some drugs which are used in the treatment of heart failure variably modulate the production of cytokines. Higenamine, a positive inotropic isoquinoline alkaloid, is traditionally used as a cardiac stimulant, and has been reported to reduce nitric oxide (NO) and inducible nitric oxide synthase (iNOS) expression in LPS- and/or cytokine-activated cells in vitro and in vivo. Therefore, we investigated the issue of whether higenamine modulates the production of proinflammatory cytokines during myocardial infarction (MI). The effects of higenamine on antioxidant action and antioxidant enzyme expression (MnSOD) were also examined. MI was confirmed by the measuring left ventricular (LV) pressure 5 weeks after the occlusion of the left anterior descending coronary artery (LAD) in rats. Higenamine treatment (10 mg/kg/daily) reduced the size of theinfarct by about 35 %. This treatment was accompanied by a reduction in TNF-α and IL-6production, but not IFN-γand IL-1β in the myocardium. The expression of TNF-α mRNA in an infracted myocardium was significantly reduced by treatment with higenamine. Although iNOS mRNA was not detected, nitrotyrosine staining was significantly increased in the myocardium of MI compared to the higenamine-treated group, indicating that peroxynitrite-induced damage occurs during MI. Cytochrome c oxidation by peroxynitrite was reduced by higenamine in a concentration-dependent manner, an effect which was similar to glutathione. Higenamine treatment increased the expression of MnSOD mRNA in both myocardial tissues and perimayocardial tissues during MI, but was reduced in tissues of contralateral regions. Moreover, it is likely that the regulation of MnSOD mRNA possibly via cytokines, in particular, IL-6, may be an important protective mechanism of higenamine. Collectively, the findings herein suggest that higenamine may be beneficial in conditions of oxidative stress, such as ischemic-reperfusion injury and MI due to antioxidant action as well as the modulation of cytokines. (This work was supported by HMP-98-D-4-0045)

[PA1-52] [10/18/2001 (Thr) 14:00 ~ 17:00 / Hall D]

SPP002-induced stimulation of spontaneous contraction of pregnant rat uterus

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The SPP002 is a mixture of extracts from Cervi parvum Cornu, Angelicae gigantis Radix and Cnidii Rhizoma. The objective of this study was to characterize in vivo the effect of SPP002 on the contractile functions in the non-pregnant and pregnant rat uterus. Pregnancy was confirmed by presence of the deep vaginal plug at 12 hr after mating and uterine contractility was measured at 21 days. Non-pregnant rats were excited by pretreatment of 6-estradiol benzoate for 2 days. After anesthetization, the lower abdomen was incised and a stainless steel cannula with suspended balloon was inserted in the right upper angle of uterus after one fetus was removed. The contractile force and frequency of the uterine contraction were recorded with a pressure transducer and a polygraph. A single (300, 900 mg/kg) and repeated (300, 600 mg/kg) treatment with SPP002 selectively increased uterine contractile functions in pregnant rat while oxytocin (500 mU/ml) increased uterine contractile functions in both pregnant and non-pregnant rat. Our findings suggest that SPP002 may have a beneficial uterotonic effect for labor.

[PA1-53] [10/18/2001 (Thr) 14:00 ~ 17:00 / Hall D]

The Effects of Chondroitin Digestion Products on Type II Collagen-induced Arthritis in DBA/1J Mice

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The effects of chondroitin digestion products and intact chondroitin sulfate on arthritis were evaluated. Inhibition on elastase activity of chondroitin digestion products, chondroitin disaccharide, chondroitin oligosaccharide and intact chondroitin sulfate was examined *in vitro*. Chondroitin disaccharide and oligosaccharide inhibited the elastase activity but intact chondroitin sulfate did not influence the elastase activity. And the effects of these digestion products and intact one were examined on type II collagen-

induced arthritis in DBA/1J mice. Mice were immunized with type II collagen emulsified in Freund's complete adjuvant, followed by a booster injection 21 days later.
Chondroitin disaccharide, oligosaccharide and intact chondroitin sulfate at respective doses of 50, 300 and 1,200 mg/kg were administrated orally once daily beginning 14 days before initial immunization. The index of swelling and hind paw edema was significantly decreased in the group of treatment with chondroitin disaccharide and chondroitin oligosaccharide. Levels of anti-type II collagen antibodies, TNF-a and IL-6 in serum were shown the similar trends. It was also confirmed that chondroitin digestion products including chondroitin disaccharide and a mixture of oligosaccharides, have preventive and/or therapeutic effects compared to the group of arthritis control. The result was clearly demonstrated through histological evaluation of joint tissues.

[PA1-54] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Renal protective effect of Jahagur in STZ induced diabetic rats

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Jahagur(JHG) is an oriental medicine which has been used to treat woman's disease. We have studied the renal protective effect of JHG in STZ(75mg/kg in citrate buffer) induced diabetic rats. Rats were grouped and treated for 2 weeks as follow : control group was injected saline by s.c , treated groups were injected JHG by s.c , positive control group received captopril(CAP), 50mg/kg by oral administration. JHG did not lower plasma glucose level. JHG and CAP-treated rats exhibited lowered urinary albumin excretion and blood urea nitrogen, indicative of renal glomerular damage, as compare to the control. mRNA of TGF-β and protein of fibronectin in kidney were investigated. There were significant difference between control and treated group. We examined the morphology of glomerulus by H&E staining. From these results we may conclude that JHG showed the renal protective effect and it suppressed Fibronectin expression in kidney .

[PA1-55] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Comparative Study of KHU-1 and Simplified Prescription of KHU-1(KHU-2) in Ob/Ob mice

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KHU-1, which is on record in chinese ancient writings (Entrance to Medical Science), has been known as improvement in the functions of gastrointestinal tract and kidney. We had studied antidiabetic effect and mechanism of KHU-1 in male ZDF rats, KHU-1 had shown the excellent hypoglycemic activity. In these studies, we have tried to simplify prescription of KHU-1. The first stage, prescription was divided into 4 parts and anti-hyperglycemic activities of each part were investigated In high-fat diet induced diabetic mice. We prepared simplified prescription with just herbs which have hypoglycemic activity. Subsequently, we have made a comparative study of KHU-1and simplified prescription of KHU-1(KHU-2) in male Ob/Ob mice. Mice were grouped and treated for 9 weeks as follows : lean control (C57/BL6J black mice) and Ob/Ob control groups received powdered standard chow , KHU-1 group was fed with a diet of chow supplemented with 8 g/kg KHU-1 , KHU-2 group was fed with a diet of chow supplemented with 4 g/kg KHU-2(KHU-2 form 50% of KHU-1). KHU-2 lowered plasma glucose from a week after treatment and the hypoglycemic activity was superior to KHU-1. Total cholesterol, triglyceride, free fatty acid and LDL cholesterol were decreased and HDL cholesterol was increased similarly in KHU-1 and KHU-2-treated groups at the end of treatment. While the Ob/Ob control group showed elevated level of insulin and C-peptide concentration, KHU-1 and KHU-2-treated groups lowered insulin and C-peptide concentration respectively. In the mechanism study, mRNA and protein expression of GLUT-4 and PPAR-γ in muscle and epididymal fat were studied by RT-PCR and western blot. We have also investigated Insulin contents in pancreas by immunohistochemistry. We may suggest