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Cannabidiol and cannabigerol effect on cognitive deficit induced by intracerebroventricular administration of amyloid beta 42 in experimental Alzheimer's disease model

Arda Can Aydin[1], Ayse Nur Hazar-Yavuz[1], Naziye Ozkan[2], Sarfraz Ahmad[3]*, Rezzan Gulhan[4], Levent Kabasakal[1] & Hatice Kubra Elcioglu[1]*

[1]Department of Pharmacology, Faculty of Pharmacy, Marmara University, Istanbul 34854, Turkey

[2]Department of Medical Services and Techniques, Vocational School of Health Services, Marmara University, Istanbul 34854, Turkey

[3]AdventHealth Medical Center, Orlando, FL 32804, USA

[4]Department of Medical Pharmacology, Faculty of Medicine, Marmara University, Istanbul 34854, Turkey

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Alzheimer's disease (AD) causes amyloid beta (Aβ) plaque formation in regions such as the cerebral cortex and hippocampus, which have a cognitive function. Besides oxidative stress, neuroinflammation and acetylcholine, the degeneration of glutamatergic pathways in individuals with AD causes acetylcholine accumulation in the cortex and hippocampus, leading to the formation of Aβ plaque. Herein, we investigated the effects of cannabidiol (CBD) and cannabigerol (CBG) which are *Cannabis sativa* components on AD-like cognitive deficit induced by intracerebroventricular (*icv*) administration of $A\beta_{1-42}$. Sprague Dawley rats were divided into four groups: i) Control, ii) Alzheimer, iii) Alzheimer+CBD, and iv) Alzheimer+CBG. The AD model was induced by icv injection of $A\beta_{1-42}$ and then CBD and CBG treatments were administrated for 2 weeks. Open field test, passive avoidance test, and Morris' water maze test were performed, and on 15th day, the rats were decapitated. Hippocampus and cerebral cortex were removed from the brain, and levels of interleukin-1β (IL-1β) and tumour necrosis factor-α (TNF-α) were measured by ELISA, and $A\beta_{1-42}$ expression was evaluated immunohistochemically. There was no significant difference between the groups in the parameters evaluated by the open field test. In passive avoidance and Morris's water maze tests, both CBD and CBG enhanced the learning-memory functions impaired by AD. CBD and CBG treatments successfully reduced the levels of TNF-α and IL-1β in AD. Immunohistochemical analysis revealed decreased expression of $A\beta_{1-42}$ in CBD and CBG treatment groups. CBD and CBG treatments improved learning and memory deficits in the $A\beta_{1-42}$ induced AD model. We implicate that these experimental findings would lead to better avenues for targeted studies on *C. sativa* (a natural product of herbal origin and its components) that can potentially be developed for AD treatment.

Keywords: Alzheimer's disease, Rat model, Cannabidiol, Cannabigerol, Inflammatory cytokine, Amyloid beta