CBD: Diabetes

Autoimmunity. 2006 Mar;39(2):143-51.

Cannabidiol lowers incidence of diabetes in non-obese diabetic mice.

Weiss L[1], Zeira M, Reich S, Har-Noy M, Mechoulam R, Slavin S, Gallily R.

Abstract

Cannabidinoids are components of the Cannabis sativa (marijuana) plant that have been shown capable of suppressing inflammation and various aspects of cell-mediated immunity. Cannabidiol (CBD), a non-psychoactive cannabidinoid has been previously shown by us to suppress cell-mediated autoimmune joint destruction in an animal model of rheumatoid arthritis. We now report that CBD treatment significantly reduces the incidence of diabetes in NOD mice from an incidence of 86% in non-treated control mice to an incidence of 30% in CBD-treated mice. CBD treatment also resulted in the significant reduction of plasma levels of the pro-inflammatory cytokines, IFN-gamma and TNF-alpha. Th1-associated cytokine production of in vitro activated T-cells and peritoneal macrophages was also significantly reduced in CBD-treated mice, whereas production of the Th2-associated cytokines, IL-4 and IL-10, was increased when compared to untreated control mice. Histological examination of the pancreatic islets of CBD-treated mice revealed significantly reduced insulitis. Our results indicate that CBD can inhibit and delay destructive insulitis and inflammatory Th1-associated cytokine production in NOD mice resulting in a decreased incidence of diabetes possibly through an immunomodulatory mechanism shifting the immune response from Th1 to Th2 dominance.
PMID:16698671DOI:10.1080/08916930500356674
[Indexed for MEDLINE]

Type-1 Diabetes: CBD

“Cannabidiol Arrests Onset of Autoimmune Diabetes in NOD Mice”

Hebrew University Medical School, Jerusalem, 2009: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2270485/

ABSTRACT: We have previously reported that cannabidiol (CBD) lowers the incidence of diabetes in young non-obese diabetes-prone (NOD) female mice. In the present study we show that administration of CBD to 11–14 week old female NOD mice, which are either in a latent diabetes stage or with initial symptoms of diabetes, ameliorates the manifestations of the disease. Diabetes was diagnosed in only 32% of the mice in the CBD-treated group, compared to 86% and 100% in the emulsifier-treated and untreated groups, respectively. In addition, the level of the proinflammatory cytokine IL-12 produced by splenocytes was significantly reduced, whereas the level of the anti-inflammatory IL-10 was significantly elevated following CBD-treatment. Histological examination of the pancreata of CBD-treated mice revealed more intact islets than in the controls. Our data strengthen our previous assumption that CBD, known to be safe in man, can possibly be used as a therapeutic agent for treatment of type 1 diabetes.

CBD: Diabetes

Inhibition of aldose reductase activity by Cannabis sativa chemotypes extracts with high content of cannabidiol or cannabigerol.

Fitoterapia. 2018 Jun;127:101-108. doi: 10.1016/j.fitote.2018.02.002. Epub 2018 Feb 7.
Author information

Abstract Aldose reductase (ALR2) is a key enzyme involved in diabetic complications and the search for new aldose reductase inhibitors (ARIs) is currently very important. The synthetic ARIs are often associated with deleterious side effects and medicinal and edible plants, containing compounds with aldose reductase inhibitory activity, could be useful for prevention and therapy of diabetic complications. Non-psychotropic phytocannabinoids exert multiple pharmacological effects with therapeutic potential in many diseases such as inflammation, cancer, diabetes. Here, we have investigated the inhibitory effects of extracts and their fractions from two Cannabis sativa L. chemotypes with high content of cannabidiol (CBD)/cannabidiolic acid (CBDA) and cannabigerol (CBG)/cannabigerolic acid (CBGA), respectively, on human recombinant and pig kidney aldose reductase activity in vitro. A molecular docking study was performed to evaluate the interaction of these cannabinoids with the active site of ALR2 compared to known ARIs. The extracts showed significant dose-dependent aldose reductase inhibitory activity (>70%) and higher than fractions. The inhibitory activity of the fractions was greater for acidic cannabinoid-rich fractions. Comparative molecular docking results have shown a higher stability of the ALR2-cannabinoid acids complex than the other inhibitors. The extracts of Cannabis with high content of non-psychotropic cannabinoids CBD/CBDA or CBG/CBGA significantly inhibit aldose reductase activity. These results may have some relevance for the possible use of C. sativa chemotypes based preparations as aldose reductase inhibitors.

