ABSTRACT

Cardiac gene and protein expression in sucrose-fed rodent models of insulin resistance: preventive effect of anthocyanins

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Diabetes mellitus (DM) is a global health problem associated with multiple complications, including diabetic cardiomyopathy (DCM) which is mainly characterized by contractile dysfunctions. The molecular basis of DCM is largely unknown, but delineation of underlying biochemical defects could provide insights into functional aberrations; this was the major goal of this project and several studies were undertaken. Firstly, the streptozotocin model of type 1 DM showed decreased expression of SERCA and PLN, and depressed Ca^{2+}-ATPase activity and heart rate. Secondly, insulin resistance (IR) was induced by 32% sucrose in drinking water. This significantly increased ($p<0.05$) plasma TAGs, insulin and levels of Akt and cTnI: ratios of p*-IRec/IRec and p*-AMPK/AMPK were also significantly decreased ($p<0.05$). In a repeat experiment with sucrose-fed rats, changes in the gene expression along the insulin signaling pathway were quantitated using focused RT-PCR arrays. In cardiac, hepatic and skeletal muscle tissues expression of several genes were significantly changed ($p<0.05$). Next, adult rat cardiomyocytes were incubated with 200 mg/dL glucose; this significantly down-regulated 21 genes ($p<0.05$), and up-regulated 11 ($p<0.05$) when compared to controls (100 mg/dL).

In separate experiments 300 mg/dL glucose significantly decreased Akt expression ($p<0.05$) and increased the p*-Akt/Akt ratio ($p<0.05$). Finally, in another model of type 2 DM, rats were fed an AIN control diet or a modified isocaloric diet in which sucrose provided 55% of energy. The potential for an anthocyanin rich food extract to augment metabolic defects associated with IR and DCM was also explored. Sucrose feeding significantly decreased antioxidant capacity ($p<0.05$), increased PLN ($p<0.05$) and decreased p*-cTnI expression and the p*-cTnI/cTnI ratio ($p<0.05$). Several genes involved in insulin signaling were significantly down-regulated ($p<0.05$). Anthocyanins attenuated the antioxidant capacity and significantly up-regulated ($p<0.05$) adipsin, PI3K and SREBF1. It is concluded that changes in protein and gene expression contribute to physiological alterations observed in DCM, and some changes can be modulated by anthocyanins.

Keywords:

type 2 diabetes mellitus, type 1 diabetes mellitus, insulin resistance, pre-diabetes, diabetic cardiomyopathy, sucrose-fed, anthocyanins, cardiomyocytes, PCR arrays,