CBD: Transplants

Biol Blood Marrow Transplant. 2015 Oct;21(10):1770-5. doi: 10.1016/j.bbmt.2015.05.018. Epub 2015 May 30.

Cannabidiol for the Prevention of Graft-versus-Host-Disease after Allogeneic Hematopoietic Cell Transplantation: Results of a Phase II Study.

Yeshurun M[1], Shpilberg O[2], Herscovici C[2], Shargian L[2], Dreyer J[3], Peck A[3], Israeli M[4], Levy-Assaraf M[5], Gruenewald T[6], Mechoulam R[7], Raanani P[2], Ram R[2].

Abstract

Graft-versus-host-disease (GVHD) is a major obstacle to successful allogeneic hematopoietic cell transplantation (alloHCT). Cannabidiol (CBD), a nonpsychotropic ingredient of Cannabis sativa, possesses potent anti-inflammatory and immunosuppressive properties. We hypothesized that CBD may decrease GVHD incidence and severity after alloHCT. We conducted a phase II study. GVHD prophylaxis consisted of cyclosporine and a short course of methotrexate. Patients transplanted from an unrelated donor were given low-dose anti-T cell globulin. CBD 300 mg/day was given orally starting 7 days before transplantation until day 30. Forty-eight consecutive adult patients undergoing alloHCT were enrolled. Thirty-eight patients (79%) had acute leukemia or myelodysplastic syndrome and 35 patients (73%) were given myeloablative conditioning. The donor was either an HLA-identical sibling (n = 28), a 10/10 matched unrelated donor (n = 16), or a 1-antigen-mismatched unrelated donor (n = 4). The median follow-up was 16 months (range, 7 to 23). No grades 3 to 4 toxicities were attributed to CBD. None of the patients developed acute GVHD while consuming CBD. In an intention-to-treat analysis, we found that the cumulative incidence rates of grades II to IV and grades III to IV acute GVHD by day 100 were 12.1% and 5%, respectively. Compared with 101 historical control subjects given standard GVHD prophylaxis, the hazard ratio of developing grades II to IV acute GVHD among subjects treated with CBD plus standard GVHD prophylaxis was .3 (P = .0002). Rates of nonrelapse mortality at 100 days and at 1 year after transplantation were 8.6% and 13.4%, respectively. Among patients surviving more than 100 days, the cumulative incidences of moderate-to-severe chronic GVHD at 12 and 18 months were 20% and 33%, respectively. The combination of CBD with standard GVHD prophylaxis is a safe and promising strategy to reduce the incidence of acute GVHD. A randomized double-blind controlled study is warranted. (clinicaltrials.gov: NCT01385124).

KEYWORDS:

Allogeneic hematopoietic cell transplantation; Cannabidiol; Cannabis sativa; Graft-versus-host disease; Prophylaxis
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Free full text

CBD: Innate and Humoral Immunity

Pharmacology. 1983;26(1):1-11.

Effects of delta 9-tetrahydrocannabinol, cannabinol and cannabidiol on the immune system in mice. I. In vivo investigation of the primary and secondary immune response.

Baczynsky WO, Zimmerman AM.

Abstract
The effects of the cannabinoids delta 9-tetrahydrocannabinol (THC), cannabinol and cannabidiol on the primary humoral immune response, the secondary humoral immune response and the memory aspect of humoral immunity in response to sheep red blood cell (SRBC) immunization was investigated. Mice treated with THC (10 and 15 mg/kg) during the primary immunization period exhibited a suppression of the primary humoral immune response. Mice treated with THC during the secondary immunization period showed no measurable suppression of the secondary humoral immune response to the immunizing antigen. The memory aspect of humoral immunity was assessed when treatment with cannabinoids was carried out during the primary immunization period and the ability of mice to undergo a secondary immune response was evaluated; suppression of the secondary humoral immune response was evident with THC treatment (10 and 15 mg/kg). Cannabinol and cannabidiol (10 and 25 mg/kg) treated mice showed no impairment in the ability to undergo primary or secondary immune responses with any treatment protocol. In vivo investigations of the effects of cannabinoids on the thymus were also carried out. Thymus weight and thymus cell number were depressed in mice undergoing a primary humoral immune response when treated with THC (10 and 15 mg/kg) during this period. THC treatment, however, did not alter these parameters in mice not challenged with antigen. In both challenged and unchallenged animals, cannabinol and cannabidiol did not measurably alter the thymus.

