In this study, effect of CAD on heterologous passive cutaneous anaphylaxis (PCA) were studied by the method of Levine and Vaz(1970). Anti-serum was prepared from OA-sensitized male Balb/c mouse at two weeks after the last challenge of ovalbumin (OA) and alumina gel, and these serum diluted with HEPES buffer by means of the heterologous PCA titer, i.e. the highest dilution inducing PCA in rats. Heterologous PCA test in rats were carried out to determine the width and contents of pigment leakaged in the dorsal skin 30 minutes after i.v. injection of 0.2 ml of 1 % egg albumin and 1 % Evans blue mixture (1 : 1). It shows that all of CAD inhibited the heterologous PCA : Quinic acid, ferulic acid and coumaric acid at a dose of 25 mg/kg, and sinapinic acid and cinnamic acid at a dose of 50 mg/kg,, inhibited significantly the contents of leaked pigments and width of pigmented skin as compared with control, respectively ($p<0.01$). These activity were lees than that of prednisolone acetate at a dose of 10 mg/kg. Quinic acid has more inhibitory activity of PCA than chlorogenic acid. These results indicated that CAD inhibited dose-dependently the anaphylactic hypersensitivity, and also the more hydrogen radical in benzene ring of CAD have, the more inhibitory activity on PCA have.

[PB2-7] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Inhibitory Action of Cinnamic Acid Derivatives on Reversed Cutaneous Anaphylasis and Hemolysin Titer

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Cinnamic acid derivatives(CAD) originating from vegetable kingdom have some biological activity. Effect of CAD on reversed cutaneous anaphylaxis (RCA) and hemolysin (HY) titer were studied in rats. Experiments were carried out to determine RCA as the skin edema induced at 2 hours after injection of 0.05ml/site of anti-rat serum rabbit serum. Drugs were orally administered at one hour before antigen challenge. HY titer determined the hemlysis of sRBC to spleen cells. Two weeks after sensitization of i.p. injection of sRBC (4x10(8) cells), mice were challenged by i.p. injection of sRBC. On day 5 after sRBC challenged, spleen cells were isolated by cytosieve. HY titer exhibited as log2X (X is the highest dilution). Drugs were orally administered one hour before the last challenge of antigen. It shows that all of CAD have generally the dose-dependently inhibitory action on RCA and HY titer. Sinapinic acid at a dose of 12.5 mg/kg, and coumaric acid, quinic acid, chlorogenic acid, cinnamic acid and ferulic acid at a dose of 50 mg/kg inhibited significantly the RCA as compared with control, respectively ($p<0.01$). Quinic acid at a dose of 12.5 mg/kg inhibited significantly HY titer as compared with control ($p<0.01$), and it's activity was one half of prednisolone acetate. Sinapinic acid and chlorogenic acid at a dose of 25 mg/kg have the significant inhibition of HY tier. These results indicated that the more methoxy or hydroxyl radical in benzene ring of CAD have, the more inhibitory activity of RCR and HY titer have.

Poster Presentations - Field B3. Neuroscience

[PB3-1] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

ROLE OF ERK1/2 IN 6-HYDROXYDOPAMINE-INDUCED APOPTOSIS IN SK-N-SH HUMAN NEUROBLASTOMA CELLS

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Parkinson's disease (PD) is a widespread neurodegenerative disorder. Even though PD has been studied in many aspects, it is still unknown the molecular signaling mechanisms linking reactive oxygen species (ROS) and neuronal apoptosis in PD. A better understanding of cellular mechanisms that occur in Parkinson's disease is essential for development of new therapies. In this study we investigated the signaling molecules involved in neuronal apoptosis induced by 6-hydroxydopamine (6-OHDA) in human SK-N-SH neuroblastoma cells as a model cellular system. Treatment of SK-N-SH cells with 6-OHDA increased nitric oxide generation and apoptosis. N(G)-monomethyl-L-arginine (NMMA), a NOS inhibitor, prevented 6-OHDA-induced cell death. In addition, 6-OHDA also induced time-dependent phosphorylation of extracellular signal-regulated protein kinase (ERK1/2) and cyclic AMP regulatory binding protein (CREB), which was not dependent on phosphatidylinositol 3-kinase(PI3-K). Furthermore, 6-OHDA also increased Bax expression but decreased bcl-2 level. Blocking of ERK1/2 activation with the upstream inhibitor PD98059 prevented 6-OHDA-induced cell death and changes of the ratio between Bax and Bcl-2. These data suggest that ERK1/2 play an important role in 6-OHDA-induced neurotoxicity.

[PB3-2] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

A novel potassium channel opener, KR-31378, protects cortex neurons from oxidative injury by restoring antioxidant enzyme activities and glutathione levels

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Neuronal hyperexcitability followed by high level of intracellular calcium and oxidative stress play critical roles in neuronal cell death in stroke and neurotrauma. Hence, KR-31378, a novel benzopyran derivative was designed as a new therapeutic strategy for neuroprotection possessing both anti-oxidant and potassium channel modulating activities. In the present study, we tested for its neuroprotective efficacy against oxidative stress-induced cell death in primary cortical cultures and further investigated its neuroprotective mechanism.
Incubation of cortical neurons with KR-31378 protected FeSO4-induced apoptotic as well as necrotic cell death in a concentration dependent manner. The protective effect of KR-31378 was neither mimicked by other potassium channel openers nor abolished in the presence of KATP channel blockers, indicating that its effect was not related K+ channel opening activity. The mechanism of protection is rather attributable to the antioxidant property of KR-31378 since it suppressed the intracellular accumulation of ROS and ensuring lipid peroxidation caused by FeSO4. We further studied its effect on antioxidant defense, enzymatic and nonenzymatic system. Prooxidant, FeSO4, resulted in decrease of catalase and glutathione peroxidase activities, which were restored by KR-31378 treatment. In addition, it attenuated the depletion of glutathione contents caused by FeSO4. Taken together, modulation of antioxidant enzyme activities and glutathione metabolism may contribute to the antioxidant property of KR-31378 by which it exerts a beneficial effect in oxidative stress-induced brain injury and it represents a potentially useful therapeutic agent for the ischemic brain injury

[PB3-3] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]