https://en.wikipedia.org/wiki/GSK3B – upregulates – GSK3B is involved in **energy metabolism,** neuronal cell development, and body pattern formation.[9][10] It might be a new therapeutic target for ischemic stroke.

https://en.wikipedia.org/wiki/Aldose_reductase – inhibits – target for diabetes – this enzyme induces glucose metabolism - In enzymology, **aldose reductase** (or **aldehyde reductase**) (EC 1.1.1.21) is a cytosolic NADPH-dependent oxidoreductase that catalyzes the reduction of a variety of aldehydes and carbonyls, including monosaccharides. It is primarily known for catalyzing the reduction of glucose to sorbitol, the first step in polyol pathway of glucose metabolism.[1] **Aldose reductase inhibitors** are a class of drugs being studied as a way to prevent eye and nerve damage in people with **diabetes.**

CBD:improved insulin sensitivity

J Hepatol. 2015 Jun;62(6):1382-90. doi: 10.1016/j.jhep.2015.01.001. Epub 2015 Jan 13.

Two non-psychoactive cannabinoids reduce intracellular lipid levels and inhibit hepatosteatosis.

Silvestri C[1], Paris D[1], Martella A[1], Melck D[1], Guadagnino I[1], Cawthorne M[2], Motta A[1], Di Marzo V[3].

Abstract

BACKGROUND & AIMS:
Obesity and associated metabolic syndrome have quickly become a pandemic and a major detriment to global human health. The presence of non-alcoholic fatty liver disease (NAFLD; hepatosteatosis) in obesity has been linked to the worsening of the metabolic syndrome, including the development of insulin resistance and cardiovascular disease. Currently, there are few options to treat NAFLD, including life style changes and insulin sensitizers. Recent evidence suggests that the cannabinoids Δ(9)-tetrahydrocannabivarin (THCV) and cannabidiol (CBD) improve insulin sensitivity; we aimed at studying their effects on lipid levels.

METHODS:
The effects of THCV and CBD on lipid levels were examined in a variety of in vitro and in vivo systems, with special emphasis on models of hepatosteatosis. Transcriptional, post-translational and metabolomic changes were assayed.

RESULTS:
THCV and CBD directly reduce accumulated lipid levels in vitro in a hepatosteatosis model and adipocytes. Nuclear magnetic resonance- (NMR) based metabolomics confirmed these results and further identified specific metabolic changes in THCV and CBD-treated hepatocytes. Treatment also induced post-translational changes in a variety of proteins such as CREB, PRAS40, AMPKa2 and several STATs indicating increased lipid metabolism and, possibly, mitochondrial activity. These results are supported by in vivo data from zebrafish and obese mice indicating that these cannabinoids are able to increase yolk lipid mobilization and inhibit the development of hepatosteatosis respectively.

CONCLUSIONS:
Our results suggest that THCV and CBD might be used as new therapeutic agents for the pharmacological treatment of obesity- and metabolic syndrome-related NAFLD/hepatosteatosis.

CBD: Metabolic syndrome

Orv Hetil. 2012 Apr 1;153(13):499-504. doi: 10.1556/OH.2012.29308.

[The potential use of cannabidiol in the therapy of metabolic syndrome].

[Article in Hungarian]

Kleiner D[1], Ditrói K.