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6298841
DOI:
10.1159/000137763
[Indexed for MEDLINE]

THC/CBD/CBN: Spleen function

Pharmacology. 1977;15(1):10-23.

delta1-tetrahydrocannabinol, cannabidiol and cannabinol effects on the immune response of mice.

Zimmerman S, Zimmerman AM, Cameron IL, Laurence HL.

Abstract

delta1-tetrahydrocannabinol (THC) elicited a dose-dependent (1, 5, 10 mg/kg) depression of the immune response, of immature mice, stimulated with sheep red blood cells. The impairment of humoral immunity was specific for THC but not for cannabidiol at 25 mg/kg or cannabinol at 25 mg/kg. The mice were given four daily doses (i.p.) of either drug or vehicle (Tween 80-propylene glycol in 1% saline) or a single injection (i.p.) of sheep red blood cells in addition to four daily doses (i.p.) of drug or vehicle. Suppression of the antigenic response by THC was reflected as a reduction of splenic weight, reduction in the number of splenic antibody-forming cells, lowered hemagglutination titer and reduction in the percentage of splenic white pulp of total spleen volume.

PMID:
320608
DOI:
10.1159/000136658

CBD: modulates autoimmune

J Neuroinflammation. 2016 Jun 3;13(1):136. doi: 10.1186/s12974-016-0603-x.

Pathways and gene networks mediating the regulatory effects of cannabidiol, a nonpsychoactive cannabinoid, in autoimmune T cells.

Kozela E1,2, Juknat A3,4, Gao F5, Kaushansky N4, Coppola G5, Vogel Z3,4.
Author information

Abstract
BACKGROUND:
Our previous studies showed that the non-psychoactive cannabinoid, cannabidiol (CBD), ameliorates the clinical symptoms in mouse myelin oligodendrocyte glycoprotein (MOG)35-55-induced experimental autoimmune encephalomyelitis model of multiple sclerosis (MS) as well as decreases the memory MOG35-55-specific T cell (TMOG) proliferation and cytokine secretion including IL-17, a key autoimmune factor. The mechanisms of these activities are currently poorly understood.
METHODS:
Herein, using microarray-based gene expression profiling, we describe gene networks and intracellular pathways involved in CBD-induced suppression of these activated memory TMOG cells. Encephalitogenic TMOG cells were stimulated with MOG35-55 in the presence of spleen-derived antigen presenting cells (APC) with or without CBD. mRNA of purified TMOG was then subjected to Illumina microarray analysis followed by ingenuity pathway analysis (IPA), weighted gene co-expression network analysis (WGCNA) and gene ontology (GO) elucidation of gene interactions. Results were validated using qPCR and ELISA assays.
RESULTS:
Gene profiling showed that the CBD treatment suppresses the transcription of a large number of proinflammatory genes in activated TMOG. These include cytokines (Xcl1, Il3, Il12a, Il1b), cytokine receptors (Cxcr1, Ifngr1), transcription factors (Ier3, Atf3, Nr4a3, Crem), and TNF superfamily signaling molecules (Tnfsf11, Tnfsf14, Tnfrsf9, Tnfrsf18). "IL-17 differentiation" and "IL-6 and IL-10-signaling" were identified among the top processes affected by CBD. CBD increases a number of IFN-dependent transcripts (Rgs16, Mx2, Rsad2, Irf4, Ifit2, Ephx1, Ets2) known to execute anti-proliferative activities in T cells. Interestingly, certain MOG35-55 up-regulated transcripts were maintained at high levels in the presence of CBD, including transcription factors (Egr2, Egr1, Tbx21), cytokines (Csf2, Tnf, Ifng), and chemokines (Ccl3, Ccl4, Cxcl10) suggesting that CBD may promote exhaustion of memory TMOG cells. In addition, CBD enhanced the transcription of T cell co-inhibitory molecules (Btla, Lag3, Trat1, and CD69) known to interfere with T/APC interactions. Furthermore, CBD enhanced the transcription of oxidative stress modulators with potent anti-inflammatory activity that are controlled by Nfe2l2/Nrf2 (Mt1, Mt2a, Slc30a1, Hmox1).
CONCLUSIONS:

Microarray-based gene expression profiling demonstrated that CBD exerts its immunoregulatory effects in activated memory TMOG cells via (a) suppressing proinflammatory Th17-related transcription, (b) by promoting T cell exhaustion/tolerance, (c) enhancing IFN-dependent anti-proliferative program, (d) hampering antigen presentation, and (d) inducing antioxidant milieu resolving inflammation. These findings put forward mechanism by which CBD exerts its anti-inflammatory effects as well as explain the beneficial role of CBD in pathological memory T cells and in autoimmune diseases.

