month-old PHT. This study showed that the early development of vascular dysfunction in the endothelial cells as well as vascular smooth muscle cells in PHT rabbits. These results suggest that post-prandial hypertriglyceridemia may become an important risk factor for promoting atherosclerosis.

Keywords: Endothelium; Metabolism; Smooth muscle

doi:10.1016/j.yjmcc.2007.03.691

Losartan ameliorates diabetic vascular hyper-reactivity to angiotensin II by reducing ROCK1 expression and activity

Laura Raimondi, Sergio Franchi-Micheli, Elisabetta Cerbai, Alessandro Mugelli, Paola Failli. Department of Pharmacology, University of Florence, Italy

We investigated the effect of an *in vivo* treatment with losartan, an angiotensin type 1 receptor antagonist (ARB), on the angiotensin II (ATII) contracture elicited in phenylephrine pre-contracted aortic strips isolated from normo (groups A and B) and hyperglycemic rats (STZ injected, 55 mg/kg; group C and D) not treated (groups A and C) and treated with losartan (20 mg kg^{-1} day^{-1}; groups B and D). While ATII showed similar E50 values in all the preparations tested, its maximum effect (expressed as % of maximum phenylephrine contraction) reached 360% in group C, 250% in group D and only 175% in groups A and B. Aortas from all the animal groups responded similarly to irbesartan, an ARB, added to superfusion medium (50% reduction of the ATII maximum effect). The ATII contracture in groups C and D were reduced (32% and 22% respectively) by fasudil, an inhibitor of the RhoA/ROCK1 pathway. Exposure to the same drug left unchanged the ATII contracture in the aortas from groups A and B. ROCK1 enzyme activity (mU/mg of tissue proteins) was 0.04±0.01 in normoglycemic, 1.42±0.22* ($p<0.001$ vs. groups A and B) in diabetic aortas and only 0.72±0.05§ ($^{\S}p<0.05$ vs. groups A and B) in the aortas from losartan-treated diabetic rats.

In diabetes, ROCK1 overexpression is functionally coupled with aorta hyper-reactivity towards ATII. We provide evidence stating that losartan ameliorates vascular response to ATII reducing ROCK1 activity and expression.

Keywords: Diabetes mellitus; Renin angiotensin system; Pharmacology

doi:10.1016/j.yjmcc.2007.03.692

Synthetic flavonol preserves postischemic endothelial function after 7 days reperfusion in conscious sheep

Sheng Wang, Colleen J. Thomas, Greg J. Dusting, Owen L. Woodman, Clive N. May. Howard Florey Institute and Melbourne University, Australia

Myocardial ischemia–reperfusion impairs endothelium-dependent dilatation due to oxidative stress. The synthetic flavonol, 3′,4′-dihydroxyflavonol (DiOHF), is an effective antioxidant which reduces infarct size. This study in conscious, instrumented sheep subjected to experimental myocardial infarction investigated the ability of DiOHF to preserve post-ischemic coronary endothelial function. Acetylcholine (ACh, 10 μg/kg/min iv) increased coronary conductance (CC) before ischemia (ΔCC, ACh, 34±4%). In vehicle-treated sheep ($n=4$) following prolonged (1 h) ischemia and 24 h reperfusion, vasodilatation of the coronary vascular bed to ACh was significantly reduced (ΔCC, 7±2%). $p<0.05$). This impairment of endothelial function persisted even after 7 days of reperfusion (ΔCC 15±2%). In DiOHF-treated sheep (2 mg/kg i.v. bolus 5 min before reperfusion, $n=4$), however, coronary vasodilatation in response to acetylcholine was partly preserved after 24 h of reperfusion (ΔCC 18±5% n.s.) and completely recovered (ΔCC 31±7% n.s.) after 7 days of reperfusion. Animals in both groups maintained vascular responses to SNP during reperfusion, confirming normal function of vascular smooth muscle. DiOHF also significantly decreased infarct size expressed as a percentage of area at risk by approximately 40% (vehicle=80±7%, DiOHF=46±11%). In conclusion, this study provides functional evidence that DiOHF protects against endothelial dysfunction caused by ischemia and reperfusion.

Keywords: Coronary endothelial dysfunction; Flavonol; Ischemia–reperfusion injury

doi:10.1016/j.yjmcc.2007.03.693

Endothelium-dependent prothrombotic and fibrinolytic factors in patients with chronic heart failure

K.A. Khmelnitskaya, E.V. Shlyakhto, M.U. Sitnikova. Pavlov State Medical University, Almazov Research Institute of Cardiology, Saint-Petersburg, Russia

Along with disturbance of blood flow, a hypercoagulable state, endothelium plays an important regulatory role thromboembolic pathophysiology and produces prothrombotic and antithrombotic factors in the chronic heart failure (CHF). In study we have investigated endothelial-dependent hemostasis [von Willebrand factor (vWf), tissue plasminogen activator (tPA)] and endothelial damage [circulating endothelial cells (CECs), an index of endothelial damage] in 108 patients with ischemic heart disease and CHF I–IV class (NYHA), who were compared with 30 age-matched patients with ischemic heart disease without CHF and 27 age-matched healthy control subjects.

Results: There was an increase plasma levels CECs in patients with CHF compared without CHF ($p=0.002$) and healthy controls ($p=0.001$). Patients with more severe symptoms CHF (class III–IV) had higher CECs ($p=0.01$), vWf ($p=0.02$), lower tPA-antigen ($p=0.1$), than class I–II. A significant increase