The inhibitory effects of (1R,9S)- and (1S,9R)-enantiomers of β-hydrastine (BHS) on dopamine biosynthesis in PC12 cells were investigated. (1R,9S)-BHS decreased the intracellular dopamine content with the IC_{50} value of 14.3 μM at 24 h, but (1S,9R)-BHS did not. In these conditions, (1R,9S)-BHS inhibited TH activity mainly in a concentration-dependent manner (33% inhibition at 20 μM) and decreased TH mRNA level. (1R,9S)-BHS at 10-50 μM also reduced the intracellular cyclic AMP level and Ca^{2+} concentration. In addition, treatment of L-DOPA at 20-50 μM for 24 h increased the intracellular dopamine content to 198-251% compared with the control value in PC12 cells, however, the increase in dopamine levels induced by L-DOPA was significantly reduced when L-DOPA (20-50 μM) was associated with (1R,9S)-BHS (10-50 μM). These results indicate that (1R,9S)-BHS, but not (1S,9R)-BHS, inhibited dopamine biosynthesis and L-DOPA-induced increase in dopamine content, in part, through the inhibition of TH activity and TH gene expression in PC12 cells: thus, (1R,9S)-BHS proved to have a function to regulate dopamine biosynthesis.

[PA1-29] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Inhibitory Effects on Dopamine Biosynthsis and Protective Effect on L-DOPA-induced Neurotoxicity of liriodenine in PC12 cells

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The effects of liriodenine, an aporphine isoquinoline alkaloid, on dopamine biosynthesis and L-DOPA-induced neurotoxicity in PC12 cells were investigated. Treatment of PC12 cells with liriodenine at 10 μM showed 33.6% inhibition of dopamine content decreased at 3 h and reached a minimal level at 12 h after the exposure to liriodenine at 10 μM. Under these conditions, tyrosine hydroxylase (TH) and aromatic amino acid decarboxylase (AADC) activities were also reduced inhibited at 10 μM of liriodenine by 10.1% and 20.2% relative to control, respectively. However, TH mRNA level was not altered by liriodenine treatment. Intracellular level of cAMP and $[Ca^{2+}]i$ were also decreased by liriodenine at 10 μM. Liriodenine induced a time- and concentration- dependent decrease in cell viability. Liriodenine at non-cytotoxic concentration (10 μM) significantly inhibited L-DOPA-induced the decrease in cell viability. These results suggest that liriodenine contributes partially to the decrease in dopamine biosynthesis and L-DOPA-induced increase in dopamine content by inhibition of TH and AADC activities in PC12 cells, which may be due to inhibition of cAMP production and $[Ca^{2+}]i$. In addition, liriodenine may attenuate decrease the L-DOPA-induced death of PC12 cells.

[PA1-30] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Antimicrobial and Antioxidative Activities of Cornis fructus Extracts

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Tannin-rich fruit of Cornus officinalis Sieb. et Zucc has been used as an ingredient in several prescriptions of Oriental medicine. Cornis fructus was extracted by successive extraction. Cornis fructus extracts were investigated for antimicrobial and antioxidative activities. Antimicrobial effects used disk diffusion method. All extracts were examined against Streptococcus mutans, Staphylococcus aureus and Phseudomonsa putida. Methanol extract showed the highest antimicrobial activity. Antioxidant effects used DPPH method. Antioxidative activities of the methanol extract were stronger than the others.

[PA1-31] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Isolation of diterpene acid from Anisotome lyallii

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The diterpene acid 1 was isolated from the roots of Anisotome lyallii(Apiaceae/Umbelliferae). The structure of the compound was elucidated as anisotomenoic acid 1 on the basis of spectroscopic method. This compound was evaluated against p388 murine leukaemia and B16/F10 melanoma cells.

[PA1-32] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Sauchinone inhibits iNOS, TNF-α and COX-2 induction by LPS

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Sauchinone, a lignan isolated from *Saururus chinensis (Saururaceae)*, is a diastereomeric lignan with cytoprotective and antioxidant activities in cultured hepatocytes. The effects of sauchinone on the iNOS, TNF-α and COX-2 gene expression and on the activation of transcription factors, NF-κB, C/EBP, AP-1 and CREB were determined in Raw264.7 cells as part of the studies on its anti-inflammatory effects. Expression of the iNOS, TNF-α and COX-2 genes was assessed by Northern and Western blot analyses. Sauchinone inhibited the induction of iNOS, TNF-α and COX-2 by LPS (IC50≤10 μM) with suppression of the mRNAs. To identify the transcriptional factors affected by sauchinone, the extents of NF-κB, C/EBP, AP-1 and CREB activation were measured. Activation of the transcription factors was monitored by gel mobility shift assay, whereas p65 and I-κBα were analyzed by immunocytochemical and immunoblot analyses. Sauchinone (1-30 μM) inhibited LPS-inducible nuclear NF-κB activation and nuclear translocation of p65, which was accompanied by inhibition of I-κBα phosphorylation. LPS-inducible increase in the intensity of C/EBP binding to its consensus sequence was also inhibited by sauchinone. The AP-1, but not CREB, DNA binding activity was weakly inhibited by sauchinone. These results demonstrate that sauchinone inhibits LPS-inducible iNOS, TNF-α and COX-2 expression in macrophages through suppression of I-κBα phosphorylation and p65 nuclear translocation and of C/EBP and/or AP-1 activation, which may constitute anti-inflammatory effects of the lignan.(Supported by the fund of Plant Diversity Research Center of the 21st Frontier Research Program, PF2-4)