KEYWORDS:
Autoimmune; Cannabidiol; Gene expression; Memory T cells
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Free PMC Article

THC: T-cells and Resistance to Infection

Effects of Cannabinoids on T-cell Function and Resistance to Infection.

J Neuroimmune Pharmacol. https://www.ncbi.nlm.nih.gov/pubmed/25876735 2015 Jun;10(2): 204-16. doi: 10.1007/s11481-015-9603-3. Epub 2015 Apr 16. Temple University School of Medicine, Room 859, 3500 N. Broad St., Philadelphia, PA,

Abstract - Regarding ∆(9)-THC - Ultra-low doses offer synergistic immune modulation without psychoactive effect.

This review examines the effects of cannabinoids on immune function, with a focus on effects on T-cells, as well as on resistance to infection. The paper considers the immune modulating capacity of marijuana, of ∆(9)-THC extracted from the marijuana plant, and synthetic cannabinoids. Of particular interest are synthetic compounds that are CB2 receptor (CB2R) selective agonists. As the CB2R is principally expressed on cells of the immune system, agonists that target this receptor, and not CB1 (which is mainly expressed on neurons), have the possibility of altering immune function without psychoactive effects. The overall conclusion of the studies discussed in this review is that cannabinoids that bind to the CB2 receptor, including ∆(9)-THC and CB2 selective agonists are immunosuppressive. The studies provide objective evidence for potentially beneficial effects of marijuana and ∆(9)-THC on the immune system in conditions where it is desirable to dampen immune responses. Evidence is also reviewed supporting the conclusion that these same compounds can sensitize to some infections through their immunosuppressive activities, but not to others. An emerging area of investigation that is reviewed is evidence to support the conclusion that CB2 selective agonists are a new class of immunosuppressive and anti-inflammatory compounds that may have exceptional beneficial effects in a variety of conditions, such as autoimmune diseases and graft rejection, where it is desirable to dampen the immune response without psychoactive effects.

CBD in Acute Febrile Seizures

“Cannabidiol as a Potential Treatment for Febrile Infection-Related Epilepsy Syndrome (FIRES) in the Acute and Chronic Phases.”

J Child Neurol. 2017 Jan;32(1):35-40. doi: 10.1177/0883073816669450. Epub 2016 Sep 29.https://www.ncbi.nlm.nih.gov/pubmed/27655472#

Abstract

Febrile infection-related epilepsy syndrome (FIRES) is a devastating epilepsy affecting normal children after a febrile illness. FIRES presents with an acute phase with super-refractory status epilepticus and all patients progress to a chronic phase with persistent refractory epilepsy. The typical outcome is severe encephalopathy or death. The authors present 7 children from 5 centers with FIRES who had not responded to antiepileptic drugs or other therapies who were given cannabadiol (Epidiolex, GW Pharma) on emergency or expanded investigational protocols in either the acute or chronic phase of illness. After starting cannabidiol, 6 of 7 patients' seizures improved in frequency and duration. One patient died due to multiorgan failure secondary to isoflourane [general anesthetic]. An average of 4 antiepileptic drugs were weaned. Currently 5 subjects are ambulatory, 1 walks with assistance, and 4 are verbal. While this is an open-label case series, the authors add cannabidiol as a possible treatment for FIRES.

CBD: Herpes-type viruses

“Cannabidiol inhibits growth and induces programmed cell death in kaposi sarcoma-associated herpesvirus-infected endothelium.”

https://www.ncbi.nlm.nih.gov/pubmed/23264851 Genes Cancer. 2012 Jul;3(7-8):512-20. doi: 10.1177/1947601912466556.

