Dietary anti-oxidant rich oil protect against ischaemia/reperfusion injury by activation of PKB/Akt and p38 MAPK

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Background: Red palm oil (RPO) is known as a potent anti-oxidant rich oil. Previous results have shown that RPO can protect against the consequences of ischaemia/reperfusion. It has been shown that RPO offered protection via the NO-cGMP pathway during ischaemia (Esterhuyse et al., 2006).

Hypothesis: RPO may protect against ischaemia/reperfusion injury via the PKB/Akt and MAPK signalling pathways.

Methods: Male Wistar rats were fed RPO for 6 weeks. Hearts were excised and mounted on a working rat heart perfusion system. Hearts were exposed to ischaemia for 25 min and reperfused for 20 min. Functional recovery was measured and biochemical analysis was performed in a different set of freeze clamped hearts to determine the degree of kinase phosphorylation.

Results: Aortic output recovery was improved (72.1±3.2% in RPO vs. 54.0±3.2% in control, $p<0.05$). No changes in activation of PKB/Akt and p38 could be found during ischaemia. The improved functional recovery was associated with an increased phosphorylation of PKB/Akt$^{(Ser473)}$ and p38 during reperfusion. During reperfusion RPO significantly decreased phosphorylation of both JNK54 and JNK46 and attenuated PARP cleavage.

Discussion: The results in this study show that dietary RPO supplementation can protect against the consequences of ischaemia/reperfusion. This protection may be caused by the ability of RPO to increase phosphorylation of PKB/Akt and p38 MAPK and dephosphorylation of JNK, which might be associated with inhibition of apoptosis.

Keywords: Ischaemia/reperfusion; Antioxidants; Signal transductions

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Heart rate reduction induced with ivabradine in middle-aged post-infarcted rats improves myocardial perfusion

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This study assessed the impact of pure heart rate reduction (HRR) induced with ivabradine (IVA), a selective inhibitor of cardiac pacemaker I_f current, on left ventricular (LV) function, angiogenesis and coronary perfusion, in middle-aged post-myocardial infarction rats. MI was induced in 12-month-old male Sprague–Dawley rats by left coronary artery ligation. Post-MI rats received IVA (10.5 mg/kg/day, 1month, MI+IVA) or placebo (MI) via i.p. osmotic pumps. Sham-operated older rats (Shams) served as control. In MI+IVA rats, HR was consistently reduced by 25% ($P<0.001$) compared to Shams. One month after MI and treatment cessation, ejection fraction in MI+IVA rats was 34% higher ($P<0.05$ vs. MI rats). Maximal coronary conductance in LV free wall and septum was greater in MI+IVA rats by 35% ($P<0.01$) and 28% ($P<0.05$), respectively. Arteriolar length and volume densities were similar in MI+IVA and MI rats but MI+IVA rats demonstrated significantly reduced interstitial and perivascular collagen content compared to non-treated MI rats by 21.6% ($P<0.01$) and 37% ($P<0.01$) in free wall and by 33.1% ($P<0.01$) and 35.7% ($P<0.01$) in septum, respectively. IVA prevented the increase in plasma level of angiotensin II, angiotensin II type 1 receptor and TGFβ1 protein expression in the non-infarcted LV myocardium observed in MI rats ($P<0.05$ vs. MI rats). In conclusion, HRR induced with IVA in post-MI middle-aged rats substantially reduces both interstitial and perivascular fibrosis via inhibition of renin–angiotensin system. This effect may be the anatomical basis for the preservation of maximal coronary conductance and possibly the improvement of LV function.

Keywords: Myocardial infarction; Ivabradine; Coronary microcirculation

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Cardioprotective effect of poly(ADP-ribose) polymerase inhibition: Role of PI3K/Akt

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Aims: We investigated the cardioprotective effect of the PARP inhibitor, DP264 (Inotek, Beverly, Ma) in an isolated working rat heart model of donor heart preservation.

Methods: Hearts were treated with 1 μM DP264 before, during or after hypothermic storage. Hearts not exposed to DP264 served as controls. Another group was pretreated with the PI3-k inhibitor, Wortmannin, (0.1 μM), before storage in DP264-supplemented Celsior. After baseline measurement of aortic flow, heart rate, coronary flow and cardiac output were taken, hearts were arrested and stored in Celsior at 2–3 °C for 6 h. After storage, hearts were reperfused for 15 min before performing work for a further 30 min at which time post-storage indices of cardiac function were remeasured and heart tissue stored at −80 °C for Western blot analysis.

Results: The presence of DP264 during pre-storage perfusion or during cardioplegia and storage significantly improved post-storage cardiac function. Protection was completely abolished by Wortmnanin pre-treatment. Western blots showed a significant increase in phospho-Akt and phosphorylated phospholamban in presence of DP264, which was also inhibited by Wortmannin.

Conclusions: These results show that the known effect of PARP inhibition on Akt activation also holds true for ischemia–reperfusion as it directly pertains to heart procurement and