(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 (ED_{20}: 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 (ED_{20} 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

synthetic compound SY014 exhibited a neuroprotective effect on global ischemia induced 4-vessel occlusion in rat. Also Compound SY014 inhibited the production of NO in BV2 cell line responded to LPS in a dose dependent manner. Furthermore, we investigated whether Compound SY014 can produce protective effect against hypoxia induced oxidative damage in brain slice culture. ATP is estimated as a parameter of cellular injury. With treatment of Compound SY014, production of ATP in brain slice culture was significantly decreased. In conclusion, the present results that compound014 have a neuroprotective effect on global ischemia induced 4-VO in rat, and that this may be involved in antioxidative effect against hypoxia-induced cell death.

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

The effects of quercetin-3-O-β-D-glucuronopyranoside on the Reflux Esophagitis Induced Surgically in Rats

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It has been shown that quercetin-3-O-β-D-glucuronopyranoside (QGC) extracted from Rumex aquatica has increased vascular permeability and reduced on PBQ-induced writhing syndrome induced by in mice (Hwang et al, 1999). We studied QGC may increase inhibiting effects on the development of the reflux esophagitis induced surgically and on gastric secretion in rats. Intraduodenally administered QGC significantly and dose-dependently prevented the development of reflux esophagitis. QGC dose-dependently inhibited the gastric secretion. We investigated the influence of reflux esophagitis on lipid peroxidation by measuring esophagitis mucosa thiobarbituric acid reactive substances (TBARS), which is a marker of oxidative stress. Malonyldialdehyde content, the end product of lipid peroxidation, increased significantly after the induction of reflux esophagitis. These results suggest that QGC can inhibit the development of reflux esophagitis.

[PA1-21] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

The Mechanism on Diuretic Action Induced by SKF 81297, Dopamine D1 Receptor Agonist, in Dog

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It had been reproted previously that (±)6-chloro-7,8-dihydroxy-1-phenyl 2,3,4,5-tetrahydro-1H-3 benzazepine (SKF 81297), dopamine D1 receptor agonist, produced diuresis by both indirect action through central function and direct action being induced in kidney. This study was attempted in order to examine the diuresis mechanism of such SKF 81297. Diuretic action of SKF 81297 given into the vein or the carotid artery was not affected by renal denervation, whereas diuretic action of SKF 81297 administered into a renal artery was blocked completely by renal denervation, and then diuretic action of SKF 81297 injected into carotid artery was inhibited by SCH 23390, dopamine D1 receptor antagonist, given into carotid artery. Above results suggest that central diuretic action of SKF 81297 elicites through central dopamine D1 receptor and direct diuresis in kidney by influence of renal nerves.

[PA1-22] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

GABA-gated chloride channels modulate morphine-induced hyperactivity, reverse tolerance and dopamine receptor supersensitivity.