anti-rat serum rabbit serum in SD rat. Drugs were orally administered one hour before antigen challenge. HY titer were determined the hemolysis of sheep red blood cell (sRBC) to spleen cells. Two weeks after sensitization of i.p. injection of sRBC, the mice were challenged with sRBC. On five day after the mice were rechallenged, spleen cells were isolated by cytosieve (100 mesh), the viability of spleen cells was determined by trypan blue exclusion test immediately before used. HY titer to sRBC were carried out to determine hemolysis in inactivated mice serum added guinea-pig complement, and exhibited as $\log_2 X$ (X is the highest dilution). Drugs were orally administered one hour before the last challenge of antigen. It shows that Compound-A has dose-dependently inhibited the RCA as compared with control : Its inhibitory activity at a dose of 25 and 50 mg/kg were 18.0±2.4 and 23.4±1.4 %, respectively ($p<0.05$). Its activity at a dose of 50mg/kg was same as prednisolone acetate at a dose of 10 mg/kg and its activity at a dose of 25 mg/kg was same as disodium cromoglycate at a dose of 20 mg/kg. And Compound-A at a dose of 50 mg/kg inhibited significantly the HY titer as compared with control (34.1±3.0 %, $p<0.05$), but its activity was more active than disodium cromoglycate (20 mg/kg) and less active than prednisolone acetate (10 mg/kg). Compound-A has the dose-dependently inhibitory action on RCA and HY titer. These results showed that Compound-A has the inhitory acivity of type II hypersensitivity such as RCA and CDH.

[PB2-6] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Compound-A inhibited the Asthmatic Responses in the Conscious Guinea Pigs

JiYun Lee°, JinHee Lee, YounJoung Kim, SangSoo Sim, ChangJong Kim
Department of Pathophysiology, College of Pharmacy, Chung Ang University

Effect of Compound-A, a phenylpropanoid isolated from Arctium lappa fruit, on the early- (EAR) and late-phase asthmatic responses (LAR) of guinea pigs were studied in vivo. Guinea pigs were sensitized by injection of 100 mg of ovalbumin (OA). Twenty-one days after sensitization, animals were challenged with exposure to aerosolized 1 % OA for five minutes in double-chambered plethysmograph box with jet nebulizer. Immediately and twenty-four hours after challenge, EAR and LAR asthmatic responses were determined the tidal volume (TV), respiration rate (RR) and specific airway resistance (sRaw), and then animals anethetized and taken the bronchoalveolar lavage fluid (BALF) by lavage the lung with HEPES buffer through cannulation into trachea. BALF cytospined and stained by Wright"s stain, and the contents of leukocytes, histamine, phospholipase A_2 (PLA_2), eosinophil peroxidase (EPO) and protein were measured in BALF. The TV at a dose of 25 mg/kg inhibited 42.1±9.3 % in EAR, 21.1±6.3 % in LAR as compared with control, respectively ($p<0.05$). sRaw at a dose of 25 mg/kg increased 187.5±33.4 % in EAR, 97.1±15.5 % in LAR as compared with control, respectively ($p<0.05$). but its activity was less than dexamethasone (5 mg/kg) and disodium cromoglycate (10 mg/kg). And Compound-A at a dose of 50 mg/kg inhibited significantly recruitment of total leukocytes and neutrophils ($p<0.05$), and inhibited significantly recrument of eosinophils at a dose of 25 mg/kg, but its activity was less than dexamethasone (5 mg/kg) and disodium cromoglycate (10 mg/kg). Also Compound-A at a dose of 50 mg/kg inhibited significantly protein exudation and PLA_2 ($p<0.05$), its activity was same as dexamethasone (5 mg/kg) and disodium cromoglycate (10 mg/kg), respectively. Compound-A dose-dependently inhibited the histamine release ($p<0.05$), but its activity was less than dexamethasone (5 mg/kg). These results showed that Compound-A dose-dependently inhibited asthmatic responses.

