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THE INFLUENCE OF CANNABIDIOL ON LIPID METABOLISM AND INFLAMMATION DEVELOPMENT IN THE HEART

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Background. Cannabidiol (CBD) is a phytocannabinoid derived from *Cannabis* species, which is devoid of psychoactive activity. It exerts analgesic, anti-inflammatory, antineoplastic and chemopreventive activities. It binds to a wide variety of physiological targets of the endocannabinoidome within the body, mainly cannabinoid receptor 1 (CB1R), cannabinoid receptor 2 (CB2R) and vanilloid receptor 1 (TRPV1). It is used in the treatment of a number of medical conditions ranging from anxiety to epilepsy. CBD is being intensively studied in many potential medical uses, but little is known about its influence on lipid metabolism regulation, particularly accumulation of fatty acids in the heart.

Aims: the aim of this study was to evaluate the impact of CBD on accumulation of lipid precursors of inflammation and concentration of pro-inflammatory proteins in rat heart during lipid-overload state.

Materials and methods. The study was performed on male Wistar Crl:WI (cmdb) rats which were divided into two groups namely group fed with standard rat chow and group fed with high-fat diet (HFD) during 7 weeks. Half of animals from each group was intraperitoneally injected with vehicle or CBD (10 mg/kg of body mass) for last 14 days of feeding. After animal anesthetizing the harts were collected and frozen in liquid nitrogen. The concentration of arachidonic acid in free fatty acids (FFA), di- (DAG) and tri- (TAG) acylglycerol fraction was measured using Gas-Liquid Chromatography (GLC). The concentration of pro-inflammatory proteins (TNF-α, IL-6) and the expression of enzymes involved in eicosanoids and prostanoids production (COX-1,COX-2, 5-LOX) were evaluated using Bio-Rad Multiplex assay and Western Blot, respectively.

Results and discussion. Administration of CBD significantly decreased the expression of enzymes responsible for the synthesis of proinflammatory prostaglandins and leukotrienes: COX-1, COX-2 and 5-LOX, in rats fed with high fat diet. Moreover, the concentration of proteins involved in development of inflammation namely TNF-α and IL-6, were significantly decreased in this group. The concentration of arachidonic acid (AA) in DAG fraction was significantly decreased in rats treated with CBD and HFD, in comparison to HFD group. Moreover, CBD alone decreased the concentration of AA in DAG and FFA fractions compared to control and HFD groups. Concentration of AA in TAG fraction did not differ significantly in both CBD and CBD+HFD groups.

Conclusions. The outcome of this study pointed that cannabidiol exerted strong anti-inflammatory potential in rat heart during lipid overload state. Moreover, it attenuated the accumulation of lipid precursors of inflammation. These findings suggested potential use of CBD in prevention of cardiac inflammation and steatosis development, which both may lead to an impairment in energetic and mechanical efficiency of myocardium. Undoubtedly, our study opened the field for further research into the use of CBD and other phytocannabinoids as a supportive factors in the treatment of heart diseases.