PRE-CLINICAL RESEARCH

Cannabidiol Attenuates Cardiac Dysfunction, Oxidative Stress, Fibrosis, and Inflammatory Cell Death Signaling Pathways in Diabetic Cardiomyopathy

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Objectives: In this study, we have investigated the effects of cannabidiol (CBD) on myocardial dysfunction, inflammation, oxidative/nitrative stress, cell death, and interrelated signaling pathways, using a mouse model of type 1 diabetic cardiomyopathy and primary human cardiomyocytes exposed to high glucose.

Background: Cannabidiol, the most abundant nonpsychoactive constituent of Cannabis sativa (marijuana) plant, exerts anti-inflammatory effects in various disease models and alleviates pain and spasticity associated with multiple sclerosis in humans.

Methods: Left ventricular function was measured by the pressure-volume system. Oxidative stress, spasticity associated with multiple sclerosis in humans.

Results: Diabetic cardiomyopathy was characterized by declined diastolic and systolic myocardial performance associated with increased oxidative/nitrative stress, nuclear factor-κB and mitogen-activated protein kinase (c-Jun N-terminal kinase, p-38, p38α) activation, enhanced expression of adhesion molecules (intercellular adhesion molecule-1, vascular cell adhesion molecule-1), tumor
Cannabidiol attenuates cardiac dysfunction, oxidative stress, fibrosis...

Remarkably, CBD attenuated myocardial dysfunction, cardiac fibrosis, oxidative/nitrative stress, inflammation, cell death, and interrelated signaling pathways. Furthermore, CBD also attenuated the high glucose-induced increased reactive oxygen species generation, nuclear factor-κB activation, and cell death in primary human cardiomyocytes.

Conclusions: Collectively, these results coupled with the excellent safety and tolerability profile of CBD in humans, strongly suggest that it may have great therapeutic potential in the treatment of diabetic complications, and perhaps other cardiovascular disorders, by attenuating oxidative/nitrative stress, inflammation, cell death and fibrosis.

Key Words: cannabinoids • diabetic complications • inflammation • oxidative stress

Abbreviations and Acronyms
ADP = adenosine diphosphate
CBD = cannabidiol
HCM = human cardiomyocytes
HG = high glucose
HNE = hydroxynonenal
ICAM = intercellular adhesion molecule
ICB-α = inhibitor of nuclear transcription factor nuclear factor-κB
iNOS = inducible nitric oxide synthase
JNK = c-Jun N-terminal kinase
MAPK = mitogen-activated protein kinase
MMP = matrix metalloproteinase
NADPH = nicotinamide adenine dinucleotide phosphate
NF-κB = nuclear factor kappa B
NT = nitrotyrosine
PARP = poly(ADP-ribose) polymerase
ROS = reactive oxygen species
SOD = superoxide dismutase
THC = delta 9-tetrahydrocannabinol
TNF = tumor necrosis factor
TUNEL = terminal deoxynucleotidyl transferase dUTP nick end labeling
VCAM = vascular cell adhesion molecule

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