[PD1-1] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

3D-QSAR Study of Isoquinoline Analogs and Designing New Topoisomerase I Inhibitors

Kim EK°, Lee CH, Cho WJ

전남대학교 약학대학

Recently, we found that a 3-arylisoquinoline derivative, 3-(2-methylphenyl)-6-methylisoquinolinamine, exhibited very strong topoisomerase I inhibition activity. This finding attracted us to explore the relationship between 3-arylisoquinoline derivative and topoisomerase I. We performed the 3D-QSAR study using both comparative molecular field analysis (CoMFA) and LeapFrog on the basis of recently determined topoisomerase I-DNA crystal structure and 3-arylisoquinoline derivatives as topoisomerase I inhibitors.
CoMFA is a ligand-based drug design method and could be a powerful tool for designing new ligands when the receptor site is unrecognized. On the other hand, LeapFrog is a receptor-based drug design method and it is useful when the structure of receptor is determined.
CoMFA procedure was performed with a set of 53 3-arylisoquinoline derivatives for A-549 tumor ce line (human lung cancer), and resulted in a good cross-validated R^2 value (0.837). By using this result we could perform LeapFrog with topoisomerase I-DNA complex structure. A synthesis of 3-arylisoquinoline derivatives, CoMFA, and LeapFrog study will be discussed.

[PD1-2] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis of 2-(allylthio)pyrazine to confirm the structure of drug metabolite

Choi BE , Kim DH*, Jeong JH

Department of Pharmaceutical Science, College of Pharmacy,Kyung Hee University, *Doping contro center,Korea Institute of Science and Technology

Organosulfur compounds have been found to possess protective effects against experimental carcinogenesis and mutagenesis. A series of compounds have been synthesized with the aim of developing potential chemopreventive organosulfur compounds active against hepatotoxicity and chemical carcinogenesis.
A series of pyrazine derivatives such as 2-(Allylthio)pyrazine(2-AP),which is known as the most effective against toxicants, were prepared as shown in the following scheme.