Topic category: Cardiovascular Physiology

Involvement of Protein Kinase B (Akt) in Cardioprotection Carried out by Oral Administration of Stevioside

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Introduction: *Stevia rebaudiana bertoni* is an herbaceous plant widely distributed and used in Paraguay and Brazil, known for its sweetener character. Stevioside (E), a diterpenoid glycoside, is the main non-caloric sweetener extracted from Stevia leaves. Several papers have been published about stevia and its properties as antihypertensive, insulinotropic, antihyperglycemic and antitumor. However, there are few documented findings on cardiovascular effects mediated by stevioside. In previous studies carried out in our laboratory, we demonstrated that oral administration of E improved the recovery of contractile activity in hearts subjected to I-R and decreased the infarct size. These effects were, at least in part, reverted by the administration of Wortmannin (W), an upstream inhibitor of Akt.

Objective: The aim of the present study was to investigate the mitochondrial morphology and the rate of ATP synthesis after oral administration of E (168 mg/kg for 15 days) and its relation with the activation profile of Akt and GSK3β, in Langendorff perfused rat hearts subjected to I-R.

Material and Methods: Hearts from female Wistar rats (200-250g) fed ad libitum were used. W (100nM) was added 15 min before I. Mitochondrial ultrastructure was analyzed by electron microscopy, the measurement of mitochondrial ATP synthesis was made by the luciferin-luciferase method and the activation profile of Akt and GSK3β were studied by western blot considering Akt-P/Akt-T and GSK3β-P/GSK3β-T, respectively. ANOVA, n=8/group.

Results: At the end of reperfusion, results showed an increase in mitochondrial ATP synthesis rate of hearts treated with E that was partly canceled by the administration of W

(C: 66.3±6.5, W: 59.5±6.1, E: 87.3±3.7*, E+W: 64.6±6.9 nmol/min/mg mitochondrial protein; *p<0.05 vs all groups) Likewise, electron micrographs showed better mitochondrial conservation in the group treated with E. Akt presented higher phosphorylation with E treatment (C: 1.26±0.19, W: 1.16±0.07, E: 1.80±0.16*, E+W: 0.86±0.16 AU; *p<0.05 vs all groups). Moreover, GSK3β phosphorylation was higher in the E group with respect to the control group, being partially reverted with W (C: 1.03±0.11, W: 1.04±0.15, E: 1.88±0.05*, E+W: 1.63±0.18 AU; *p<0.05 vs C and W).

Conclusions: These findings suggest that oral administration of E presents cardioprotective effects which includes greater preservation of mitochondrial function and morphology and could be partly mediated by Akt activation.

Keywords: Wistar rats, electron microscopy, cardioprotection, protein kinase B, stevioside