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研究论文

六钼酸盐有机胺杂化衍生物与SARS-CoV 3CL^{pro}相互作用的分子动力学模拟

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摘要 采用分子动力学模拟方法, 在分子水平上探讨六钼酸盐有机杂化衍生物潜在的抗SARS病毒活性. 3CL^{pro}主蛋白酶是冠状病毒复制和转录过程中起关键作用的功能蛋白, 因此采用SARS-CoV 3CL^{pro}作为靶标进行抗SARS病毒的药物设计. 使用Insight II软件包中的Biopolymer, Discover 3, Profile-3D和Affinity等模块, 研究POMs/3CL^{pro}相互作用的结合位点和作用性质. 研究其能量变化规律, 探讨了多酸化合物对SARS病毒可能的抑制机理. 研究结果表明, POMs与3CL^{pro}在酶的催化活性位点处有较强的结合力. 形成的复合物主要以静电相互作用相结合, 氢键相互作用对复合物的相对稳定性有一定影响. 对于POMs/3CL^{pro}复合物, 有机胺基团取代的POMs所带负电荷比未取代体系的高, 比3CL^{pro}的结合能更高, 这与POMs的相关量子化学计算结果吻合.

关键词 SARS 3CL^{pro} 多金属氧酸盐 分子动力学 对接

分类号 0641

Interactions of $[Mo_6O_{19}]^{2-}$ and Its Derivatives Substituted with Organic Groups Inhibitor with SARS-CoV 3CL^{pro} by Molecular Modeling

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Abstract Polyoxometalates(POMs) were proved with the properties of both anti-tumor and anti-HIV. The potential anti-SARS activities of the polyoxometalates $[Mo_6O_{19}]^{2-}$ and its derivatives substituted with organic groups were investigated in this paper by molecular modeling method. The 3c like(3CL)protease hydrolyze, namely 3CL^{pro}, is the key protease for virus replication as well as transcription, and thus can be taken as one of the key targets for anti-SARS drug design. InsightII/Dicover 3, affinity, Profile-3D modules were used to explore possible binding locations and properties for POMs/3CL^{pro} interaction. We studied the energy changing tend and investigated the possible inhibiting mechanism of POMs' with SARS-CoV. The results show that POMs bind with 3CL^{pro} in the active site with a high affinity, mainly *via* electrostatic interactions and H-bond interactions. For the POMs/3CL^{pro} complex, POMs substituted with organic groups with higher negative charge are prefer to bind with 3CL^{pro} than non-substituted ones, and this agrees well with relative quantum chemical calculations. Organic substitutions in ligands have an influence on the stability of complexes by steric hindrance. Our study may provid

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e theoretical reference and illustrations to anti SARS-CoV drug design.

Key words SARS 3CL^{pro} Polyoxometalate Molecular dynamics Docking

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