Author information

Abstract

Cannabidiol, a cannabinoid and serotonin receptor antagonist, may alleviate hyperphagia without the side effects of rimonabant (for example depression and reduced insulin sensitivity). Similar to the peroxisome proliferator-activated receptor-gamma agonists, it may also help the differentation of adipocytes. Cannabidiol has an immunomodulating effect, as well, that helps lessen the progression of atherosclerosis induced by high glucose level. It may also be effective in fighting ischaemic diseases, the most harmful complications of metabolic syndrome. However, it can only be administered as an adjuvant therapy because of its low binding potency, and its inhibiting effect of cytochrome P450 enzymes should also be considered. Nevertheless, it may be beneficially used in adjuvant therapy because of its few side effects.

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22430005
DOI:
10.1556/OH.2012.29308
[Indexed for MEDLINE]

CBD: Insulin resistance

Phytother Res. 2018 Jun;32(6):1080-1089. doi: 10.1002/ptr.6047. Epub 2018 Feb 21.

Time-dependent effect of phytocannabinoid treatments in fat cells.

Ramlugon S[1], Levendal RA[1], Frost CL[1].

Abstract

The objectives of this paper is to investigate, demonstrate, and compare the mechanism of action of phytocannabinoids as antidiabetic and anti-obesity agents in preadipocytes and adipocytes, relative to rosiglitazone and metformin. Briefly, cannabis extract, Δ^9 -tetrahydrocannabinol and cannabidiol (in very low dosages) were shown to promote glucose uptake higher or to equivalent levels, reduce fat accumulation, and reverse the insulin-resistant state of 3T3-L1 cells more effectively, relative to rosiglitazone and metformin. The phytocannabinoids had a more pronounced effect in preadipocytes undifferentiated model rather than the differentiated model. They induced a protective effect at the mitochondrial level by preventing overactivity of the succinate dehydrogenase pathway ($p < .01$), unlike rosiglitazone, through activation of the glycerol-3-phosphate dehydrogenase shuttling system. An increase in oxygen consumption and an increased expression of beta to alpha adrenoceptors ($p < .05$) in treated cells were noted. These findings contribute toward understanding the mechanism of action of phytocannabinoids in fat cells and highlight the antidiabetic and anti-obesity properties of various phytocannabinoids that could potentially support the treatment of obesity-related insulin resistance.

KEYWORDS:
beta/alpha adrenoceptors; glycerol-3-phosphate dehydrogenase shuttling system; insulin-resistance; obesity; phytocannabinoids
PMID: 29464872 DOI: 10.1002/ptr.6047

Clin Hemorheol Microcirc. 2016;64(4):655-662. doi: 10.3233/CH-168021.

Experimental cannabidiol treatment reduces early pancreatic inflammation in type 1 diabetes.

Lehmann C[1,2,3,4], Fisher NB[5], Tugwell B[6], Szczesniak A[2], Kelly M[2], Zhou J[1,3].

Abstract

BACKGROUND: Destruction of the insulin-producing beta cells in type 1 diabetes (T1D) is induced by invasion of immune cells causing pancreatic inflammation. Cannabidiol (CBD), a phytocannabinoid, derived from the plant, Cannabis sativa, was shown to lower the incidence of diabetes in non-obese diabetic (NOD) mice, an animal model of spontaneous T1D development. **OBJECTIVE:** The goal of this study was to investigate the impact of experimental CBD treatment on early pancreatic inflammation in T1D by intravital microscopy (IVM) in NOD mice. **METHODS:** Seven-week-old female NOD mice were prophylactically administered daily 5 mg/kg CBD or control vehicle i.p. five times weekly for ten weeks. Animals underwent IVM following confirmation of T1D diagnosis by blood glucose testing. Leukocyte activation and functional capillary density (FCD) were quantified via IVM. **RESULTS:** CBD-treated NOD mice developed T1D later and showed significantly reduced leukocyte activation and increased FCD in the pancreatic microcirculation. **CONCLUSIONS:** Experimental CBD treatment reduced markers of inflammation in the microcirculation of the pancreas studied by intravital microscopy.

KEYWORDS: Type 1 diabetes; adhesion molecules; cytokines; functional capillary density; inflammation; intravital microscopy; leukocyte adherence
PMID:27767974 DOI: 10.3233/CH-168021 [Indexed for MEDLINE]