

THE THERAPEUTIC USE OF CANNABIS

CARDIOVASCULAR BENEFITS OF CBD

CBD does not affect blood pressure, heart rate, body temperature, glucose levels, pH, pCO₂, pO₂, hematocrit, and K⁺ or Na⁺ levels in doses up to 30mg per kg body weight in animals; however, it exerts beneficial effects on the cardiovascular system through multiple target sites for the following conditions:

Heart failure

Hypertension

Atherosclerosis

Isquemic / Reperfusion injury

Hypertension

CBD vasoactive responses are endothelium dependent and highly dependent also on the vascular tone. It induces Vasorelaxation through:

- Calcium activated potassium channels
- Through a putative novel receptor called endothelial cannabinoid receptor as an agonist
- The PPAR_γ receptor

-CB1 receptor activation in vascular smooth muscle and endothelium via inhibition of FAA and thus increasing anandamide

- Releasing vasorelaxant mediators: NO, COX1-COX2 derived products,

-Reduction of ROS through implementing the activity of SOD

In addition, CBD causes bradycardic and negative inotropic actions inhibiting Ca⁺⁺ channels in ventricular myocytes

Atherosclerosis

CBD and its methylated forms have a selective inhibitory effect on 15-LOX which directly oxidizes the cholesterol ester in the LDL particle, and oxidation of the LDL molecule is the first step in the development of atherosclerosis, with 15-LOX having a well established role in the both the oxidation of LDL and the progression of atherosclerosis.

ROS play a pivotal role in the development of the atheroma and macrophages are the major source of ROS, with cicloxygenases, lipoxygenases, iNOS and myeloperoxidases contributing. ROS which cause LDL oxidation, activate stress signaling pathways, apoptosis and plaque rupture.

In addition, when monocytes turn into macrophages they change their CB receptor profile to a more CB1, and its activation attracts more cholesterol and generates more ROS and TNF α . In contrast CB2 activation attenuates the proinflammatory actions of CB1. Cannabinoids might be able to abrogate atherosclerosis by different approaches.

Heart Failure

CBD decreases the infarct size associated with a reduction in the inflammatory infiltration in infarct zones. In Diabetic Cardiomyopathy also prevents and attenuates complications in cardiomyocytes exposed to high glucose levels, like cardiac fibrosis and myocardial dysfunction through decreasing ROS and nitrogen species, and inhibiting the potent pro inflammatory actions of NF- κ B.

Ischemia / reperfusion injury

CBD has a protective action reducing the accumulation of neutrophils and reducing the activity of myeloperoxidase; and it shows vascular-stabilizing effects mediated by its potent immunosuppressive effects on the production of TNF α , other cytokines, and COX2 expression.

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