

[PA1-26] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **A Random Amplified Polymorphic DNA (RAPD) primer to assist the Identification of Panax ginseng in Commercial Ginseng Granule Products**

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Previously, we found the operon random primer (OP-5A) that is characteristic the genus Panax by randomly amplified polymorphic DNA (RAPD) analysis. However, OP-5A primer is limited to apply on the differentiation of only crude herbal plants. To construct more sensitive and unique primers on the genus Panax, ginseng-specific DNA profile (350 bp) that was amplified by OP-5A primer were inserted in a plasmid vector in the TA cloning method and sequenced. We designed the PCR primers (Forward: 5"-AGGGGTCTTGCTAT AGCGGAAC-3", Reverse: 5"-AGTCTTAATTTTCATATTTTCGTATG-3") and identified the unique ginseng band (350 bp) in commercial granule products including ginseng extracts as well as crude ginseng plants by nascent PCR. Therefore, these results support that ginseng-specific DNA sequence could be used as a molecular marker to distinguish ginseng extract products from others at the molecular level.

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### **Effects of $\beta$ -carbolines on Dopamine Biosynthesis and L-DOPA-Induced Cytotoxicity in PC12 Cells**

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In vivo aromatic  $\beta$ -carbolines, such as harman and norharman, may easily be formed by cyclization of indoleamines with e.g. aldehydes. Because of the structural similarity to MPTP,  $\beta$ -carbolines have been proposed as endogenous toxins. In this study, we have investigated the effects of harman and norharman on dopamine biosynthesis and L-DOPA-induced cytotoxicity in PC12 cells. Treatment of PC12 cells with harman and norharman showed 48.8% and 49.5% inhibition of dopamine content at a concentration of 20  $\mu$ M and 100  $\mu$ M for 48 h. The IC<sub>50</sub> values of harman and norharman were 18.8  $\mu$ M and 96.7  $\mu$ M, respectively. Next, the intracellular mechanism of harman and norharman were examined. tyrosine hydroxylase (TH) activity decreased at 6 h maintained for up to 48 h and then recovered to the control level at about 72 h after exposure of PC12 cells to 20  $\mu$ M harman and 100  $\mu$ M norharman. Under the same conditions, TH mRNA level and intracellular Ca<sup>2+</sup> concentration also decreased by harman and norharman. Treatment with harman and norharman at concentrations higher than 100  $\mu$ M and 200  $\mu$ M caused a cytotoxicity in PC12 cells. Harman at 20-150  $\mu$ M and norharman at 100-300  $\mu$ M enhanced L-DOPA-induced cytotoxicity (L-DOPA concentrations, 20-100  $\mu$ M). These results suggest that harman and norharman contribute to the decrease in dopamine content by the inhibition of TH activity, the regulation of TH gene expression, the reduction of intracellular Ca<sup>2+</sup> concentration, and stimulate L-DOPA-induced cytotoxicity at higher concentrations in PC 12 cells.

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### **C/EBP $\beta$ mediated inhibition of PAH-inducible CYP1A1 expression by Oltipraz, a cancer chemopreventive agent**

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Oltipraz, a cancer chemopreventive agent, induces CYP1A1 to a certain extent by transactivation of the gene via the Ah receptor (AhR)-xenobiotic response element (XRE) pathway. Previously, we showed that oltipraz promoted CCAAT/enhancer binding protein  $\beta$  (C/EBP $\beta$ ) activation, which leads to the induction of glutathione S-

transferase. Given that oltipraz activates C/EBP $\beta$  for gene transactivation and that the putative C/EBP binding site is located in the CYP1A1 promoter region, this study investigated the effect of oltipraz on CYP1A1 induction by 3-methylcholanthrene (3-MC). 3-MC induced CYP1A1 in H4IIE cells in a time- and concentration-dependent manner. Gel shift analysis showed that 3-MC increased the band intensity of protein binding to the XRE. Immunocompetition analysis verified the specificity of AhR-XRE binding. Oltipraz (30  $\mu$ M) induced CYP1A1 and CYP1A1 promoter-luciferase gene and increased AhR DNA binding activity, which were 10-20% of those in 3-MC (100 nM)-treated cells. However, AhR-XRE binding was not increased after 10  $\mu$ M oltipraz treatment. Oltipraz (10  $\mu$ M) significantly inhibited CYP1A1 and CYP1A1-luciferase gene induction by 3-MC with no increase in AhR DNA binding. Oltipraz enhanced protein binding to the C/EBP binding site in the gene promoter and the binding complex comprised of C/EBP $\beta$  and partly C/EBP $\delta$ . Overexpression of dominant-negative mutant C/EBP significantly abolished the ability of oltipraz to suppress 3-MC-inducible CYP1A1 and CYP1A1-reporter gene expression. Consistently, C/EBP $\beta$  overexpression blocked CYP1A1-reporter gene induction by 3-MC. These results provided evidence that oltipraz suppresses 3-MC induction of the CYP1A1 gene expression and that activation of C/EBP $\beta$  by oltipraz contributes to suppression of 3-MC-inducible AhR-mediated CYP1A1 expression.

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#### **Anti-stress effect of Archoke juice in ICR mice.**

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High-dose extracts from artichoke leaves are traditionally used for treatment of stress related disorder, that is, hepatic disease, dyspeptic disorder, hyperlipidemic disorder and diuretic disorder. The aim of this study was to investigate anti-stress effects of Artichoke extract (Archoke juice produced from Choa company). The experiments were performed with the use of young (6-8 weeks of age) male mice of ICR strain weighing between 20 and 25 g at the time of first treatment with Archoke juice. They were grouped normal, control, Ginseng, diazepam and Archoke juice group. The normal ones were provide normal water and not exposed to stress. The control ones were provide normal water and exposed to stress. Ginseng, diazepam and Archoke juice ones were provide Ginseng extract 0.01%, diazepam 0.005% and Archoke juice 5% containing water for 12 days and exposed to stress for 5 days. They were stressed by immobilization for 30 minutes and electro-shock (1mA/20 secs) for 5 minutes. At first, they were pretreated with Ginseng extract, diazepam and Archoke juice for 7 days, and followed by the treatments in combination with the exposure to stress for 5 days. We recorded stress related behavioral changes of experimental animals induced by over stress using Etho-vision system. Smelling and grooming activity, plus maze moved distance and rearing, and Y-maze moved distance decreased by stress were increased by treatment of Archoke juice. Freezing activity, plus maze-staying time in closed area increased by stress were decreased by treatment of Archoke juice. But total activity and activities of face washing, burrowing and rearing were not significantly changed although there were recovering trends from stress induced behavioral change. These results suggest that Artichoke protect partially the living organism from stress attack in some case.

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#### **Antifibrotic and Antioxidative Effect of Solanum lycopersicum in Liver fibrosis (Cirrhosis) induced Rats**

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Introduction: Liver fibrosis is defined unbalance of collagen metabolism, especially a stimulation of collagen