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Five allylthiopyridazine derivatives were synthesized and their chemoprotective activities were screened by aflatoxin B1 administration. Male Sprague-Dawley rat were treated with five allylthiopyridazine derivatives at the daily oral doses of 50 mg/kg for 10 consecutive days, and during this period three repeated doeses of aflatoxin B1(1.0 mg/kg, i.p.) injected. The group of aflatoxin B1 (1.0 mg/kg, 3 times) administration showed the striking increase in body and liver weight, whereas the body and liver weight of allylthiopyridazine derivatives was normal as compared with vehicle. And the allylthiopyridazine derivatives showed remarkable inhibition for the AST and ALT activities of rat serum exposed by aflatoxin B1 toxin. But propoxy substituent compound, K18, did not show any activity, whereas other four allylthiopyridazine derivatives, K6, K8, K16 and K17 showed strong hepatoprotective activity.

[PD1-29] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Modeling of Binding Modes and Inhibition Mechanism of Apicidin Derivatives, Histone Deacetylase Inhibitors : A flexible Docking Study

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A novel fungal metabolite, apicidin has growth inhibition and detransforming activity against cancer cells. It is known that the biological activity of apicidin is due to the inhibition of histone deacetylase (HDAC) in low nanomolar concentration. Hydrazone, semicarbazone and carbohydrazone derivative of apicidin were synthesized and characterized in a human HDAC inhibition assay. All compounds have shown IC_{50} values between 0.17 and 0.71 μM, and revealed the HDAC inhibition activity comparable to apicidin.
In this study, we examined a possible mode of interaction between those compounds and HDAC by docking analysis. We conducted flexible docking of each compound into the histone deacetylase-like protein (HDLP) catalytic domain using a FlexX docking program. FlexX binding energy scores of the compounds were analyzed using consensus scoring method (CScore), which combines multiple scoring functions in binding affinity estimation.
The docked models predicted the interactions of the compound with the amino acid residues and Zn^{2+} at the active site of HDLP, and the data obtained from the CScore analysis correlated well with the HDAC inhibitory activity of the apicidin derivatives.

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Diversity of compounds in Korea Chemical Bank

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Korea Chemical Bank project has started as an "infra" supporting the new drug development strategy of high efficiency and low costs. Now Korea Chemical Bank holds 50,000 compounds consigned from the domestic institutions.
We examined the consigned compounds to verify that the compounds have the adequate structure to new drug using Lipinski's rule. As a result, about 95% of compounds are validated as having proper structure for new drug.
And we compared the physical properties and diversity of compounds with the compounds of international compounds supplier(160,000 compounds from ChemDiv and 145,000 compounds from SPECS and BIOSPECS).