

[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) has 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 has 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, [³H]-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 transcription 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