

expression of bax and bid suggest that mitochondria pathway is primarily involved in NOCF induced apoptosis.

[PA1-56] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Antidiabetic Activity of Formular containing an Euonymus alata and Mori Folium in Multiple Low Dose Streptozotocin-induced Rats**

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Antidiabetic activity of formular containing an Euonymus alata (EA) and Mori Folium (MF) was investigated in oral glucose tolerance test (OGTT) and multiple low dose Streptozotocin (MLDSTZ)-induced rats. Optimum ratio between EA and MF was found to be 1:1 in OGTT, and two strengths (250 and 500 mg/kg for each medicinal plant) were coadministered with 20 mg/kg of STZ in 5 consecutive days. At 3rd week, water and food intakes were compared between groups and polydipsia and polyphagia shown in diabetic control were markedly improved in dose dependent manner. Plasma glucose level in E2M2 (500 mg/kg for EA and MF)-treated group was significantly lowered to 153 mg/dl from 300 mg/dl in diabetic control (49% inhibition). Plasma insulin levels in E1M1 (250 mg/kg for EA and MF) and E2M2-treated groups were increased by 13% and 26%, respectively, when compared to the diabetic control, suggesting that the formular may protect the pancreas beta cell from destruction by STZ administration. Beta cell sparing effect of the formular was confirmed by HE staining of pancreata. Protein expression of glucose transporter 4 (GLUT4) was examined by Western blot analysis, and 45% reduction of GLUT4 expression in diabetic control group compared to the normal control was recovered by 2 and 3.5-fold in E1M1 and E2M2-treated groups, respectively.

[PA1-57] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Effects of (1R,9S)-(β)-Hydrastine on Intracellular Calcium Concentration in PC12 Cells**

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(1R,9S)-(β)-Hydrastine (HS) at 10-50 μM has been proven to have an inhibitory effect on dopamine biosynthesis in PC12 cells by the inhibition of tyrosine hydroxylase (TH) activity and TH gene expression. In the present study, therefore, the effects of HS on the basal and K<sup>+</sup>-induced dopamine release, and Ca<sup>2+</sup> influx induced by high K<sup>+</sup> and caffeine in PC12 cells were investigated. The dopamine release by high K<sup>+</sup> (56 mM) was inhibited by co-incubation of 20 μM HS. Application of HS also significantly reduced the magnitude of the maintained Ca<sup>2+</sup> influx induced by K<sup>+</sup> depolarization. In addition, when the cells were exposed to 2 μM nifedipine after the treatment with 50 μM HS, the reduction of [Ca<sup>2+</sup>]<sub>i</sub> was continued. The reduction of basal [Ca<sup>2+</sup>]<sub>i</sub> was also observed in response to HS when PC12 cells were bathed in Ca<sup>2+</sup>-free KRH solution, suggesting that HS inhibits Ca<sup>2+</sup> release from intracellular Ca<sup>2+</sup> stores. The application of 20 mM caffeine in Ca<sup>2+</sup>-free KRH solution caused a rapid rise of [Ca<sup>2+</sup>]<sub>i</sub>. The pretreatment with HS reduced caffeine-induced rise of [Ca<sup>2+</sup>]<sub>i</sub>, leading to the activation of store-operated Ca<sup>2+</sup> entry. In the presence of extracellular Ca<sup>2+</sup> (2.5 mM), the application of 20 mM caffeine also caused a rapid Ca<sup>2+</sup> influx compared with Ca<sup>2+</sup>-free condition. The application of HS after caffeine treatment also reduced the magnitude of the maintained Ca<sup>2+</sup> influx induced by caffeine. When 50 μM HS was added after the treatment of 1 μM thapsigargin, a slight decrease in [Ca<sup>2+</sup>]<sub>i</sub> was observed in PC12 cells. These results newly suggest that HS is an inhibitor of, working on the modulation of L-type Ca<sup>2+</sup> channels, Ca<sup>2+</sup> release from intracellular Ca<sup>2+</sup> stores and store-operated Ca<sup>2+</sup> channels in PC12 cells.

