An ideal antiarrhythmic drugs for atrial fibrillation extracted from plants

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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. The number of patients suffering from atrial fibrillation is increasing and many cardiologists is trying to develop the ideal antiarrhythmic drugs for atrial fibrillation. Previously, we found out that the extracts from plants selectively inhibited the hKv1.5 current expressing predominantly in human atrium without affecting the HERG current expressing mainly in ventricle. From those results, we proposed that the extracts from plants would be one of the leading compound in developing the ideal antiarrhythmic drugs for atrial fibrillation.
In this study, we examined the effects of the extracts on the action potentials in rabbit heart using conventional microelectode technique. The extracts prolonged the action potential durations of atrial, ventricular myocytes and Purkinje fibers in a dose-dependent manner. However, the effect of the extract on atrial APD was frequent dependent whereas the effect of the extract on the APDs of ventricular myocytes and Purkinje fibers was not frequency dependent. Additionally, the extract-induced hKv1.5 block was frequency-dependent and the extract inhibits the human atrial K+ current. These results stongly suggest that the extract could be an ideal compound for atrial fibrillation.

[PA1-30] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Resverotrol inhibits the degranulation of mast cells by interfering the IgE receptor-mediated regulation of pyruvate kinases in RBL-2H3 cells

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Previously we have reported the structure-activity relationship of hydroxystilbens on the inhibtion of mast cell degranulation, and resveratrol was one of the most potent compounds tested. Here we examined the effect of resveratrol on tyrosine phosphorylation of several signaling components of Fcε RI, the high affinity IgE receptor. Resveratrol did not affect the tyrosine phosphorylation of Syk, and showed some variable effects on PLC-γ2, and consistent inhibition on pyruvate kinase and MAPK. The pyruvate kinase is known to be inhibited and tyrosine-phosphorylated when FcεRI is cross-linked. Resveratrol, when tested for the pyruvate kinase activity, inhibited the FcεRI-mediated inhibition of pyruvate kinase activity (disinhibition). These results show that, when we consider that MAPK is not important for the regulation of the degranulation of mast cells, resveratrol inhibits mast cell degranulation by interfering with the FcεRI-mediated inhibition the pyruvate kinase.

[PA1-31] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Antimicrobial activity of the ethyl aceate extract of Sophora flavescens Ait

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The ethyl acetate extract from Sophora flavescense Ait. had strong antimicrobial activity against S. mutants, S. epidermidis, S. aureus and P. putida. The extract was subfractionated by C18 reverse-phase silica gel chromatography with various solvents. The activity was retained in H2O: CH3CN, 1 : 3 fractions. The subfraction was further chromatographed on silica gel with MeOH : CHCl3 and the maximum acitivity was found in the fraction eluted with 1 : 10 - 3 : 10 (5-4-5-4-3). The maximum MIC was 3.125 ㎍/㎖ for S. mutants, S. epidermidis and S. aureus and 6.25 ㎍/㎖ for P. putida. The 5-4-5-4-3 subfraction was further fractionated by silica gel column chromatography and recycle-high performance liquid chromatography. The isolation and NMR spectral data of (2s)-2'-methoxykurarinone and kurarinone were reported. They demonstrated antimicrobial activities in a broth dilution bioassay.

[PA1-32] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Flavonoids of Inula britannica attenuate the glutamate-induced toxicity in primary cultures of rat cortical cells

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We previously reported that twelve antioxidative flavonoids from the *n*-BuOH extract of *Inula britannica* (Asteraceae). This prompted us to investigate further whether these flavonoids also showed antioxidative activity in live cells of culture system. Among twelve flavonoids tested, only patuletin, nepetin and axillarin protected primary cultures of rat cortical cells from oxidative stress induced by glutamate. These flavonoids exerted more neuroprotective activity when pre-treated than post-treated after the oxidative stress. Treatment of these flavonoids maintained the activities of antioxidant enzymes such as catalase, glutathione-peroxidase, glutathione reductase which play important role in antioxidative defense mechanism. Moreover, these three flavonoids also attenuated the significant drops of GSH induced by glutamate through the inhibition of GSH diminution as a result of oxidative stress, which is demonstrated by using buthionine sulfoximine or diethyl maleate. However, these flavonoids did not stimulate the synthesis of GSH. Regarding the structure-activity relationship, our results indicated that 3',4'-hydroxyl groups in the B ring are crucial for the protection against the oxidative stress and glycosylation greatly reduced their protective activities. Collectively, these results indicated that patuletin, nepetin and axillarin strongly protect primary cultured neurons against glutamate-induced oxidative stress.

[PA1-33] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Antidiabetic effect and mechanism of Ginseng Radix Rubra, Ginseng Radix Alba, and Ginseng Radix Palva in KKAy mice

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To elucidate antidiabetic effect and mechanism of Ginseng Radix Rubra(GRR), Ginseng Radix Alba (GRA) and Ginseng Radix Palva(GRP) in hyperglycemic and hyperinsulinemic KKAy mice, GRR, GRA, GRP were administered orally for 4 weeks and effects on BMI, plasma glucose, HbA1c, insulin, total cholesterol, HDL, Triglyceride, genetic expressions of PPARγ in epididymal fat, intestinal sodium-glucose cotransporter (sGLT1) and glucose transporter in quardriceps muscle (GLUT4) were examined in this study. GRR, GRA, GRP lowered significantly plasma glucose from a week after treatment and the hypoglycemic activity was retained for 4 weeks. GRR, GRA, GRP also lowered insulin dramatically 4 weeks after treatment. GRR and GRA treated group reduced HbA1c level. We found no significant difference in BMI, total cholesterol, HDL, and triglyceride with any of treatments. α-glycosidase