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苯并呋喃／噻吩联二苯类**PTP1B**抑制剂三维构效关系研究

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摘要　主要采用比较分子力场分析方法（CoMFA）对苯并呋喃／噻吩联二苯类PTP1B (protein tyrosine phosphatase 1B)抑制剂进行了三维构效关系的研究，考察了 静电场、立体场和氢键场对构效关系的影响，交叉系数q^2的值达到0．58，表明 CoMFA得到的构效关系模型比较理想，同时test set中分子的预测活性也表明，模 型具有较好的预测能力，研究还表明，氢键场的加入不一定有利于模型的改善，通 过对分子场等值面图的分析，可以观察到叠合分子周围立体场和静电场对化合物活 性的影响，为改进原有化合物的结构，提高它们的活性提供了指导，还尝试采用比 较分子相似性指数分析方法（CoMFA）对这一系列化合物作了研究，结果表明虽然 CoMFA中加入了疏水场，但是对于研究的体系，CoMFA的模型质量并没有显著提高。

关键词　苯并呋喃　噻吩 P　联苯 P　构效关系　酪氨酸　蛋白质　磷酸酯酶　糖尿病

分类号　R91

3D-QSAR analyses of novel benzofuranyl and benzothiophenyl biphenyls as PTP1B inhibitors

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Abstract　Comparative molecular field analysis (CoMFA) was performed to study the structure-activity relationship of novel benzofuranyl and benzothiophenyl biphenyls as protein tyrosine phophatase IB (PTP1B) inhibitors. In this analysis, three molecular fields were considered: electrostatic field, steric field and H-bond field. The value of cross-validated coefficient q~2 was found to be 0.58, showing that the model from CoMFA was good and the predictive biological activity of molecules in the test set indicated the predictive potential of the model for the untested compounds. It also indicated that the addition of H-bond field did improve the quality of the QSAR model. From analysis of the CoMFA coefficient contour plots, steric and electrostatic properties were identified, which were very helpful for designing new compounds. In addition, a newly developed approach, comparative molecular similarity indices analysis (CoMSIA), was tried. However, the results show that CoMSIA does not lead to any improvement compared with CoMFA for the system examined in this work.

Key words　BENZOFURAN　THIOPHENE P　DIPHENYL P　STRUCTURE ACTIVITY RELATIONSHIP　TYROSINE　PROTEIN　DIABETES MELLITUS

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