

transferase. Given that oltipraz activates C/EBP β for gene transactivation and that the putative C/EBP binding site is located in the CYP1A1 promoter region, this study investigated the effect of oltipraz on CYP1A1 induction by 3-methylcholanthrene (3-MC). 3-MC induced CYP1A1 in H4IIE cells in a time- and concentration-dependent manner. Gel shift analysis showed that 3-MC increased the band intensity of protein binding to the XRE. Immunocompetition analysis verified the specificity of AhR-XRE binding. Oltipraz (30 μ M) induced CYP1A1 and CYP1A1 promoter-luciferase gene and increased AhR DNA binding activity, which were 10-20% of those in 3-MC (100 nM)-treated cells. However, AhR-XRE binding was not increased after 10 μ M oltipraz treatment. Oltipraz (10 μ M) significantly inhibited CYP1A1 and CYP1A1-luciferase gene induction by 3-MC with no increase in AhR DNA binding. Oltipraz enhanced protein binding to the C/EBP binding site in the gene promoter and the binding complex comprised of C/EBP β and partly C/EBP δ . Overexpression of dominant-negative mutant C/EBP significantly abolished the ability of oltipraz to suppress 3-MC-inducible CYP1A1 and CYP1A1-reporter gene expression. Consistently, C/EBP β overexpression blocked CYP1A1-reporter gene induction by 3-MC. These results provided evidence that oltipraz suppresses 3-MC induction of the CYP1A1 gene expression and that activation of C/EBP β by oltipraz contributes to suppression of 3-MC-inducible AhR-mediated CYP1A1 expression.

[PA1-29] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Anti-stress effect of Archoke juice in ICR mice.

Kim M.K., Han J.S., Park E.Y., Han S.W., Yu K.Y., Tan Blendyl, Cheong Jae Hoon^o

Department of Pharmacy, Samyuk University and, Department of Chemistry, Samyuk University

High-dose extracts from artichoke leaves are traditionally used for treatment of stress related disorder, that is, hepatic disease, dyspeptic disorder, hyperlipidemic disorder and diuretic disorder. The aim of this study was to investigate anti-stress effects of Artichoke extract (Archoke juice produced from Choa company). The experiments were performed with the use of young (6-8 weeks of age) male mice of ICR strain weighing between 20 and 25 g at the time of first treatment with Archoke juice. They were grouped normal, control, Ginseng, diazepam and Archoke juice group. The normal ones were provide normal water and not exposed to stress. The control ones were provide normal water and exposed to stress. Ginseng, diazepam and Archoke juice ones were provide Ginseng extract 0.01%, diazepam 0.005% and Archoke juice 5% containing water for 12 days and exposed to stress for 5 days. They were stressed by immobilization for 30 minutes and electro-shock (1mA/20 secs) for 5 minutes. At first, they were pretreated with Ginseng extract, diazepam and Archoke juice for 7 days, and followed by the treatments in combination with the exposure to stress for 5 days. We recorded stress related behavioral changes of experimental animals induced by over stress using Etho-vision system. Smelling and grooming activity, plus maze moved distance and rearing, and Y-maze moved distance decreased by stress were increased by treatment of Archoke juice. Freezing activity, plus maze-staying time in closed area increased by stress were decreased by treatment of Archoke juice. But total activity and activities of face washing, burrowing and rearing were not significantly changed although there were recovering trends from stress induced behavioral change. These results suggest that Artichoke protect partially the living organism from stress attack in some case.

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

Antifibrotic and Antioxidative Effect of Solanum lycopersicum in Liver fibrosis (Cirrhosis) induced Rats

Kim Kiyoung*,^{#o}, Oh Semi*, Kim Jinsook**, Somasundaram Rajan##, Ruehl Martin##, Matthes Burkhard[^]

**,# Dept. of Pathology, Medical School and *Professional Graduate School of Oriental Medicine, Wonkwang University, Iksan, Korea, * Professional Graduate School of Oriental Medicine, Wonkwang University,*

*** Dept. of Herbal Pharmaceutical Develop, Institut of Oriental Medicine, Seoul, Korea, ## Gastroenterologie/ Infektiologie/Rheumatologie/Liver Research, Universitaetsklinikum der Charite Universitaetsmedizin Berlin, Germany, ^ Forschungsinstitut Havelhoehe, Berlin, Germany*

Introduction: Liver fibrosis is defined unbalance of collagen metabolism, especially a stimulation of collagen

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), malondialdehyde (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.

Kim Eun-Joo, Seo Joung-Wook, Choi Gyu-Kap, Park Eun-Kyung, Kim Ki-Suk, Shin Won-Ho, Han Sang-Seop
Korea Institute of Toxicology, KRRICT

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

Lim Dong-Yoon^o, Lee Eun-Sook

Laboratory of Pharmacology, College of Medicine, Chosun University

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