ZR-75-1 human breast cancer cells to study the mechanism of action of PAHs

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Recent industrial society has human widely exposed to PAHs that are comming from the incomplete combustion of organic material as widespread environment contaminants. Biological activities of PAHs are not known although PAHs are considered as carcinogens. PAHs in the mammalian cells affect CYP1A1 gene expression as well as other phase II drug metabolizing enzymes as UDPGTT, N-MOR etc. The mechanism of action of PAHs has been studied extensively; however it is not clear how PAHs turn on CYP1A1 in human breast cancer.

Our laboratory have been studied the effect of PAHs in the human breast cancer cell line MCF7. In this study, we examined the ZR-75-1 human breast cancer cells as a new system to evaluate bioactivity of PAHs. ZR-75-1 human breast cancer line has been established from the breast cancer patient, has estrogen receptors and progesteron receptors. We have been able to establish long term culture system of this cell then used for the study to observe the effect of PAHs. We demonstrate that PAHs induced the transcription of an aryl hydrocarbon responsive reporter vector containing the CYP1A1 promoter and 7-ethoxyresolufin-O-deethylase(EROD) activity of CYP1A1 enzyme in a concentration-dependant manner. RT-PCR analyses indicated that PAHs significantly up-regulate the constitutive level of CYP1A1 mRNA. Apparently, ZR-75-1 cells have Aryl hydrocarbon receptors, therefore it would be good experimental tool to study the cross-talk between PAHs and steroid actions.

The Screening of Hepatic Functional Improvement, Liver Protection and Antifibrotic Effect from Dried Extracts of Concha Cipangopaludinae

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Oxidative stress and its consequent lipid peroxidation exert harmful effects, which have been currently involved in the generation of carbon tetrachloride(CCl4)-induced fibrosis(cirrhosis). In this study, it was investigated whether dried extract of Concha Cipangopaludinae: CC is liver functional improvement, antioxidative and antifibrotic effect under the liver fibrotic(cirrhotic) condition by CCl4 administration. The female Sprague-Dawley rats were divided into 3 groups(Normal: AC: AC-CC), and were observed for 3 weeks. Except for normal group, the rats rendered fibrotic(cirrhotic) by CCl4 administration(0.8ml/rat/week) for 3 weeks. And the prepared CC was treated p. o. 2ml/day/rats in 3 weeks for AC-CC groups. At the time of sacrifice, the liver, kidney, spleen were weighted and the ratio of organ weight/body weight was calculated. The MDA, the hyp and biochemical parameters(AST, ALT, ALP, t-bili) were measured in sera and liver tissue of rats. In the result, the strong yellow color of urine was observed in all CCl4-treated group compared with in normal group but jaundice didn't appeared in CCl4-treated group. Also, mortality of CCl4-treated group during 3 weeks of observation time is very low(<13%). The ratio of liver/body as well as the weight of liver in CCl4-treated rats significantly increased compared with that in normal group(p<0.001). The level of clinical parameters in sera of all liver fibrosis(cirrhosis) developed rats were significantly higher than in normal group(p<0.001 ~ 0.05). Especially the value of BUN, ALP, t-bilirubin in AC-CC group showed 20.9%, 19.6%, 47.9% lower than that in AC group. The content of hyp in CCl4-treated rats was significantly higher than in normal group(p<0.001 ~ 0.05), and showed 12.2% lower value in the AC-CC group than in AC group(p<0.05). The product of lipid peroxidation(MDA) in sera and liver tissue significantly increased under the fibrotic(cirrhotic) condition(p<0.001 ~ 0.05). Especially the MDA value of AC-CC group in sera significantly 46.5% decreased compared with that of AC group(p<0.05), and the MDA value of AC-CC in liver tissue showed 21.4% lower than that of AC group. In the histological change, the excessive lipid droplet, septum formation, lysis of cytoplasm and crushed down of nucleus were observed in CCl4-treated group compared with in normal group. In conclusion, Concha Cipangopaludinae can be improved hepatic function, and may be have effect of liver protection and antifibrosis.
Chronic exposure of nicotine modulate the expressions of cerebellar glial glutamate transporters in rats

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To study the expressions of glutamate transporter subtypes in cerebellar astrocytes following the chronic exposure of nicotine from mating, rats were treated with nicotine (25 ppm) from the beginning of mating through drinking water. After delivery, each group was divided into two groups. Groups were exposed to either distilled water or nicotine. From 7 day-old pups at each group, cerebellar astrocytes were prepared. Ten days after culture, the expressions of glutamate transporter subtypes (GLAST and GLT-1) were determined using immunochemistry and immunoblot. In addition, the developmental expressions of glutamate transporter subtypes in cerebellum were also determined from 2, 4 and 8 weeks-old rats during the continuous treatments. The expressions of GLAST in cultured astrocytes from either pre- or post-natally exposed groups were higher, but those from continuously exposed group were lower than those from control. The expressions of GLT-1 were higher in all nicotine–treated group, especially in continuously treated group. The expressions of cerebellar GLAST and GLT-1 in all nicotine–treated groups were lower than in the control group at each age using immunochemistry. However the expressions of cerebellar GLT-1 in all nicotine–treated groups were higher than those in the control except 8 weeks of continuously treated group using immunoblot. These results indicate that the expressions of glial glutamate transporters are differently altered depending on the initial exposure time and periods of nicotine and nicotine exposure during gestation have persistent effects on glial cells.

Safety pharmacology study of AS2–006A, a new wound healing drug


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The safety pharmacological core battery studies of AS2–006A, a newly developed wound healing drug. The studies were investigated according to the ICH S7A guidelines in compliance with Good Laboratory Practice(GLP) Regulations. The doses given were 0, 100, 300 and 1000 mg/kg and drugs were administered subcutaneously. The animals used for this study were mice, rats and guinea pigs. AS2–006A showed no effects on the central nervous system such as motor activity, behavioral changes, coordination, sensory/motor reflex responses and body temperature, no effects on blood pressure(BP), heart rate(HR), and EOG profiles and respiratory system. It was concluded that AS2–006A possess no general pharmacological effects at all doses tested.

The toxicity of Aceporol 460 as a novel high loading capacity solubilizer of paclitaxel

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Previously, we reported a novel polymeric micellar solubilizer, Aceporol 330, that showed relatively low toxic effects when it was compared with that of Cremophor EL which is currently being used for paclitaxel. In this study, we have developed a new micellar solubilizer, Aceporol 460, that has 3–4 times higher loading capacity for paclitaxel than Aceporol 330. The single–dose and the repeated–dose toxicity of Aceporol 460 were evaluated in ICR mice. For single dose toxicity test, male and female mice were randomly assigned to one of five study groups to receive, and injected intravenously with dosages of 0, 3, 4mL Cremophor EL/kg body weight, and 3, 4mL Aceporol 460/kg body weight, respectively. In both male and female mice, LD50 for Aceporol 460 can not be