

[PA1-15] [04/20/2001 (Fri) 10:30 – 11:30 / Hall 4]

Antidiabetic activity and mechanisms of acarbose in KKAY mice

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To elucidate antidiabetic effect and mechanism of acarbose in a polygenic spontaneous hyperglycemic and hyperinsulinemic diabetic animal model, KKAY mice, acarbose was administered orally for 4 weeks and effects on body weight, plasma glucose and insulin levels, genetic expressions of intestinal sucrase-isomaltase(SI), sodium-glucose cotransporter (sGLT1) and glucose transporter in quadriceps muscle (GLUT4) were examined in this study. Although no differences in body weight were detected between control and acarbose-treated groups, plasma glucose level in acarbose-treated group was markedly reduced as compared to the control. In the mechanism study, acarbose downregulated the SI and sGLT1 mRNA expressions and upregulated the GLUT4 mRNA and protein expressions when compared to the control group. In conclusion, the data obtained strongly implicate that acarbose can prevent the hyperglycemia in KKAY mice possibly through blocking intestinal glucose absorption by downregulations of SI and sGLT1 mRNA expressions, and upregulation of skeletal muscle GLUT4 mRNA and protein expressions.

[PA1-16] [04/20/2001 (Fri) 10:30 – 11:30 / Hall 4]

Comparisons of Renal Dysfunction in normal and STZ-induced diabetic rats

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The characteristic early changes of the diabetic nephropathy are increased renal size and glomerular volume, hyperfiltration, and fibrotic changes in glomeruli. And the cytokine transforming growth β (TGF- β) has emerged as having a key role in the development of renal hypertrophy and accumulation of extracellular matrix in diabetes. To investigate the expression of TGF- β in early stage of diabetes, SD rat was administered with 75 mg/kg streptozotocin. We measured blood glucose level every three days and plasma creatinine and blood urea nitrogen(BUN) were measured on days 7 and 14 after STZ injection. The urinary albumin excretion(UAE) in 24-hour urine collections was determined by Biuret method. Glomeruli were isolated from kidney by differential sieving method. TGF- β mRNA and protein of glomeruli were determined by RT-PCR and Western blot, respectively. BUN and UAE increased dramatically time dependently as compared to those of the normal SD rat. TGF- β mRNA and protein levels were also upregulated in STZ-treated group.

[PA1-17] [04/20/2001 (Fri) 10:30 – 11:30 / Hall 4]

Renal Action of SKF 81297, Dopamine D1 Receptor Agonist, in Dog

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This study was attempted to investigate on renal effect of (\pm)-6-chloro-7,8-dihydroxy-1-phenyl 2,3,4,5-tetrahydro-1H-3 benzazepine (SKF 81297), dopamine D1 receptor agonist, in dog. SKF 81297, when given intravenously, produced diuretic action along with the increases of renal plasma flow (RPF), glomerular filtration rate (GFR), amounts of Na⁺ and K⁺ excreted into urine (ENa, EK) and osmolar clearance (Cosm). It also decreased the reabsorption rates of Na⁺ and K⁺ in renal tubule

(RNa, RK) and free water clearance (CH₂O), whereas ratios of K⁺ agonist Na⁺ in urine and filtration fraction (FF) was not changed. SKF 81297, when administered into a renal artery, elicited diuresis both in experimal kidney given the SKF 81297 and control kidney not given, while the effect was remarkable in experimal kidney than those exhibited in control kidney. SKF 81297 given into carotid artery also exhibited diuresis, the potency at this time, compared to those induced by intravenous SKF 81297, was magnusgreat. Above results suggest that SKF 81297 produces diuresis by both indirect action through central function, direct action being induced in kidney. Central diuretic action is mediated by improvement of renal hemodynamics, but direct action by inhibition of electrolytes reabsorption in renal tubule.

[PA1-18] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Cardioprotective and hemodynamic effects of KR-31378, a cardioselective ATP-sensitive potassium channel activator

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The hemodynamic profiles of KR-31378, a cardioselective ATP-sensitive potassium channel activator, were compared with those of BMS-191095. The cardioprotective effects of KR-31378 were evaluated in rat and dog models of coronary artery occlusion and reperfusion. In conscious rats, KR-31378 slightly increased blood pressure only at high dose (100 mg/kg), unlike BMS-191095 that dose-dependently decreased blood pressure (ED₂₀: 2.03±0.62 mg/kg). In anesthetized dogs, KR-31378 was about 100-fold less potent than BMS-191095 for most hemodynamic parameters including blood pressure (ED₂₀ for MAP: 33.7±11.1 and 0.37±0.03 mg/kg, respectively), left ventricular pressure, +dP/dt_{max}, and coronary flow, despite similar hemodynamic profiles to BMS-191095. In rats subjected to 45-min coronary occlusion and 90-min reperfusion, KR-31378 (bolus i.v., 30 min before ischemia) reduced infarct size from 58.6±1.9% of the area at risk in controls to 36.6±4.1 and 34.3±1.2% for 0.3 and 1.0 mg/kg, respectively (p<0.05). The reduction in infarct size afforded by KR-31378 was inhibited by pretreatment with glibenclamide and sodium 5-hydroxydecanoate, selective ATP-sensitive potassium channel antagonists. In dogs that underwent 2-h occlusion followed by 4.5-h reperfusion, KR-31378 (i.v. infusion of 2 mg/kg over 40 min, starting 10 min before ischemia) markedly reduced infarct size from 48.7±1.4% in controls to 19.1±6.5 (p<0.05). These results indicate that KR-31378 is a potent cardioprotective agent with potentially minimal hypotensive effects. Thus, it could be useful in the prevention and treatment of acute myocardial infarction.

[PA1-19] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Neuroprotective Effects of Resveratrol derivative, Compound SY014 Against Ischemic Damage in Rat

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Neuroprotective Effects of Resveratrol derivative, Compound SY014 Against Ischemic Damage in Rat. One of the ingredients of *Vitis vinifera* L., that are responsible for potential cardioprotective effect is believe to be resveratrol, which belong to the stilbene group. Resveratrol has been reported to have strong protective for ischemia reperfusion injury in isolated rat hearts. However not much amount of resveratrol in grapes is limited and its synthetic approach is not well established. In this work, the compound SY014, which is a stilbene derivative was synthesized by simple step process. The