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五味子素类抑制**HIV**活性的三维定量构效关系研究

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摘要　建立了五味子活性成分木脂素类和联苯类化合物抑制HIV活性的三维定量构效方程。采用联苯环原子和苯环质心两种叠合方式，并区分联苯化合物的不同构型，共建立了四类CoMSIA模型，其中训练集中联苯类为S构型并叠合联苯环原子建立的 CoMSIA模型相关性最好，交叉验证相关系数q~2为0.71，非交叉验证相关系数r~2 = 0.99，标准偏差SE = 0.051, F = 1000.6。CoMSIA方法采用Gaussian函数计算 场能，并在CoMFA方法的立体和静电场基础上加入疏水场，PLS分析结果更为准确。 该模型三维等势图证实了某些结构和活性规律，如联苯基共面性越好，活性越高，同时给出了苯环上取代基的体积、电性和疏水性要求，为该类化合物的结构改造提 供了依据。

关键词　五味子　木质素　联苯 P　环辛二烯　定量构效关系

分类号　R93

3D-QSAR Study of schizandrins for Anti-HIV Using Comparative Molecular Similarity Indices Analysis

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Abstract The present study constructs a model of three-dimensional quantitative structure and bioactivity of anti-HIV for a Chinese traditional medicine-Schizandrins, by implementing a new 3D-QSAR technique: comparative molecular similarity indices analysis (CoMSIA). Here four models are built based on different form of biphenyl and two aligned methods. The results of PLS analyses indicate that a good 3D- QSAR model can be obtained if biphenyl prefers S form and all the compounds are aligned according to the atoms in biphenyl group. After field expressions in terms of similarity indices in CoMSIA instead of the conventionally used Lennard-Jones and Coulomb-type potentials in CoMFA, the cross-validated q~2 and predictive ability are significantly improved. The CoMSIA coefficient contour plots identify several key features that the torsion angel of two benzene planes is a critical factor for the activity and the substituent at cyclooctadiene is also related to the activity, which are very valuable for designing and optimizing new active structures.

Key words SCHISANDRA CHINENSIS　LIGNIN　DIPHENYL P　CYCLOOCTADIENE　QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIP

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