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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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

high-throughput screening (HTS) in drug discovery. It mainly consists of handling and screening of large chemical databases, in order to reduce the number of chemicals for which prediction of a specific biological activity has been previously made using clustering and similarity searching. After this process, other molecular modeling techniques, such as docking and molecular superposition can be applied to the selected chemicals. These techniques involve using computers to dock each chemical from the database to the active site of a drug target, to identify new drug leads through evaluation of the chemical's binding modes.
We have performed virtual screening of Chemical Diversity Inc. (ChemDiv) database of 300,000 commercially available chemicals to identify the agonists of *Peroxisome Proliferator-Activated Receptors Gamma* (PPAR-γ). The PPAR-γ □, receptor is an attractive target for anti-diabetic therapy. Among the chemicals identified through our virtual screening, four chemicals activated PPAR-γ □, in RAW264.7 cells. These activities were comparable to that of *Troglitazone*, a known PPAR-γ agonist.
This result demonstrates the validity of the virtual screening as a tool for identifying drug leads and the feasibility of this technique to drug targets such as PPAR-γ □, receptor.

[PD1-46] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Inhibitory Effects of Pyridyloxyphenoxy- or Phenoxylphenoxy alkanoic Acid Derivatives on Rat Lens Aldose reductase and Rat Platelet Aggregation

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Thirty six pyridyloxyphenoxy- or phenoxylphenoxyalkanoic acid derivatives synthesized were evaluated for their inhibitory effects on rat lens aldose reductase (RLAR) and rat platelet aggregation *in vitro*. Among compounds tested, 2-(4'-(2'',6''-dichloro-3''-methylphenoxyl)-2'-(nitrophenoxy)propanoic acid (**3**, IC_{50} = 3.0 μM), one of phenoxylphenoxyalkanoic acid derivatives was found to exhibit the most potent inhibition of RLAR, its inhibitory potency, being two times stronger than that of tetramethyleneglutarate, a positive reference drug(IC_{50} = 6.1μM). Inhibitory activities of this compound against rat platelet aggregation induced by ADP and collagen as indicated by IC_{50} values were 93 μg/ml and 32 μg/ml,respectively, whereas, the IC_{50} values of aspirin, a positive drug, at the same conditions, were 150 μg/ml and 47 μg/ml, respectively.

[PD1-47] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Heterocyclic bibenzimidazole derivatives as topoisomerase I poisons

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Topoisomerase I poisons are recognized as an attractive class of pharmacological agents, which have the potential to exhibit antineoplastic activity as well as selective antibacterial, antifungal, antiprotozoal, anthelmintic, and antiviral activity. Several benzimidazole derivatives, including Hoechst 33342, and terbenzimidazoles are unique classes of topoisomerase poisons. A series of 2'-heterocyclic derivatives of 5-phenyl-2,5'-1H-bibenzimidazoles were evaluated for their cytotoxicity and their ability to poison topoisomerase I. The topo I poisoning activity was associated with 2'-derivatives that possessed a hydrogen atom capable of hydrogen bond formation, suggesting that the interatomic distance between such hydrogen atoms and the heteroatoms on the adjacent benzimidazole influence activity.