QUERCETIN REDUCES PRO-HYPERTROPHIC SIGNALING AND MITIGATES DIASTOLIC DYSFUNCTION IN OBESE DIABETIC RATS

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With its potent anti-inflammatory and ROS scavenging properties, quercetin (Que) is being implicated in spectrum of different pathological phenotypes including cardiac remodeling. However, the precise mechanism of its action remains far from being clarified as well as the exact molecular pathways Que interferes with in certain cardiac pathologies. For that reason, we tested out the effects of Que in the model of 1-year-old Zucker Diabetic Fatty rats which combines type 2 diabetes mellitus and obesity. Animals were divided into the following experimental groups: control (fa/+) vehicle-treated, diabetic (fa/fa) vehicle-treated, control (fa/+) Que-treated and diabetic (fa/fa) Que-treated group. Que was administered to respective groups at a dose of 20 mg/kg/day during 6 weeks. Echocardiography examination was performed prior to the onset of the treatment and at the end of sixth week. Subsequently, we carried out a series of assays in excised left ventricular tissues – hydroxyproline assay, SDS-PAGE and immunoblotting. On the level of echocardiography, Que was able to normalize increased E/A ratio, suggesting diastolic dysfunction, in diabetic rats to the level of controls. In addition, Que promoted a decrease in overall wall's mass. Moreover, a significant decrease in total collagen content was associated with such reduction. On the protein level, Que significantly reduced pro-hypertrophic transcriptional pathway – MEF2/HDAC4 in diabetic animals as well as other transcriptional factors – GATA4, NFAT3 and its regulator Calcineurin A. Taken altogether, Que showed capability to ameliorate diastolic dysfunction and to suppress pro-hypertrophic signalization and therefore produced beneficial effects in obese diabetic rat hearts.

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