. Investigators at The Scripps Research Institute in California have reported that THC administration inhibits the enzyme responsible for the aggregation of amyloid plaque — the primary marker for Alzheimer's disease — in a manner "considerably superior" to approved AD drugs such as donepezil and tacrine. "Our results provide a mechanism whereby the THC molecule can directly impact Alzheimer's disease pathology," researchers concluded. "THC and its analogues may provide an improved therapeutic [option] for Alzheimer's disease by... simultaneously treating both the symptoms and the progression of [the] disease." Investigators at the Salk Institute in 2016 reported similar findings in a series of exploratory studies.

The administration of both THC and synthetic cannabinoid agonists have been shown to influence memory loss in animal models. For example, investigators at Ohio State University, Department of Psychology and Neuroscience, reported that older rats administered daily doses of WIN 55,212-2 for a period of three weeks performed significantly better than non-treated controls on a water-maze memory test. Writing in the journal *Neuroscience*, they reported that rats treated with the compound experienced a 50 percent improvement in memory and a 40 to 50 percent reduction in inflammation compared to controls. Israeli researchers in 2017 reported that THC administration can reverse age-related memory impairment in rats, and may offer a potential treatment option in patients with dementia and other neurodegenerative illnesses.

Previous preclinical studies have demonstrated that cannabinoids can prevent neuronal cell death. Some experts believe that these neuroprotective properties could play a role in moderating AD.
Writing in the British Journal of Pharmacology, investigators at Ireland's Trinity College Institute of Neuroscience concluded, "[C]annabinoids offer a multi-faceted approach for the treatment of Alzheimer's disease by providing neuroprotection and reducing neuroinflammation, whilst simultaneously supporting the brain's intrinsic repair mechanisms by augmenting neurotrophin expression and enhancing neurogenesis. ... Manipulation of the cannabinoid pathway offers a pharmacological approach for the treatment of AD that may be efficacious than current treatment regimens."\(^9\)

Clinical trials demonstrate that cannabinoid therapy can mitigate certain AD symptoms. For instance, investigators at Berlin Germany's Charite Universitatmedizin, Department of Psychiatry and Psychotherapy, reported that the daily administration of 2.5 mg of synthetic THC over a two-week period reduced nocturnal motor activity and agitation in AD patients in an open-label pilot study.\(^10\)

Clinical data presented at the 2003 annual meeting of the International Psychogeriatric Association reported that the oral administration of up to 10 mg of synthetic THC reduced agitation and stimulated weight gain in late-stage Alzheimer's patients in an open-label clinical trial.\(^11\) Improved weight gain and a decrease in negative feelings among AD patients administered cannabinoids were previously reported by investigators in the International Journal of Geriatric Psychiatry in 1997.\(^12\)

Most recently, Israeli researchers assessed the safety and efficacy of THC-infused oil in Alzheimer's patients in a four-week trial. Participants experienced decreased incidences of delusions, agitation, irritability, and apathy following treatment. Their quality of sleep also improved. "Adding medical cannabis oil to AD patients' pharmacotherapy is safe and a promising treatment option," investigators concluded.\(^13\)

REFERENCES


