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The potential therapeutic effects of THC on Alzheimer's disease.

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Abstract

The purpose of this study was to investigate the potential therapeutic qualities of Δ9-tetrahydrocannabinol (THC) with respect to slowing or halting the hallmark characteristics of Alzheimer's disease. N2a-variant amyloid-β protein precursor (AβPP) cells were incubated with THC and assayed for amyloid-β (Aβ) levels at the 6-, 24-, and 48-hour time marks. THC was also tested for synergy with caffeine, in respect to the reduction of the Aβ level in N2a/AβPPswe cells. THC was also tested to determine if multiple treatments were beneficial. The MTT assay was performed to test the toxicity of THC. Thioflavin T assays and western blots were performed to test the direct anti-Aβ aggregation significance of THC. Lastly, THC was tested to determine its effects on glycogen synthase kinase-3β (GSK-3β) and related signaling pathways. From the results, we have discovered THC to be effective at lowering Aβ levels in N2a/AβPPswe cells at extremely low concentrations in a dose-dependent manner. However, no additive effect was found by combining caffeine and THC together. We did discover that THC directly interacts with Aβ peptide, thereby inhibiting aggregation. Furthermore, THC was effective at lowering both total GSK-3β levels and phosphorylated GSK-3β in a dose-dependent manner at low concentrations. At the treatment concentrations, no toxicity was observed and the CB1 receptor was not significantly upregulated. Additionally, low doses of THC can enhance mitochondria function and does not inhibit melatonin's enhancement of mitochondria function. These sets of data strongly suggest that THC could be a potential therapeutic treatment option for Alzheimer's disease through multiple functions and pathways.

KEYWORDS: Alzheimer's disease; CB1 receptor; CB2 receptor; amyloid-β peptide; cannabinoid; delta(9)-tetrahydrocannabinol; neurodegeneration

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