[PB2-7] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Effect of Ascorbic Acid on the Activity and Gene Expression of Cytochrome P450 in Sepsis

Kim Joo-Young°, Park Sang-Won, Lee Sun-Mee
College of Pharmacy, Sungkyunkwan University

Sepsis remains common surgical problems with high morbidity and mortality despite improvement in the management for septic patient. Although hepatocellular dysfunction occurs during sepsis, the mechanism responsible for this remains unclear. In sepsis, a state of severe oxidative stress is encountered, with host endogenous antioxidant defenses overcome. Therefore, the aim of this study was to determine whether specific

abnormality exists in cytochrome P450 (CYP)-mediated metabolizing function associated with polymicrobial sepsis and whether role of ascorbic acid (AA) in the alterations during sepsis. Rats were subjected to polymicrobial sepsis by cecal ligation and puncture (CLP). AA (100 mg/kg) was immediately injected intravenously after CLP. Liver and blood samples were taken 24 h after CLP for measurement of the extent of hepatocellular damage and activities of CYP-related isozymes. In addition, Western immunoblotting and RT-PCR analysis in liver tissue were conducted to investigate the expression of protein and mRNA levels for CYP isozymes. The level of serum alanine aminotransferase activity was markedly increased after CLP, which were suppressed by AA. Serum aspartate aminotransferase activity and lipid peroxidation level were significantly increased; an increase which was not suppressed by AA. Total CYP content significantly decreased but was restored by AA. NADPH-P450 reductase activity, its protein and mRNA expression were reduced after CLP; a decrease was prevented by AA. CYP1A1, 1A2, 2B1 and 2E1 activities also decreased. This decrease in CYP1A1 and 2B1 acitivity was prevented by AA, but not in CYP1A2 and 2E1. The mRNA levels of CYP2B1 and 2E1 significantly decreased, which was prevented by AA. Also, their protein expression decreased after CLP; a decrease was prevented by AA. Our findings suggest that AA reduces hepatocellular dysfunction, as indicated by abnormalities in CYP isozyme activities and its gene expression in sepsis.

[PB3-1] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Phosphorylation by Ca^{+2}/calmodulin-dependent Kinase II Regulates Binding of Capsaicin to VR1

Koo Jae Yeon°, Kim Sang Sung, Kim Man Soo, Park Seung Pyo, Shim Won Sik, Yang Youngduk, Cho Hwawon, Kim Mi Sook, Kim Byung Moon, Oh Uhtaek
College of Pharmacy, Seoul National University

VR1, a capsaicin receptor, is now known to play a major role in mediating inflammatory thermal nociception. Although the physiological role or biophysical properties of VR1 are known, its activation mechanisms by ligands are poorly understood. Here, we show that VR1 requires phosphorylation by Ca^{2+}-calmodulin-dependent kinase II (CaMKII) for its activation by capsaicin. In contrast, dephosphorylation by calcineurin, leads to desensitization of the receptor. Point mutation of VR1 at two putative consensus sites for CaMKII fails to elicit capsaicin-sensitive currents with concomitant reduction in phosphorylation of VR1 in vivo. The mutant also lost the high-affinity binding of ^{3}H-resiniferatoxin, a potent capsaicin-receptor agonist. We conclude that the dynamic balance between phosphorylation and dephosphorylation of the channel by CaMKII and calcineurin controls the activation/ desensitization state by regulating the binding property. Furthermore, since sensitization by protein kinase A and C converges on these sites, phosphorylation stress in the cell appears to control a wide range of excitability in response to various adverse stimuli.

[PB3-2] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Involvement of PLA_2 Isoforms in Muscarinic Receptor-Mediated sAPP Release and Store-Operated Calcium Entry in SH-SY5Y Cells.

HYE-WON CHO°, JIN-HYUNG KIM, SHIN-KYU CHOI, HWA-JUNG KIM
College of Pharmacy, Ewha Womans University

We previously reported that phospholipaseA_2 (PLA_2)-related pathway and capacitative calcium entry (CCE) via store-operated calcium channel (SOC) were involved in the regulation of muscarinic receptor- mediated sAPP release. We also observed that stimulation of muscarinic receptor associated with the inositol phosphate cascade resulted not only in increase of CCE but also in activation of PLA_2 in SH-SY5Y cells. In this study, we further investigated whether the PLA_2 isoforms differently regulate the muscarinic receptor- mediated sAPP release, and examined the relationships between activation of PLA_2 isoforms and CCE mediated by muscarinic receptors in SH-SY5Y cells. Treatment of the three isoform-selective PLA_2 inhibitors, [thioether amide-PC (TEA-PC; an inhibitor of secretary PLA_2, sPLA_2), haloenol lactone suicide substrate (Helss or BEL; an inhibitor of calcium independent PLA_2, iPLA_2), arachidonyl trifluoromethyl ketone (AACOCF3; an inhibitor of calcium dependent