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-