[PD1-46] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

The 3D-QSAR study of non-peptide bradykinin antagonists by CoMFA

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Bradykinin is an autocoid related to acute and chronic pain and inflammation. The non-peptide bradykinin antagonists are of interest as novel anti-inflammatory therapeutics. Some active compounds such as FR 173657, LF 160687, and bradyzide were reported very recently. In our search for the new bradykinin antagonists, we designed and synthesized the iminodiacetic acid derivatives having two or three amide bonds and lipophilic ring system in each molecule. Liquid phase combinatorial synthesis using the iminodiacetic acid template gave diverse individual compounds rapidly and efficiently on a 10-50 mg scale.To understand the structural basis for the antibradykinin activity and to guide the design of more potent compounds we performed three-dimensional quantitative activity relationship (3D-QSAR) studies for this series using comparative molecular field analysis (CoMFA) The bradykinin inhibition activity (%) at 0.1 M concentration on the guinea-pig ileum contraction exhibited a strong correlation with steric and electrostatic factors of the molecules. The statistical results of the traning set, cross-validated q2 (0.703) and conventional r2 (0.997) values, gave reliability to the prediction of the antibradykinin activities of this series. The relative contribution of steric and electrostatic field were 33.8% and 47.9% respectively.

[PD1-47] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis of TZD Analogs as PPARγ Specific Ligands

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PPARs (peroxisome proliferator activated receptors) are member of nuclear hormone receptors superfamily. Activations of PPARs upon binding with ligands modulate glucose metabolite, differentiation of adipocyte, inflammation response, and so on. Thiazolidinedione analog is one of the potential antidiabetic drug that binds and activates PPAR selectively and enhances insulin sensitivity. In an effort to develop novel and effective antidiabetic thiazolidindione analogs, we have synthesized tetrahydroquinoline and para-substituted benzene-linked thiazolidinedione analogs by coupling reaction of the hydrophobic segments with hydroxybenzylthiazolidinedione.

[PD1-48] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

The 3D-QSAR Studies on the Indolinones Derivatives of PTKIs: CoMFA& CoMSIA

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The three-dimensional quantitative structure-activity relationship (3D-QSAR) study using the comparative molecular field analysis (CoMFA) was performed on indolinones derivatives as an inhibitor of the protein tyrosine kinase of fibroblast growth factor receptor (FGFR). In the training set, twenty-four indolinone derivatives were aligned based on the indole fragment and the steric and electrostatic fields were included in the analysis. The best predicted model showed the cross-validated coefficient (r^2_{cv}) of 0.804 and non-cross validated coefficient (r^2) of 0.942. The CoMFA study can be used to predict several new inhibitors of the FGFR.

[PD1-49] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Approach to the Total Synthesis of Acanthoside-D

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