stereochemistry of C3' position, starting from chiral amino acid, (-)-L-serine methyl ester. In this meeting, the asymmetric synthesis of one of the enantiomers, (2S,4R)-LJ-45 and its anti-HBV activity will be discussed in detail.

[PD1-40] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Construction of Indole Library for Serotonin Related Drugs

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There is an ample hope for the success of hetero cyclic compounds, known to have pharmacological activity and comparatively low chiral carbon, passed great candidate of drug. Indole compounds known as serotonin related drugs have infinite adaptation of different physiological activity.
The study developed linker that gives variety to hetero cycles and comes with swelling as choosing method to use traceless linker. Construction of whole library synthesized compounds designed linker and benzene ring are linked by combination with silicone and made maker it into hydrazine gave variety of ketone compounds. The problem of swelling was eliminated by inducing silicon with the lithiation of bromoaniline and oxygen in the middle of the linker.

[PD1-41] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

CoMFA Analysis of 2-Alkylureido-1-phenyl propanols for Cytotoxicity

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The structure of 2-alkylureido-1-phenyl propanol derivatives have been studied and optimized for their cytotoxic activity. The three dimensional quantitative structure activity relationship (3D-QSAR) was investigated using comparative molecular field analysis (CoMFA). The result suggested that electrostatic and steric factors of 2-alkylureido-1-phenyl propanol derivatives were correlated well with cytotoxic activity.

[PD1-42] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Novel Platinum(IV) compound, K101, having octahedral structure as Anticancer agent II-Cell signaling mechanism of Apoptosis in Human colon cancer cell line

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Chemotherapeutic drugs comprising cisplatin cause DNA damage and kill cancer cells mainly by apoptosis. In particular, the study of apoptosis induced by cisplatin became active research area to understand the molecular basis of CDDP-mediated apoptosis and to improve therapeutic benefits. Recently, novel Pt(IV) compound, trans,cis-[Pt(acetato)2Cl2(1,4-butanediamine)] (K101) was synthesized and characterized its octahedral structure. Anticancer activity of K101 was screened in vitro and in vivo, already. In this study, we sought to investigate the signalling mechanism of novel Pt(IV) compound-induced apoptosis. As the results of FACS analysis and immunoblotting, we confirmed several observations : 1) novel Pt(IV) complex (K101) increased Fas, p53 and ERK expression in HCT

116 colon cell line. 2) U0126, MEK inhibitor, decreased ERK and p53 response to K101, 3) ERK was up-stream regulator of the p53 sensitivity to K101. 4) in both U0126 and K101 treated cancer cells, cell death rate incresed relative to U0126 untreated cells. These results suggest that novel Pt(IV) complex-induced apotosis in colon cell line is mediated by Fas signalling system as well as ERK / p53 pathway.

[PD1-43] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

In vitro antitumor activity and nephrotoxicity of a new platinum(II) complex on cancer cell-lines and normal kidney cells

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Our platinum-based drug discovery program has been aimed at developing drugs capable of diminishing toxicity and improving selective cytotoxicity. We recently synthesize new platinum(II) complex analog containing trans-l-1,2-diaminocyclohexane(DACH) as a carrier ligand and glycolic acid(GA) as a leaving group. This platinum(II) coordination complex {Pt(II)(trans-l-DACH)(GA)} are synthesized and characterized by its high performance liquid chromatography, elemental analysis and various spectroscopic techniques (IR/NMR).PC shows acceptable and significant in vitro antitumor activity against cancer cell lines as compared with that of cisplatin. The cytotoxicity of this platinum(II) coordination complex against primary cultured proximal tubular cells of rabbit kidney and human renal cortical tissues was determined by MTT assay and the [3H]-thymidine uptake tests, and found to be quite less than those of cisplatin.

[PD1-44] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Preparation of 1,4-Oxaselenins from AgNO3/LDA-Assisted Reaction of 3-Selena-4-pentyn-1-one as Potential Antitumor Agents

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University of Ulsan, Korea and Gifu University, Japan

1,4-Oxaselenins were synthesized from 3-selena-4-pentyn-1-ones by the use of AgNO3 and LDA. Obtained 2-(4-chlorophenyl)-6-phenyl-1,4-oxaselenin indicated an inhibitory effect against the proliferation of human cancer cells revealing a typical apoptosis characteristics.

[PD1-45] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Successful Virtual Screening and Rational Design of New Drug Leads

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Virtual screening of chemical databases is a fast emerging technique and an effective alternative to