Abstract Kaposi sarcoma is the most common neoplasm caused by Kaposi sarcoma-associated herpesvirus (KSHV). It is prevalent among the elderly in the Mediterranean, inhabitants of sub-Saharan Africa, and immunocompromised individuals such as organ transplant recipients and AIDS patients. Current treatments for Kaposi sarcoma can inhibit tumor growth but are not able to eliminate KSHV from the host. When the host's immune system weakens, KSHV begins to replicate again, and active tumor growth ensues. New therapeutic approaches are needed. Cannabidiol (CBD), a plant-derived cannabinoid, exhibits promising antitumor effects without inducing psychoactive side effects. CBD is emerging as a novel therapeutic for various disorders, including cancer. In this study, we investigated the effects of CBD both on the infection of endothelial cells (ECs) by KSHV and on the growth and apoptosis of KSHV-infected ECs, an in vitro model for the transformation of normal endothelium to Kaposi sarcoma. While CBD did not affect the efficiency with which KSHV infected ECs, it reduced proliferation and induced apoptosis in those infected by the virus. CBD inhibited the expression of KSHV viral G protein-coupled receptor (vGPCR), its agonist, the chemokine growth-regulated protein α (GRO-α), vascular endothelial growth factor receptor 3 (VEGFR-3), and the VEGFR-3 ligand, vascular endothelial growth factor C (VEGF-C). This suggests a potential mechanism by which CBD exerts its effects on KSHV-infected endothelium and supports the further examination of CBD as a novel targeted agent for the treatment of Kaposi sarcoma.

CBD: meningitis

Cannabidiol reduces host immune response and prevents cognitive impairments in Wistar rats submitted to pneumococcal meningitis.

Eur J Pharmacol. 2012 Dec 15;697(1-3):158-64. doi: 10.1016/j.ejphar.2012.09.053. Epub 2012 Oct 16. https://www.ncbi.nlm.nih.gov/pubmed/23085269

Abstract Pneumococcal meningitis is a life-threatening disease characterized by an acute infection affecting the pia matter, arachnoid and subarachnoid space. The intense inflammatory response is associated with a significant mortality rate and neurologic sequelae, such as, seizures, sensory-motor deficits and impairment of learning and memory. The aim of this study was to evaluate the effects of acute and extended administration of cannabidiol on pro-inflammatory cytokines and behavioral parameters in adult Wistar rats submitted to pneumococcal meningitis. Male Wistar rats underwent a cisterna magna tap and received either 10μl of sterile saline as a placebo or an equivalent volume of S. pneumoniae suspension. Rats subjected to meningitis were treated by intraperitoneal injection with cannabidiol (2.5, 5, or 10mg/kg once or daily for 9 days after meningitis induction) or a placebo. Six hours after meningitis induction, the rats that received one dose were killed and the hippocampus and frontal cortex were obtained to assess cytokines/chemokine and brain-derived neurotrophic factor levels. On the 10th day, the rats were submitted to the inhibitory avoidance task. After the task, the animals were killed and samples from the hippocampus and frontal cortex were obtained. The extended administration of cannabidiol at different doses reduced the TNF-α level in frontal cortex. Prolonged treatment with canabidiol, 10mg/kg, prevented memory impairment in rats with pneumococcal meningitis. Although descriptive, our results demonstrate that cannabidiol has anti-inflammatory effects in pneumococcal meningitis and prevents cognitive sequel.

CBD: Sepsis - anti-inflammatory protection

Treatment with cannabidiol reverses oxidative stress parameters, cognitive impairment and mortality in rats submitted to sepsis by cecal ligation and puncture.

https://www.ncbi.nlm.nih.gov/pubmed/20561509 Brain Res. 2010 Aug 12;1348:128-38. doi: 10.1016/j.brainres.2010.06.023. Epub 2010 Jun 16.Universidade do Extremo Sul Catarinense, 88806-000 Criciúma, SC, Brazil.

Abstract: Oxidative stress plays an important role in the development of cognitive impairment in sepsis. Here we assess the effects of acute and extended administration of cannabidiol (CBD) on oxidative stress parameters in peripheral organs and in the brain, cognitive impairment, and mortality in rats submitted to sepsis by cecal ligation and perforation (CLP). To this aim, male Wistar rats underwent either sham operation or CLP. Rats subjected to CLP were treated by intraperitoneal injection with "basic support" and CBD (at 2.5, 5, or 10mg/kg once or daily for 9days after CLP) or vehicle. Six hours after CLP (early times), the rats were killed and samples from lung, liver, kidney, heart, spleen, and brain (hippocampus, striatum, and cortex) were obtained and assayed for thiobarbituric acid reactive species (TBARS) formation and protein carbonyls. On the 10th day (late times), the rats were submitted to the inhibitory avoidance task. After the test, the animals were killed and samples from lung, liver, kidney, heart, spleen, and brain (hippocampus) were obtained and assayed for TBARS formation and protein carbonyls. The acute and extended administration of CBD at different doses reduced TBARS and carbonyl levels in some organs and had no effects in others, ameliorated cognitive impairment, and significantly reduced mortality in rats submitted to CLP. Our data provide the first experimental demonstration that CBD reduces the consequences of sepsis induced by CLP in rats, by decreasing oxidative stress in peripheral organs and in the brain, improving impaired cognitive function, and decreasing mortality.

