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Hydroxamate类抑制剂与**MMP-2**的分子对接研究

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摘要 通过分子动力学模拟研究了MMP-2和hydroxamate抑制剂之间的作用模式。在分子动力学模拟中，对于催化区的锌离子和其共价结合的配体(包括抑制剂和组氨酸)采用了键合的模型。从模拟的结果可以看到，R^1取代基和MMP-2的S1疏水口袋中的部分残基能形成很好的几何匹配，从而可以产生很强的范德华和疏水相互作用。模拟结果也表明，两个抑制剂和MMP-2之间分别能形成5个和8个氢键，抑制剂B比A活性更高的原因就是能够形成更加有利氢键作用模式。在整个模拟过程中，催化锌都能保持好的五配位形式，配位键的长度也处于稳定的状态，预测得到的MMP-2和其抑制剂的相互作用模式对于全新抑制剂的设计提供了非常重要的结构信息。

关键词 锌络合物 酶抑制剂 白明胶酶 MMP-2 分子对接 金属蛋白酶 分子动力学

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Molecular docking simulations between hydroxamates and MMP-2

Hou Tingjun,Zhang Wei,Xu Xiaojie

Abstract The binding mode of MMP-2 with hydroxamate inhibitors was studied by using molecular dynamics (MD) simulations. In MD simulations, a bonded model for the catalytic zinc center was used to represent the bonded interactions between zinc center and enzyme/inhibitor. From the simulated results, it can be seen that the substituent on R^1 site will form good steric complementarity with the S1 hydrophobic pocket of MMP-2; consequently, produce strong van der Waals contacts and hydrophobic interactions. Moreover, the hydrogen bonds between receptor and ligand was critical for ligand binding,and two inhibitor can form 5 and 8 hydrogen bonds with MMP-2, respectively. The stronger binding affinity of B than A may be derived from the more favorble hydrogen-bonding interactions. In MD simulations, the coordination of the inhibitor's hydroxamate group to the catalytic zinc atom was maintained very well for the entire simulation time. The predicted complex structure of MMP-2 with hydroxamates will be very important for us to take into insight the potetial mechanisms of the intermolecular interactions between inhibitor and receptor, especially with respect to the design of new compouds.

Key words ZINC COMPLEX ENZYME INHIBITOR MOLECULAR DYNAMICS

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