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研究论文

HIV蛋白酶抑制剂——利迪链菌素的分子对接研究

李金涛, 李艳妮, 元英进*

(天津大学化工学院制药工程系 天津 300072)

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摘要 用分子对接的方法, 对利迪链菌素的抗HIV蛋白酶活性进行了研究.
为了更准确地反映利迪链菌素分子与酶蛋白结合的情况, 充分考虑受体活性部位的柔性, 采用了FlexX(初步对接)和Flexidock(精确对接)分两步将配体与受体进行对接. 在初步对接中,
设计了不同的受体活性部位来考察是否有结合水分子参与抑制剂与酶的结合.
对一种作用方式已知的非肽类HIV蛋白酶抑制剂Aha006进行的对接研究显示,
分子模拟的结果与实际情况吻合得较好, 证明了本文所采用的方法的可靠性.
利迪链菌素与蛋白酶活性部位的对接结果显示, 配体分子与受体之间的结合没有结合水分子的参与, 两者通过5对氢键作用结合成为稳定的复合物. 利迪链菌素占据结合腔, 覆盖了蛋白酶的活性三联体Asp25-Thr26-Gly27, 从而起到抑制其生物活性的作用.

关键词 HIV-1蛋白酶抑制剂 利迪链菌素 分子模拟 分子对接

分类号

Study of Molecular Docking of an HIV-1 Protease Inhibitor— Streptolydigin

LI Jin-Tao, LI Yan-Ni, YUAN Ying-Jin*

(*Department of Pharmaceutical Engineering, School of Chemical Engineering and Technology, Tianjin University, Tianjin 300072*)

Abstract The HIV protease-inhibiting activity of streptolydigin was studied using docking methodology. To reflect the binding state of streptolydigin and enzyme receptor more exactly, the flexibility of the active site was taken into consideration. A two-step docking method involving FlexX (for rough docking) and Flexidock (for precise docking) was used. In rough docking, in order to find out whether there is a structural water molecule mediating the contacts of the ligands and the protease, two different active site models were designed. The two-step docking result was obtained for Aha006, a non-peptide HIV-1 protease inhibitor whose binding mode in the active site is already known. The docking result coincided with actual binding state of ligand and receptor, indicating that the docking method used was reliable. The binding result of streptolydigin and active site of HIV-1 protease exhibited that the ligand binds to the active site under the help of five hydrogen bonds and no water molecule participates in the binding. Streptolydigin molecule oc-cupies the binding site and covers the active-site triad (Asp25-Thr26-Gly27), thus the biological activity of the protease is inhibited.

Key words HIV-1 protease inhibitor streptolydigin molecular modeling docking

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通讯作者 元英进 yjyuan@tju.edu.cn