CBD: Brain Infections : Cerebral Malaria

Cannabidiol increases survival and promotes rescue of cognitive function in a murine model of cerebral malaria.

https://www.ncbi.nlm.nih.gov/pubmed/25595981 Neuroscience. 2015 Mar 19;289:166-80. doi: 10.1016/j.neuroscience.2014.12.051. Epub 2015 Jan 13.

Abstract: Cerebral malaria (CM) is a severe complication resulting from Plasmodium falciparum infection that might cause permanent neurological deficits. Cannabidiol (CBD) is a nonpsychotomimetic compound of Cannabis sativa with neuroprotective properties. In the present work, we evaluated the effects of CBD in a murine model of CM. Female mice were infected with Plasmodium berghei ANKA (PbA) and treated with CBD (30mg/kg/day - 3 or 7days i.p.) or vehicle. On 5th day-post-infection (dpi), at the peak of the disease), animals were treated with single or repeated doses of Artesunate, an antimalarial drug. All groups were tested for memory impairment (Novel Object Recognition or Morris Water Maze) and anxiety-like behaviors (Open field or elevated plus maze test) in different stages of the disease (at the peak or after the complete clearance of the disease). Th1/Th2 cytokines and neurotrophins (brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF)) were measured in the prefrontal cortex and hippocampus of experimental groups. PbA-infected mice displayed memory deficits and exhibited increase in anxiety-like behaviors on the 5dpi or after the clearance of the parasitemia, effects prevented by CBD treatment. On 5dpi, TNF-α and IL-6 increased in the hippocampus, while only IL-6 increased in the prefrontal cortex. CBD treatment resulted in an increase in BDNF expression in the hippocampus and decreased levels of proinflammatory cytokines in the hippocampus (TNF-α) and prefrontal cortex (IL-6). Our results indicate that CBD exhibits neuroprotective effects in CM model and might be useful as an adjunctive therapy to prevent neurological symptoms following this disease.

CBD: myocarditis and autoimmune

Mol Med. 2016 Sep;22:136-146. doi: 10.2119/molmed.2016.00007. Epub 2016 Jan 8.

Cannabidiol Limits T Cell-Mediated Chronic Autoimmune Myocarditis: Implications to Autoimmune Disorders and Organ Transplantation.

Lee WS1,2, Erdelyi K1, Matyas C1,3, Mukhopadhyay P1, Varga ZV1, Liaudet L4, Haskú G5, Čiháková D6, Mechoulam R7, Pacher P1.
Author information

Abstract
Myocarditis is a major cause of heart failure and sudden cardiac death in young adults and adolescents. Many cases of myocarditis are associated with autoimmune processes in which cardiac myosin is a major autoantigen. Conventional immunosuppressive therapies often provide unsatisfactory results and are associated with adverse toxicities during the treatment of autoimmune myocarditis. Cannabidiol (CBD) is a nonpsychoactive constituent of marijuana that exerts antiinflammatory effects independent of classical cannabinoid receptors. Recently, 80 clinical trials have investigated the effects of CBD in various diseases from inflammatory bowel disease to graft versus host disease. CBD-based formulations are used for the management of multiple sclerosis in numerous countries, and CBD also received U.S. Food and Drug Administration approval for the treatment of refractory childhood epilepsy and glioblastoma multiforme. Herein, using a well-established mouse model of experimental autoimmune myocarditis (EAM) induced by immunization with cardiac myosin emmulsified in adjuvant resulting in T cell-mediated inflammation, cardiomyocyte cell death, fibrosis and myocardial dysfunction, we studied the potential beneficial effects of CBD. EAM was characterized by marked myocardial T-cell infiltration, profound inflammatory response and fibrosis (measured by quantitative real-time polymerase chain reaction, histology and immunohistochemistry analyses) accompanied by marked attenuation of both systolic and diastolic cardiac functions measured with a pressure-volume conductance catheter technique. Chronic treatment with CBD largely attenuated the CD3+ and CD4+ T cell-mediated inflammatory response and injury, myocardial fibrosis and cardiac dysfunction in mice. In conclusion, CBD may represent a promising novel treatment for managing autoimmune myocarditis and possibly other autoimmune disorders and organ transplantation.

