CANCER CELL-LINES AND NORMAL KIDNEY CELLS

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We recently synthesized a new platinum(II) complex analog containing *cis*-1,2-diaminocyclohexane (DACH) as a carrier ligand and 1,3-dichloropropane(DCP) as a leaving group.
Our platinum-based drug discovery program has been aimed at developing drugs capable of diminishing toxicity and improving selective cytotoxicity. These platinum(II) complex [Pt(II)(*cis*-DACH)(DCP);PC] was synthesized and characterized by its high performance liquid chromatography, elemental analysis and various spectroscopic techniques(IR, NMR). PC showed acceptable and significant *in vitro* antitumor actvity against SKOV-3 and NIH-OVCAR human ovarian cancer cells as compared with that of cisplatin. The cytotoxicity of PC against primary cultured proximal tubular cells of rabbit kidney determined using the MTT assaying techniques and thymidine uptake tests were found to be quite less than those of cisplatin. Based on the these results, this novel platinum complex appear to be a valuable lead compound with high efficacy and low nephrotoxicity.

[PA4-9] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

The single dosing acute toxicity tests for newly developed surfactants for pacritaxel

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The commercially available pacritaxel product, Taxol is currently formulated in a vehicle containing approximately a 1:1 v/v mixture of polyoxyethylated castor oil (Cremophor EL) and ethanol. Cremophor EL, a commonly used surfactant for lipophilic compounds, has been associated with many issues, such as adverse effects particularly following rapid administration, stability with the possibility for drug precipitation upon dilution, and filtering requirements. It is thus apparent that there is a need for new surfactant of paclitaxel that are efficacious and less toxic than the commercial product. We have tried to develop such a new surfactant for pacritaxel, and performed the hemolysis test for chemicals which passed the paclitaxel-stabilizing test. 5 Chemicals showing relatively low hemolytic effects were tested for a single dosing toxicity test. LD50 for these chemicals were not achieved even at the maximal administrable dose, 5ml/Kg, at which Cremophor EL reached LD50. According to data based on body weight, mortality, dissection, hemological test, and biochemical test, these chemicals exhibited much more reduced toxicity than Cremophor EL.[This study has been supported from the MHW]

[PA4-10] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Developmental immunotoxicity of di(n-butyl) phthalate in fetal rat

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Some of endocrine disruptors have sexual hormone like effects. These exogenous substances were suspected of immunodeficiency, which have been increasingly reported in many species. Phthalate esters are kinds of endocrine disruptors. Perinatal exposure to di(n-butyl) phthalate(DBP) have been reported to impair the androgen-dependent development of the male reproductive tract malformations in rat. Therefore, the immunomodulatory effect of DBP was investigated in the developing immune

system of fetal Sprague-Dawley rats in gestational period. Timed-bred pregnant SD rat were given 0, 250, 500, 750 mg/kg/day body weight by gavage once a day from gestational day(GD) 5 to 18. On GD19 or GD22/postnatal day one(PD1), the dams were euthanized, and their offspring were examined for organ weight and thymus phenotypic alteration. GD19 fetuses from the 750 mg DBP/kg/day maternal exposure group exhibited decreases in body weight. The spleen/body weight ratios were reduced in GD19 fetuses from the dams exposed to 500 and 750 mg DBP/kg/day. There were no significant changes in thymus and spleen cellularities though these cellularities showed a tendency to decrease in a dose dependent way. In the DBP-exsposed GD22/PD1 offspring, the body weights, the relative organ weights and the cellularities did not exhibit alteration. Additionally, the percentages of $CD3^+$ ($CD4^+CD8^+$, $CD4^+CD8^-$, $CD4^-CD8^+$, $CD4^-CD8^-$) and $CD3^-$($CD4^+CD8^+$, $CD4^+CD8^-$, $CD4^-CD8^+$, $CD4^-CD8^-$) thymocyte subsets also were not changed in all DBP-treated group. The mitogenic response of splenic T cell to Con A and that of B cells to LPS was decreased in all DBP-exposed GD22/PD1 offspring.

[PA4-11] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Structure and estrogenic activity relationship of flavonoids using ERE-Luc Reporter and E-screening assay

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Flavonoids are polyphenolic compounds that occur ubiquitously in foods of plant origin. Many flavonoids have been shown to mimic the biological effects of 17b-estradiol (E2). They can bind the estrogen receptor and mediate transcription of estrogen response gene.
In this study, we determined 5'-ERE-regulated transactivation and cell proliferation in MCF-7 cells by luciferase assay and SRB assay, respectively. Based on dose-response curve, we calculated EC50 and EEQ (17b-estradiol equivalent concentration).
ERE-Luc reporter gene assay system use MCF-7 cell lines stably transfected with pERE-Luc construct, which consists of three ERE (estrogen response element) and luciferase reporter gene. This assay is based on the estrogen receptor mediated mechanism of action and reporter gene expression is accumulation of a molecular cascade of event involved in receptor activation. E2 and many flavonoids induced luciferase activity in dose dependent manner. And there were some relationship between structure and activity.
To determine cell proliferative effect of chemicals, E-screening assay was performed. E2 increased SRB reading 20-30 folds over that of control and this effect was inhibited by tamoxifen treatment. When we tested a large series of flavonoids in this system, 7 compounds elicited the significant cell proliferative effect whereas remaining flavonoids were weak estrogenic or devoid of activity. [this study has been supported by KFDA]

[PA4-12] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Effect of Oxyresveratrol on Inflammatory Responses

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Mori Cortex is a dried root bark of Morus alba L. (Moraceae) and has been known as an important tranditional medicine, commonly used for antitussive, antiinflammatory, diuresis, and pyretolysis. However, the active components of Morus alba L. have not yet been identified. The present study was