

synthesis and inhibition of collagen degradation, and antifibrotic effect is delaying or inhibition of new collagen synthesis and deposition in liver tissue. In this study, we investigated the antifibrotic and antioxidative effect of Solanum lycopersicum (SL) in liver fibrosis induced rats. Methods: : Rats were randomly divided in three groups (normal, CCl₄ and CCl₄-SL group) and were received 0.6 ml mixture of CCl₄ and olive oil (1:1 v/v) 3 times/week for 4 weeks except of the normal group. And the rats in CCl₄-SL group were treated with 0.3 mg/day/rat in 4 weeks. After experiment, the liver tissues and sera were used for the measurement of hydroxyproline (hyp), malonaldehyde (MDA), superoxide dismutase (SOD) and enzyme activity as the liver function parameters. In addition, RNA expression of collagen \pm 1(III) and \pm 1(IV) was observed by RT-PCR. Results: The value of parameters such as liver function, lipid peroxidation protection and collagen deposition were significantly elevated in the CCl₄ and CCl₄-SL group compared to the normal group (p<0.0001). The significantly lower level of GOT, GPT, ALP, BUN and total-bilirubin in sera and the concentration of MDA and hyp in liver tissue showed in the CCl₄-SL group than in CCl₄ group (p<0.05-0.0001). The higher activity of SOD appeared in CCl₄-SL group than in the CCl₄ group, but the significance between two groups was not observed. And decreased mRNA expression of collagen \pm 1(III) as a parameter of collagen synthesis and increased mRNA expression of collagen \pm 1(IV) as a parameter of collagen degradation were observed in CCl₄-SL group compared to the CCl₄ group. Conclusion: Solanum lycopersicum could be in possession of antioxidative action, antifibrotic effect and the improvement of liver function.

[PA1-31] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Long-term measurement of physiological cardiovascular parameters using telemetry system in dogs.

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With the issuance of the ICH "Guidance for industry S7A Safety Pharmacology Studies For Human Pharmaceuticals" in July 2001 came the preference for the use of unanesthetized animals when evaluation the safety profile of new pharmaceutical agents. Telemetry provides a means of obtaining measurements of physiological functions in conscious animals without the problems associated with classical cardiovascular measuring methods. The Korea Institute of Toxicology (KIT) established the telemetric measurement of cardiovascular parameters, such as Blood pressure, Heart rate, ECG (PR, RR, QRS, QT and QTcB interval) under GLP conditions. In this study, we carried out the continuous monitoring of cardiovascular parameters for extended periods of time by the telemetered beagle dogs to ensure the validity of this system. We founded that the obtained data are constant and accurate throughout the measuring time. Therefore it could be concluded that our telemetry system is able to provide the appropriate measurements and that the signals being detected by the systems are highly accurate.

[PA1-32] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Pinacidil causes depressor action, catecholamine release and vasorelaxation in the normotensive rat

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The present study was conducted to investigate the effects of pinacidil, a potassium channel opener, on arterial blood pressure, catecholamine release and vascular contractile responses in the normotensive rats and to establish the mechanism of action. Phenylephrine (an adrenergic α_1 -receptor agonist) and high potassium (a membrane-depolarizing agent) caused greatly contractile responses in the isolated aortic strips, respectively. These phenylephrine (10⁻⁵ M)-induced contractile responses were dose-dependently depressed in the presence of pinacidil (25 ~ 100 μ M). Also, high potassium (5.6 x 10⁻² M)-induced contractile responses were greatly inhibited in the presence of pinacidil (25 ~ 100 μ M) in a dose-dependent fashion. Pinacidil (1 ~ 10 μ g/kg) given into a femoral vein of the normotensive rat produced a dose-dependent depressor response, which is transient (data not shown). Interestingly, the infusion of pinacidil (3 ~ 30 μ g/kg/30min) made a significant reduction in pressor

responses induced by intravenous norepinephrine. Moreover, the perfusion of pinacidil (100 μ M) into an adrenal vein of the rat for 20 min inhibited the CA secretory responses evoked by ACh (5.32 mM), high K^+ (56 mM), DMPP (100 μ M), McN-A-343 (100 μ M). Collectively, these results obtained from the present study demonstrate that intravenous pinacidil causes a dose-dependent depressor action in the anesthetized rat at least partly through the blockade of adrenergic α_1 -receptors. Pinacidil also causes vascular relaxation in the isolated aortic strips of the rat via the blockade of adrenergic α_1 -receptors, in addition to the known potassium channel opening-induced vasorelaxation. It seems that pinacidil has the inhibitory effects on CA secretion in the perfused rat adrenal gland.

[PA1-33] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

CJ-11668, a new selective and potent cox-2 inhibitor, has long-acting pharmacokinetic profiles

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CJ-11668 is a new potent and selective COX-2 inhibitor (IC_{50} COX-2 65nM; COX-1/COX-2 ratio 770). The pharmacokinetic profile of CJ-11668 (20 mg/kg, p.o.) in the rat was characterized by high bioavailability (90%) and long plasma half-life (11.7 hr) with low clearance (0.4 L/hr/kg). In the dog, the PK profiles (2 mg/kg, p.o.) also showed long plasma half-life (17.9hr) with low clearance (0.5 L/hr/kg), and the bioavailability of 60%. The inhibition of CJ-11668 in five different cytochrome P450 isozymes (1A2, 2C9, 2C19, 2D6 and 3A4) was determined in vitro and had observed no significant effect. When CJ-11668 was incubated with liver microsomes for 1hr, the parent drug was remained 68%. The protein binding in human and rat serum exhibited 98% and 96%, respectively. In conclusion, these results suggest that CJ-11668 have a good therapeutic potential for inflammation and pain in human arthritis owing to its long acting pharmacokinetic profiles.

[PA1-34] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Intracellular Ca^{2+} release mediates apoptosis induced by ascorbic acid (vitamin C) in HepG2 human hepatoma cells

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Ascorbic acid (vitamin C) has been shown to have anti-cancer actions. However, the exact mechanism of this action is not fully understood. In this study we investigated the possible mechanism of anti-cancer action of ascorbic acid in HepG2 human hepatoblastoma cells. Ascorbic acid induced apoptotic cell death in a dose-dependent manner in the HepG2 cells, assessed by the flow cytometric analysis of hypodiploid nuclei stained with propidium iodide. In addition, ascorbic acid increased intracellular Ca^{2+} concentration, whereas the level of reactive oxygen species was not significantly changed, suggesting that ascorbic acid may not alter cellular redox potential in the cells. Ascorbic acid-induced increased intracellular Ca^{2+} was not significantly altered by EGTA, an extracellular Ca^{2+} chelator, whereas dantrolene, an intracellular Ca^{2+} release blocker, completely blocked the action of ascorbic acid. Furthermore, U-73122 and manolide, phospholipase C (PLC) inhibitors, effectively prevented the ascorbic acid-induced intracellular Ca^{2+} increase. Furthermore, Ascorbic acid-induced apoptosis was also significantly suppressed by treatment with dantrolene and these PLC inhibitors. Collectively, these results suggest that ascorbic acid induced apoptosis in HepG2 cells and that PLC- IP_3 -intracellular Ca^{2+} signal may mediate the apoptotic action of ascorbic acid.

[PA1-35] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Acanthoic acid blocks production of pro-inflammatory mediators by inhibiting the ERK activation in trypsin-stimulated human leukemic mast cells