Antocyanins extracted from grape seed alleviate cardiac remodeling in rats with diabetic cardiomyopathy: possible involvement of PKC-ERK 1/2 signaling pathways

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**Purpose:** Increased consumption of anthocyanins is helpful to decrease incidence of cardiovascular morbidity. These cardioprotective activities are closely related to their antioxidant properties. In diabetic cardiomyopathy (DCM), protein kinase C (PKC) is involved in hyperglycemia-induced oxidative stress. Usually, PKC activation provokes modifications in extracellular matrix, induces myocyte hypertrophy and interstitial fibrosis. In this study, we investigated the effects of anthocyanin extracted from grape seed on cardiac remodeling and assessed mechanisms involved.

**Methods:** Diabetes was induced in male SD rats by intraperitoneal injections of streptozotocin (STZ) at a dose of 65 mg/kg. Rats were divided into four groups: normal rat, diabetic rat, normal rat with anthocyanin treatment and diabetic rat with anthocyanin treatment. Anthocyanin (95 purity) was orally administrated at a dose of 100 mg kg⁻¹ for 6 weeks. At termination, evaluation of hemodynamic parameters and oxidative stress status were performed. Left ventricular (LV) tissues were collected for the assessment of myocardial ultrastructure, collagen density, and cardiomyocyte hypertrophy. Finally, expression of PKC and ERK 1/2 in cardiac tissues were determined.

**Results:** After treatment with STZ, rats developed diabetes evidenced by hyperglycemia, while experimental DCM was indicated by LV dysfunctions. Rats with DCM showed lower body weight and higher heart-to-body weight ratio, impaired systolic and diastolic function accompanied with myocyte hypertrophy and interstitial fibrosis, as well as elevated malonaldehyde level. However, anthocyanin treatment significantly restored LV dysfunction, decreased oxidative stress status, and attenuated LV remodeling as evidenced by reduced mean myocyte diameter and interstitial collagen deposition. Meanwhile, brain natriuretic peptide mRNA expression were markedly decreased. More importantly, anthocyanin could dramatically prevent up-regualted expression of phosphorylated PKC alpha and ERK1/2 as well as TGF-β mRNA expression and NF-κB activation

**Conclusions:** Anthocyanin extracted from grape seed has protective potential for targeting cardiac hypertrophy and fibrosis through suppression of PKC-ERK pathway, highlighting a possible cardioprotective therapy for prevention of cardiac remodeling in DCM.