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

Lim SoonSung, Shin KukHyun, Jung SangHoon, Lee SangHyun, Lee YeonSil, Shin KyeJung[1], Kim DongChan[1], Park SangWoo[1]

Natural Products Research Institute, Seoul National University, [1]Division of Applied Sciences, Korea Institute of Science and Technology

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

Kim Jung Sun°, Jin Song, Liu Leroy, LaVoie Edmond J.

Dept. of Biotechnology, Dongseo University , College of Pharmacy, Rutgers University and UMDNJ, New Jersey, USA

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.