

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.

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### **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.

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