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Polygoni Radix, the root of *Polygonum cuspidatum* (Polygonaceae), has been used as treatments of dermatitis, hyperlipemia, gonorrhea, favus athlete's foot, inflammation in traditional medicine. Oxygen free radical injury and lipid peroxidation have been suggested as major causes of atherosclerosis, cancer, liver disease, and the aging process.

Oxidative modification of low density lipoprotein (LDL) has been recognized as an important process of atherosclerosis.

Methanol extract of Polygoni Radix showed antioxidant effect on LDL oxidation. In this study, we determined effect of ethylacetate fraction and subfractions (PE1-4) of Polygoni Radix on Cu⁺⁺ induced oxidative modification of LDL using in vitro system such as agarose gel electrophoresis and TBA method.

The results showed that PE3 had a similar effect to ascorbic acid on oxidative modification of LDL.

[PA1-15] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Development of the specific therapeutic drugs for atrial arrhythmias from natural products

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The therapeutic potential of currently available antiarrhythmic drugs is limited by their tendency to induce proarrhythmic and extracardiac side effects. An ideal antiarrhythmic agent would selectively prolong the action potential duration more in extraordinarily depolarized cardiac myocytes than in normal cells, and show tissue selectivity. Voltage-gated K⁺(Kv) channels play an important role in determining the length of the cardiac action potential and are the targets for antiarrhythmic drugs. Kv1.5, is one of the more cardiovascular-specific K⁺ channel isoforms identified to date and forms the molecular basis for an ultra-rapid delayed rectifier K⁺ current (I_{Kur}) found in human atrium. Thus, the blocker of hKv1.5 is expected to be an ideal antiarrhythmic drug for atrial fibrillation. In the present study, we examined the effect of many kinds of plants extract on the hKv1.5 current expressed in Ltk-cells using whole cell mode of patch clamp techniques. We found out that isoquinoline alkaloid plants selectively inhibited the hKv1.5 current expressing predominantly in human atrium without affecting the HERG current expressing mainly in ventricle. Thus our results suggest that isoquinoline alkaloid plants would be one of the leading compound in developing the ideal antiarrhythmic drugs for atrial fibrillation.

[PA1-16] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Caffeic acid Phenethyl Ester Inhibits Inducible Nitric Oxide Synthase Gene Expression in RAW 264.7 Macrophages

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Nitric oxide (NO), a multifunctional mediator produced by and acting on various cells, participates in inflammatory and autoimmune-mediated tissue destruction. Modulation of NO synthesis and

action represents a new approach to the treatment of inflammatory and autoimmune diseases. Caffeic acid phenethyl ester (CAPE), an active ingredient of honeybee propolis, has been identified to show anti-inflammatory, anti-viral and anti-cancer activities. However, the molecular basis for anti-inflammatory properties of CAPE has not been known. The present study examined effects of CAPE on iNOS expression induced by lipopolysaccharide plus interferon-gamma in RAW 264.7 macrophages. CAPE inhibited NO production, iNOS enzyme activity, and iNOS protein expression in a concentration-dependent manner. In addition, CAPE inhibited iNOS mRNA expression. The findings suggest that CAPE exerts anti-inflammatory effect by inhibiting both transcriptional expression and enzyme activity of iNOS.

[PA1-17] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Involvement of antioxidant action in the neuroprotective effects of *Acori graminei* rhizoma

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We have previously reported that the methanol extract and essential oils from *Acori graminei* rhizoma (AGR) exhibited protective action against excitotoxic neuronal death, and that the neuroprotective action was primarily due to the blockade of the NMDA receptor function. In the present study, we evaluated the effects of AGR extracts on the oxidative damage induced in primary cultured rat cortical cells, and identified the active principle through the activity-guided fractionation. The crude methanol extract inhibited the Fe²⁺-induced oxidative neuronal degeneration in a concentration-dependent manner. The oxidative damage induced by Zn²⁺ and H₂O₂ was partially inhibited by the extract. To isolate the active component(s) in AGR, the methanol extract was subsequently fractionated with butanol, chloroform, ethylacetate, hexane, and water. The potent antioxidant action was retained in the ethylacetate and chloroform fractions. Further purification and structure analyses demonstrated that the active principle is asarone, the major essential oil component in AGR. Asarone dramatically inhibited the increase in the levels of lipid peroxide in the brain homogenates. Based on these results and our previous reports, asarone is the major principle in AGR exhibiting neuroprotection against excitotoxic and oxidative neuronal death.

[PA1-18] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Methanol extracts of *Fructus Psoraleae* inhibit bradykinin-mediated pain reactions

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Methanol extracts of *Fructus Psoraleae* (FP) has been tested to determine if it has some analgesic actions. In both acetic acid writhing assays and tail flick assays, the extract has been shown to contain significant pain inhibition activities when 1 - 100 mg/Kg was administered via IP. It also contained some antiinflammatory actions in the rat paw edema tests. To explore potential mechanism of analgesic actions of FP extracts, rat ileum contraction studies were carried out. FP extracts blocked the bradykinin-induced rat ileum contractions in dose-dependent manners. Acute toxicity of the FP extracts was examined by measuring LD₅₀ value. The calculated LD₅₀ was more than 20g/Kg, suggesting that the safety margin of the methanol extract of FP is relatively wide.