[PA1-32] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Studies on General Pharmacological Properties of Rhus verniciflua

Choi KH, Rheu HM, Kim JI, Chung SY

Department of Pharmacology, National Instite of Toxicological Research, Korea Food and Drug Administration.

The general pharmacological properties of flavonoid and urushiol, in Rhus verniciflua (Anacardiaceae) were investigated in mice, rats and guinea pig. The influences of these components were evaluated on central nervous system (CNS), cardiovascular system, respiratory system, intestinal propulsion and automomic nervous system Among dose 50, 100 and 200 mg/kg, the administration of flavonoid (200 mg/kg) showed analgegic effect and extended sleeeping duration time. As well in digestive system, it significantly increased intestinal propulsion. The flavonoid pretreatment remarkably inhibited the contractile response induced by acetylcholine and histamine in isolated guinea pig ileum. On the experiment of urushiol, urushiol (50 mg/kg) showed undesirable effect (reducing spontaneous activity, relaxing muscle and increasing body temperature, etc) in central nervous system. It seems to act as a depressant in CNS. Furthermore it completely blocked the intestinal propulsion. From the above results, it is suggested that flavonoid has potential in automonic nervous. Urushiol affects central nervous system.

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Identification and Characterization of Matrix Metalloproteinase-2 (MMP-2) and Tissue Inhibitor of Metalloproteinase-2 (TIMP-2) Expressed in primary Hamster Tracheal Surface Epithelial cells

Lee WJ, Shin CY, Ryu JR, Yoo BK, Park KH, Choi JW, Jang ES, Min HW, Choi MS, Ko KH°

Department of Pharmacology, College of Pharmacy, Seoul National University

Matrix metalloproteinases (MMPs) are zinc-dependent endopeptidases and are implicated in the *remodelling of the extracellular matrix* (ECM). In several inflammatory diseases of airway, it has been known that MMPs are secreted from immune cells and play an important role in the process of inflammation. The purpose of the present study was to identify and characterize collagenolytic enzyme expressed from primary hamster tracheal surface epithelial (HTSE) cells and to study its relevance to chronic airway inflammatory diseases. To investigate characteristics of collagenolytic enzyme activity, [3H]collagen-digestion assay was used. The activity of enzyme was sensitive to EDTA which could be typically expected from the divalent cation dependency of MMPs. To identify the subtypes of MMP, Western blot, zymography and RT-PCR were performed. The data revealed that HTSE culture expresses MMP-2 along with the tissue inhibitor of metalloproteinase-2 (TIMP-2), a known endogenous inhibitor of MMP-2. Retinoic acid-depletion and phorbol 12-myristate 13-acetate (PMA) treatment, which resembles the condition of airway inflammatory diseases, increased the expression and activity of MMP-2 from HTSE cells, which implicate a possible role of the MMP-2 in the chronic airway inflammatory disease.

[PA1-34] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

THE RELAXATION IN RESPONSE TO CARBACHOL IN CAT LES MUCLE

Kim HC°, Jun CH, Youm JH, Shin CY, Lee TS, UD Sohn and Huh IH

Dept of Pharmacology, College of Pharmacy, Chung Ang University

It has been shown that SNP or SIN-1-induced decrease of the tone in cat LES is mediated via a NO/cGMP-dependent contraction. This study was performed using organ bath to define the participation of NO/cGMP signaling pathway on the relaxation in presence of contractile agent (carbachol). It was investigated the effect of soluble guanylate cyclase inhibitors, LY-83583 and 1H-[1,2,4]oxadiazolo[4,3-α]quinoxalin-1-one (ODQ), on sodium nitroprusside (SNP), 3-morpholino-sydnomine (SIN-1), or forskolin-induced muscle relaxation. SNP caused dose-dependent relaxation of the contraction induced by carbachol. Preincubation with NO synthase inhibitor N^{ω}-nitro-L-arginine (L-NNA) and LY-83583 had no influence on the relaxations induced by SNP. In contrast, the relaxation to SNP was blocked by ODQ. SIN-1 produced dose-dependent relaxation which was attenuated by L-NNA or ODQ, but not by LY-83583. Forskolin (0.1~10 mM) produced dose-dependent relaxation which was not inhibited by ODQ. These results suggest that SNP, or SIN-1-induced muscle relaxation in the presence of conteactile agent using cat LES is mediated by a cGMP/NO-dependent mechanism, which is similar to the relaxation to the resting tone

[PA1-35] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Effects of Ras farnesyltransferase inhibitor, SCH66336, on insulin actions in insulin-sensitive HIRc-B fibroblasts

Yi SJ°, Choi JE, Park SN, Ha JB, Pai JK # and Jhun BH

Laboratory of Cell Biology, Dept of Pharmacy, Pusan National University, Pusan, Korea and #Department of Tumor Biology, Schering-Plough Research Institute, New Jersey, USA

Ras has been shown to be a key regulator in the mitogenic signal transduction pathways of insulin. SCH66336, an orally bioavailable nonpeptide tricyclic farnesyltransferase inhibitor of Ras, is currently under clinical trials in cancer patients. In the present studies, we examined the effects of SCH66336 on the insulin signaling pathways in HIRc-B cells, Rat 1 fibroblast overexpressing human insulin receptors. The DNA synthesis, c-Jun expression and membrane ruffling induced by insulin were blocked by microinjection of GST-fusion dominant negative Ras, GST-RasN17, confirming that Ras protein is involved in the insulin mitogenic siganling pathways. The prenylation of an isoform of endogenous Ras in HIRc-B cells was inhibited by SCH66336 in dose-dependent manner. SCH66336 caused partial dose-dependent inhibition of DNA synthesis induced by insulin, while it did not affect cell viability, c-Jun expression, and membrane ruffling induced by insulin. These results indicate that 1) SCH66336 partly blocked insulin actions leading to mitogenesis of insulin and 2) isoform of Ras, probably K/N-Ras, which is unaffected by SCH66336, may be involved in insulin signaling pathways.

[PA1-36] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

The involvement of Kupffer cells in ischemia/reperfusion-induced hepatic injury

Lee YG°, Lee SH, Lee SM

College of Pharmacy, Sungkyunkwan University

Temporary interruption of hepatic blood flow is often required in the management of acute hepatic trauma and is obligatory during liver transplantation. Although growing evidences have been shown that Kupffer cells are involved in hepatic ischemic injury the mechanism of this injury still unclear. Therefore, these studies were designed to evaluate the role of Kupffer cells in hepatic ischemia/reperfusion in isolated perfused rat liver. Kupffer cells were destroyed selectively with gadolinium chloride treatment (GdCl3, 10mg/Kg) 2days prior to operation. Isolated rat livers from fasted 18 hours were preserved in UW (University of Wisconsin solution) at 4℃ for 24 hours after