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Safety pharmacological properties of DA-8159, a new pyrazolopyrimidinone derivative were examined in laboratory animals to investigate its safety profile. The oral administration of DA-8159 (1, 5 or 30 mg/kg) in mice and rats had no effect on general behaviors and central nervous system of the animals in test systems, such as hexobarbital-induced sleeping time, motor coordination, normal body temperature, writhing syndromes induced by 0.75% acetic acid solution, chemo-shock produced by pentetrazole solution and rotar rod test. Anesthetized cats treated intravenously with DA-8159 (0.1, 0.3, 1, 3 or 10 mg/kg) showed transient and mild decrease in blood pressure. However, heart rate, respiration rate and tidal volume were not changed by intravenous DA-8159. In the isolated organs including ileum, heart (sinus rate of atria and contractility of papillary muscle), trachea of guinea pigs and phrenic nerve of rats, DA-8159 ($10^{-8} \sim 10^{-5}$ g/mL) did not elicit any effect or inhibitory action on the chemically or electrically stimulated contraction. DA-8159 did not influence gastric secretion, pH and total acid output in rats and intestinal propulsion in mice. The administration of DA-8159 in rats had no effect on the platelet aggregation induced by ADP in rabbit plasma, urinary volume and electrolyte ion (Na^+, K^+, Cl^-) excretion in rats. Prothrombin time (PT) of the rats showed a mild but significant increase after administration of DA-8159. Activated partial thromboplastin time (APTT), however, was not affected by DA-8159. These results indicate that DA-8159 does not exert any of serious pharmacological effects.

[PA1-20] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Effect of Resveratrol on Dimethylnitrosamine-Induced Liver Fibrosis in Rats

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Resveratrol (trans-3,4',5-trihydroxystilbene), a polyphenolic compound found in grapes was reported to inhibit activation of hepatic stellate cells *in vitro*. In this study, we have evaluated the preventive effect of resveratrol on liver fibrosis induced by dimethylnitrosamine (DMN) in rats. Oral administration of resveratrol significantly prevented the DMN-induced loss in body weight and liver weight. Resveratrol inhibited dramatically the elevation of serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels in DMN-induced liver injuries, and improved the serum albumin concentrations. Resveratrol also prevented the increase collagen deposition and reduced MDA contents in the liver. These results suggest that resveratrol may be potentially useful in the prevention of the development of hepatic fibrosis.

[PA1-21] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Effects of SK-1080 on neointimal formation after rat carotid artery balloon angioplasy

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We investigated the effects of SK-1080, a novel angiotensin AT1 receptor antagonist, on neointimal proliferation in the rat carotid artery after balloon injury, together with its effects on the impaired endothelium-dependent vascular relaxation. SK-1080 (0.3 and 1.0 mg/kg/day) was orally administered in balloon injured rats for 21 days (from 6 days before to 14 days after balloon injury). SK-1080 (1 mg/kg) exerted significant effects on three important parameters associated with the intimal thickening induced by balloon injury (50.0% reduction in neointimal area, 42.7% reduction in stenosis ratio and 69.1% increase in lumen/total area ratio). Acetylcholine-induced relaxation was significantly reduced in the balloon injured carotid arteries (64.0 □, 9.1%), and this impairment of acetylcholine-induced relaxation was significantly restored by SK-1080 (Maximal relaxation: 87.1 □, 6.5 and 88.6 □, 1.9% at 0.3 and 1.0 mg/kg, respectively, $p<0.05$). However, the endothelial-independent, sodium nitroprusside-

induced relaxation was clearly demonstrated and did not differ in carotid arteries from all treatment groups. Furthermore, acetylcholine-induced relaxation was completely inhibited by L-NAME but not by indomethacin. SK-1080 caused a slight hypotension 1 day before balloon injury (8.7%), which gradually returned to the baseline 6 and 13 days after balloon injury. These results suggest that SK-1080 might be a useful candidate for the treatment of restenosis after percutaneous transluminal coronary angioplasty.

[PA1-22] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Neuroprotective and Neurotrophic Effect of a Novel Quinic Acids derivative Isolated from Aster Scaber.

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Aster scaber T. (Asteraceae) has been used to treat bruises, snakebite, headache and dizziness in the traditional Chinese medicine. We examined the neuroprotective effects and NGF-potentiating activities of quinic acid derivatives (novel quinic acid, (-) 3,5-dicaffeoyl-muco-quinic acid)from Aster scaber. By examining thier effects on the neurite outgrowth from PC12 cells and the synthesis of neurotrophic factor (NGF) in C6 glial cells. Quinic acid derivatives from Aster scaber T. (Asteraceae) increased the proportion of neurite-bearing cells. In addition, after 6h incubation of C6 cells with this compound, NGF levels in the cultured medium increased 300-fold of the control. In RT-PCR analysis, the NGF gene expression was found to reach 2-fold of the control level. We also investigated the effect of this compound on the phosphorylation of MAP kinase (Erk1,2, p38) and PI3 kinase activity, which play a crucial role in the survival and differentiation of neurons. Quinic acid derivatives from Aster scaber T. (Asteraceae) increased PI3 kinase activity and MAP kinase phosphorylation in PC12 cells. These results suggest that a novel quinic acid, (-) 3,5-dicaffeoyl-muco-quinic acid derivatives from Aster scaber T (Asteraceae) might potentially used be as a neuroprotective agent.

[PA1-23] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Anti-coagulant and/or platelet anti-aggregatory activities of MeOH extracts of Cacti

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The MeOH extracts obtained from 42 species of Cacti were tested on their anti-coagulant and/or platelet anti-aggregatory activities by aPTT assay and modified smearing method, respectively. *Obregonia denegrii Fric.* and *Chamaecereus silvestrii* showed potential inhibitory effects on adenosine 5`-diphosphate (ADP)-induced rat platelet aggregation, and *Opuntia vulgaris Mill, Euphorbia grandicornis, Crassula cv. himaturi, Euphorbia milii var. splendens, etc.* were suggested to be potential anti-coagulants.

[PA1-24] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

A newly developed antiarrhythmic drug CW-2101 is ideal in treating atrial fibrillation

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