化学学报 2001 59 (12): 2143-2147 ISSN: 0567-7351 CN: 31-1320/06

异喹啉类化合物抑制肥大细胞脱颗粒活性的**3D-QSAR**研究

陈海峰,李强,曾宝珊,董喜城,袁身刚,陈敏伯,郑崇直,孙仁山,程天民

中国科学院上海有机化学研究所.上海(200032);中国科学院计算机化学开放实 验室.上海(200032);
第三军医大学国家重点学科防原医学教研室全军复合伤研究 所

收稿日期 修回日期 网络版发布日期 接受日期

摘要 对一组抑制肥大细胞脱颗粒的异喹啉类化合物的活性及毒性进行了3D-QSAR研究，采用距离比较法(DISCO)得到了它们的药效团模型，通过选择不同的叠合方式，建立了相关性很好的比较分子力场分析(CoMFA)模型，其交叉验证参数R^2~cv分别为0.654和0.662，非交叉验证的相关系数分别为0.990与0.983，
通过查阅统计量F表，表明活性及毒性模型的置信度都大于99%，显示模型具有较强的预测能力，
并在此基础上进行了新活性先导化合物的设计，得到了预测活性高以及预测毒性低的新结构，
合成实验正在进行之中。

关键词 异喹啉P 比较分子力场分析 药效团 表面活性

分类号 06-39

3D-QSAR study on anti-mast cell degranulation of isoquinoline compounds

Chen Haifeng,Li Qiang,Zeng Baoshan,Dong Xicheng,Yuan Shengang,Chen Minbo,Zheng Chongzhi,Sun Renshan,Cheng Tianmin,Su Yongping,Liu Rongqing
Shanghai Inst Organ Chem., CAS.Shanghai(200032);Lab of Comp Chem, CAS.Shanghai(200032)

Abstract A set of isoquinoline compounds of anti-mast cell degranulation were investigated by using 3D-QSAR. Their pharmacophore model was identified by DISCO program. According to the pharmacophore model, 3D- QSAR models for the activity and toxicity were built respectively by CoMFA. The crossvalidated R^2~cv and the non-crossvalidated R^2 (correlation coefficient) for the structure-activity and structure- toxicity models are 0.654 and 0.662, 0.900 and 0.983 respectively. The confidence levels of these models are all over 99% by referring statistics F table. These models show relevant and high predictability. New bioactive lead compounds were designed on the basis of these models. Their predicted activities are the higher and the predicted toxicity are lower than known compounds. Synthesis of these new compounds is in progress.

Key words ISOQUINOLINE P SURFACE ACTIVITY

DOI:

通讯作者