3D-QSAR analyses by CoMFA and CoMSIA were conducted on a series of thiazole and triazole analogues with respect to their antifungal activities against *Microsporum gypseum*. A total of twenty analogues were used for the derivation of the 3D-QSAR models (training set). The superposition of the compounds was performed by applying the FlexS with shape-based screening method. The resulting statistical parameters revealed that the CoMFA (q^2= 0.691, r^2= 0.923) and CoMSIA (q^2= 0.590-0.686, r^2= 0.836-0.914) have similar predictability. However, the CoMSIA models were considerably better than the CoMFA ones, since they were obtained with lower number of principal components. Based upon CoMFA and CoMSIA contour maps, the structural regions responsible for the differences in antifungal activity were analyzed with reference to their electrostatic, steric and hydrophobic nature.

[PD1-44] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

CoMFA and CoMSIA 3D QSAR Studies on Pimarane Cyclooxygenase-2 (COX-2) Inhibitors

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In this work, we have conducted 3D-QSAR studies on a series of acanthonic acid derivatives that act as COX-2 inhibitors, using two different methods: comparative molecular field analysis (CoMFA) and comparative molecular similarity indices analysis (CoMSIA). CoMFA and CoMSIA analysis of twenty five pimarane analogues produced good models with high predictive abilities.The CoMSIA model showed slightly improved prediction abilities in comparison with the CoMFA model. It is well revealed that the COX-2 inhibitory activity is influenced by the character of steric, electrostatic, hydrophobic, hydrogen bonding donor, and hydrogen bonding acceptor at C4 linker and C16 of pimarane analogues. These results are consistent with our SAR studies of previous work and provide crucial information in the design and development of new pimarane analogues as anti-inflammatory agents.

[PD1-45] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Synthesis and COX-2 Inhibitory Activities of Rutaecarpine Homologues

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A series of rutaecarpine homologues were prepared from 2,3-polymethylene-4(3*H*)-quinazolinones in 4 steps [i) PhCHO/Ac_2O, ii) O_3, iii) $PhNHNH_2HCl$, and iv) PPA], in which dihedral angles of the two planar aromatic rings (indole and 4(3*H*)-quinazolinone) were controlled in a regular fashion. Their inhibitory activities on COX-1 and COX-2 were evaluated to show that the inhibitory activities were increased with the increase of the length of methylene unit while selectivities on COX-2 decreased leading a loss in trimethylene bridged system.

[PD1-46] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

Highly efficient ortho-fluoro-dimeric cinchona-derived phase-transfer catalysts