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 quardriceps 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 markedlly 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 $\beta(TGF-\beta)$ 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 $TGF-\beta$ 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, $TGF-\beta$ 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. $TGF-\beta$ 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