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CBD: a more balanced immune system

Cell Immunol. 2017 Feb;312:25-34. doi: 10.1016/j.cellimm.2016.11.006. Epub 2016 Nov 9.

Cannabidiol (CBD) induces functional Tregs in response to low-level T cell activation.

Dhital S[1], Stokes JV[2], Park N[2], Seo KS[2], Kaplan BL[3].

Abstract

Many effects of the non-psychoactive cannabinoid, cannabidiol (CBD), have been described in immune responses induced by strong immunological stimuli. It has also been shown that CBD enhances IL-2 production in response to low-level T cell stimulation. Since IL-2, in combination with TGF-β1, are critical for Treg induction, we hypothesized that CBD would induce $CD4^+CD25^+FOXP3^+$ Tregs in response to low-level stimulation. Low-level T cell stimulation conditions were established based on minimal CD25 expression in $CD4^+$ cells using suboptimal PMA/Io (4nM/0.05μM, S/o), ultrasuboptimal PMA/Io (1nM/0.0125μM, Us/o) or soluble anti-CD3/28 (400-800ng each, s3/28). CBD increased $CD25^+FOXP3^+$ cells from $CD4^+$, $CD4^+CD25^+$, and $CD4^+CD25^-$ T cells, as well as in $CD4^+$ T cells derived from FOXP3-GFP mice. Most importantly, the Us/o+CBD-induced $CD4^+CD25^+$ Tregs robustly suppressed responder T cell proliferation, demonstrating that the mechanism by which CBD is immunosuppressive under low-level T cell stimulation involves induction of functional Tregs.

KEYWORDS:
CBD; CD4(+)CD25(+)FOXP3(+) Tregs; Immunosuppression
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27865421
PMCID:
PMC5327652
DOI:
10.1016/j.cellimm.2016.11.006
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CBD: autoimmune

Exp Neurol. 2017 Dec;298(Pt A):57-67. doi: 10.1016/j.expneurol.2017.08.017. Epub 2017 Sep 1

Mechanisms of action of cannabidiol in adoptively transferred experimental autoimmune encephalomyelitis.

González-García C[1], Torres IM[2], García-Hernández R[3], Campos-Ruíz L[4], Esparragoza LR[5], Coronado MJ[6], Grande AG[7], García-Merino A[8], Sánchez López AJ[9].

Abstract

Cannabidiol (CBD) is one of the most important compounds in Cannabis sativa, lacks psychotropic effects, and possesses a high number of therapeutic properties including the amelioration of experimental autoimmune encephalomyelitis (EAE). The aim of this study was to analyse the relative efficacy of CBD in adoptively transferred EAE (at-EAE), a model that allows better delineation of the effector phase of EAE. Splenocytes and lymph nodes from mice with actively induced EAE were cultured in the presence of MOG_{35-55} and IL-12 and inoculated intraperitoneally in recipient female C57BL/6J mice. The effects of CBD were evaluated using clinical scores and magnetic resonance imaging (MRI). In the central nervous system, the extent of cell infiltration, axonal damage, demyelination, microglial activation and cannabinoid receptors expression was assessed by immunohistochemistry. Lymph cell viability, apoptosis, oxidative stress and IL-6 production were measured in vitro. Preventive intraperitoneal treatment with CBD ameliorated the clinical signs of at-EAE, and this improvement was accompanied by a reduction of the apparent diffusion coefficient in the subiculum area of the brain. Inflammatory infiltration, axonal damage, and demyelination were reduced, and cannabinoid receptor expression was modulated. Incubation with CBD decreased encephalitogenic cell viability, increasing early apoptosis and reactive oxygen species (ROS) and decreasing IL-6 production. The reduction in viability was not mediated by CB_1, CB_2 or GPR55 receptors. CBD markedly improved the clinical signs of at-EAE and reduced infiltration, demyelination and axonal damage. The CBD-mediated decrease in the viability of encephalitogenic cells involves ROS generation, apoptosis and a decrease in IL-6 production and may contribute to the therapeutic effect of this compound.

KEYWORDS:
Cannabidiol; Cannabinoid; Experimental autoimmune encephalomyelitis
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