[PA1-58] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Inhibitory effects of tetrahydropapaverine on serotonin biosynthesis in murine**

## **mastocytoma P815 cells**

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The inhibitory effects of tetrahydropapaverine on serotonin biosynthesis in serotonin-producing murine mastocytoma P815 cells were investigated. Tetrahydropapaverine at concentration ranges of 5-20  $\mu\text{M}$  decreased serotonin content in a concentration-dependent manner in P815 cells and showed 42.1 % inhibition of serotonin content at 5.0  $\mu\text{M}$  for 24 hr. The value of 50 % inhibitory concentration,  $\text{IC}_{50}$ , of tetrahydropapaverine was 6.2  $\mu\text{M}$ . Under these conditions, tryptophan hydroxylase (EC 1.14.16.4, TPH) was inhibited for 24-36 hr after treatment with tetrahydropapaverine in P815 cells (49.1 % inhibition at 7.5  $\mu\text{M}$ ). In addition, tetrahydropapaverine inhibited the activity of TPH, prepared from the P815 cells (P815-TPH), with the  $\text{IC}_{50}$  value of 5.7  $\mu\text{M}$ . Tetrahydropapaverine inhibited un-competitively P815-TPH with the substrate L-tryptophan, and inhibited non-competitively with the cofactor DL-6-methyl-5,6,7,8-tetrahydropteridin. The  $\text{K}_i$  value of tetrahydropapaverine with L-tryptophan was 10.1  $\mu\text{M}$ . These data indicate that tetrahydropapaverine leads to a decrease in serotonin content by the inhibition of TPH activity in P815 cells.

[PA1-59] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

## **Anti-inflammatory mechanism of bee venom in Raw 264.7 cells and Synoviocyte**

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Bee venom (BV) has been utilized to relieve pain and to treat inflammatory diseases such as rheumatoid arthritis (RA). However, the molecular mechanism by which BV-induced anti-arthritis effect has been not reported yet. Therefore, in the present study we investigated anti-inflammatory effect of BV in a murine macrophage cell line Raw 264.7 cell and synoviocyte obtained from RA patients. The present data showed that BV has a preventive effect on lipopolysaccharide (LPS) and sodium nitroprusside (SNP) induced induction of COX-2, cPLA2 and iNOS. BV also reduced the production of NO and PGE<sub>2</sub> dose dependently (0.5-5  $\mu\text{g/ml}$ ). BV also inactivated LPS and SNP-induced NF- $\kappa\text{B}$ , an important transcription factor regulating expression of COX-2, cPLA2 and iNOS. In addition, BV blocked NF- $\kappa\text{B}$ -dependent luciferase activity in Raw264.7 cells and THP-1 cells. Moreover, BV inhibited nuclear translocation of p50 subunit of NF- $\kappa\text{B}$ . These results showing that BV induced target disruption of p50 subunit in the activation of NF- $\kappa\text{B}$ , thereby inhibition of expression of genes involving in the inflammatory response may be critical in the anti-inflammatory effect of BV.

[PA1-60] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

## **A long duration of anticoagulant activity of acharan sulfate in vivo**

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Introduction: We previously reported that a new glycosaminoglycan, acharan sulfate (AS) from the African giant snail *Achatina fulica* showed anticoagulation activity in vitro, but it was much less than that of heparin. In the present study, the anticoagulant activity of AS was investigated in vivo. Methods: AS and heparin were administered to rats in various concentrations and anticoagulant activities were measured. Both were also compared in a thrombin-induced Results: Intravenous administration of acharan sulfate prolonged the clotting time (APTT) in mice and rats in a dose-dependent manner. Although the activity was low in rats, it could be maintained over 5h after administration of AS (30 mg/kg). In contrast, the activity of heparin (5 mg/kg) was restored to the normal level after 3 h. In a thrombin-induced lethality model in mice AS (20 mg/kg) protected the lethality by 80 percent, while heparin (20 mg/kg) did not show any protective activity after 3.5 h administration of