[PA4-6] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

IN VITRO CYTOTOXIC ACTIVITIES OF NOVEL PLATINUM(II) COMPLEX ON GASTRIC CANCER CELL-LINES AND NORMAL KIDNEY CELLS

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Platinum(II) coordination complex(cisplatin) han been currently used as one of the most effective compounds in the treatment of various solid tumors. However, its use has been limited by severe side effects such as renal toxicity. Our platinum-based drug discovery program han been aimed at developing drugs capable of diminishing toxicity and improving selective cytotoxicity. We recently synthesized a new platinum(II) complex analog(PC) containing *cis*-1,2-diaminocyclohexane(DACH) as a carrier ligand and 1,3-dichloropropane(DCP) as a leaving group. A new series of Pt(II)(*cis*-DACH)(DCP); PC was evaluated its cytotoxic activity on cancer cells and normal kidney tissues. The new platinum complex demonstrated high efficacy in the cytotoxicity on the human gastric cancer cell-lines(MKN-45/P, MKN-45/ADM and MKN-45/CDDP). The cytotoxicities of PC were found quite less than those of cisplatin in normal rabbit proximal renal tubular cells, human cortical cells and tissues of normal kidney using MTT assay, [^{3}H]-thymidine uptake and glucose consumption tests. Based on the result, Pt(II)(*cis*-DACH)(DCP) was considered as a better valuable lead compound for improving antitumor activity with low nephrotoxicities in the development of a new clinically available anticancer chemotherapeutic agent.

[PA4-7] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Down-regulation of c-fos expression, AP-1 activation and p53-p21 response pathway by glycolic acid in cultured HaCaT cells

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Glycolic acid, an alpha-hydroxy acid derived from fruits and milk sugars, has been commonly used as a cosmetic ingredient since it was known to have photo-protective and anti-inflammatory effects, and anti-oxidant effect on UVB-irradiated skin. However, little has been known about functional role of glycolic acid on UV-induced skin tumorigenesis. We previously found that glycolic acid reduced UV-induced skin tumor development in hairless mouse. In this study we extended our study to investigate anti-tumor promoting mechanism of glycolic acid on the UV-induced skin carcinogenesis. Changes in the UV-induced cytotoxicity, apoptosis, expression of apoptosis-regulatory genes and c-fos, and activation of transcription factor AP-1 were examined in cultured HaCaT cells. Glycolic acid treatment attenuated UV-induced cytotoxicity as well as apoptosis. Glycolic acid also caused an attenuation of UV-induced expression of c-fos and the activation of transciption factor AP-1 as well as down-regulation of P53 and P21. These results suggest that glycolic acid may exert inhibitory effect on the UVB-induced tumorigenesis by down regulation of c-fos expression (AP-1 activation) in addition to the p53-p21 response pathway.

[PA4-8] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

SELECTIVE CYTOTOXICITIES OF NOVEL PLATINUM(II) COMPLEX ON OVARIAN

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