[PA1-1] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Compound SY006, Stilbene Derivative as a Potent Inhibitor of Melanin Production

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Traditionally, the Mori cortex has been used for skin whitening purpose. One of the ingredients of Mori cortex that are responsible for the whitening activity is believe to be oxyresveratrol, which belong to the stilbene group. Oxyresveratrol has been reported to have strong tyrosinase inhibitory effects than kojic acid, which is widely used for manufacturing the whitening cosmetics recently. However not much amount of oxyresveratrol in the Mori cortex is limited, and its synthetic approach is not well established. Even in the synthetic aspect, the manufacturing of the whitening ingredient has many difficulties because oxyresveratrol was has to be passed through many synthetic steps. Therefore an attempt to search for alternative materials like stilbene derivatives, which have high bioactivities and can be easily obtained, is warranted. In this work the compound SY 006, which is a stilbene derivative, was synthesized by single step process. The compound 006 exibited inhibitory effects on tyrosinase that is involved in melanin biosynthesis, UV blocking effect, and SOD-like activity. These results suggested that compound SY 006 might be used as a skin whitening agent.

[PA1-2] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Doxorubicin inhibits the production of NO by colon tumor cells

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Doxorubicin is an active and broad spectrum chemotherapeutic agent. The relationship between doxorubicin treatment and the enzymatic activity of eNOS is well characterized. However, little is known about the effects of adriamycin on the expression of iNOS. In the present study, we characterized the effects of doxorubicin on nitric oxide (NO) production by colorectal cancer cells, DLD-1. IFN-γincreased the production of NO and pretreatment of doxorubicin inhibited the production of NO in response to IFN-γin a dose dependent manner. The increased expressions of iNOS mRNA and protein by IFN-γwere completely blocked by doxorubicin without affecting the iNOS mRNA stability. However,doxorubicin activated nuclear factor-kB in response to IFN-γ. In summary, doxorubicin inhibited the production of NO by DLD-1 cells which is not linked to well known transcription factor, NF-kB. These data suggest that inhibition of nitric oxide biosynthesis in colon tumor cells by doxorubicin may, at least in part, the efficacy of this antitumor agent.

[PA1-3] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Enhanced rate of DNA repair and expression of anti -apoptotic protein in cisplatin-resistant K562 cells

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cis-Diamminedichloroplatinum(II) (cisplatin or cis-DDP) is one of the most widely used cytotoxic anticancer drugs. The therapeutic effect is believed to arise from consequence of cisplat in binding to DNA. However, its clinincal efficacy is often limited due to the induction of secondary resistance. Classical anti-cancer drug resistance mechanism is frequently associated with overexpression of P-glycoprotein, a member of the ATP binding cassette family of transmembrane transport proteins capable of expelling certain cytotoxic drugs and maintaining their non-lethal intracellular level. Recently the finding that acquired multidrug resistance occurs in the absence of ATP binding cassette family protein overexpression has provided support for the existence of other mechanisms. We established cisplatin-resistant cell lines to study mechanisms of cisplatin resistance. Acquired resistant cells were obtained by growing K562 cells in stepwise increasing concentrations of cisplatin to produce resistant cell lines (K562/CDDP). The resistant cells represent resistant factor of 4.87. No differences were noted on drug accumulation between cisplatin resistant and sensitive cells. In addition, the levels of cisplatin bound to DNA in K562/CDDP decreased more rapidly than sensitive cells, suggesting that increased DNA repair capacity plays a partial role in the acquired resistance. Additionally, K562/CDDP cells were more resistant to apoptosis. DNA fragmentation and Western blot analysis showed that K562/CDDP cells had significantly more resistant to proteolytic activation of caspase-3 with higher levels of the anti-apoptotic protein Bcl-2. These results suggest that blocking of apoptosis through the suppression caspase-3 activation in K562 cells may be responsible for cisplatin resistance.

[PA1-4] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Comparison of antitumor activity between oxaliplatin and cisplatin given alone and in combination with 5-fluorouracil in human gastric cancer cells with different mismatch repair enzyme status.

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Oxaliplatin (LOHP) approved for metastatic colorectal cancers showed activity against various tumors including cisplatin (CDDP)-resistant tumors. Although its activity against gastric cancer has been suggested, no preclinical data are available to support its clinical application. We evaluated antitumor activity of LOHP alone and in combination with 5-FU and then compared with that of CDDP in five human gastric cancer cell lines *in vitro*. LOHP showed cytotoxicity similar to CDDP as determined by XTT assay with IC_{50} ranging from 1.58 to 17.0㎍/㎖. Deficiency of mismatch repair (MMR) enzyme causes resistance to many cytotoxic drugs including CDDP and 5-FU. SNU-1 cells are hMLH1-deficient due to a non-sense mutation resulting in protein truncation. However, no significant resistance to CDDP was observed in SNU-1 when compared with MKN-45 cells expressing hMLH1 abundantly. When combined with 5-FU, synergistic interaction of both LOHP and CDDP was dependent on cell line, dose ratio, and fraction affected. In MKN-45, both LOHP+5-FU and CDDP+5-FU showed similar synergistic interaction profiles. In MMR deficient-SNU-1, however, the synergism of LOHP+5-FU was greater than that of CDDP+5-FU. In summary, LOHP alone was as active as CDDP against human gastric cancer cells and its synergistic interaction with 5-FU was superior to that of CDDP. The present study indicates that LOHP may be a promising agent not only as monotherapy but also in combination with 5-FU against human gastric cancers.

[PA1-5] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Mechanism of Epibatidine-Induced Catecholamine Secretion in the Perfused Rat Adrenal Gland

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