Theoretical Chemistry Colloquium

May 1, 2014 (Thu), 16:00-17:00

RCMS, 2nd floor, Chemistry Gallery

Rational design of InhA inhibitors as highly potential anti-tubercular agents, based on computer aided molecular design

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Abstract: A series of diphenyl ether derivatives have been developed and shown promising potency for inhibiting InhA, an essential enoyl acyl carrier protein reductase involved in mycolic acid biosynthesis, leading to the lysis of *Mycobacterium tuberculosis*. To understand the structural basis of diphenyl ether derivatives for designing more potent inhibitors, 3D-QSAR using CoMSIA approach and molecular dynamics (MD) simulations were performed. Based on the obtained results, the structural requirements derived from the obtained CoMSIA model related with the inhibitor-enzyme interactions as well as the binding site of diphenyl ether derivatives in the InhA pocket investigated from MD simulations. The dynamic behaviour in terms of flexibility, binding free energy, binding energy decomposition, conformation and the inhibitor-enzyme interaction of diphenyl ether inhibitors were elucidated. Based on the integrated results, our results could provide the structural concept to design new diphenyl ether inhibitors with the better enzyme inhibitory activity against *M. tuberculosis* InhA. The present work facilitated the design of new and more potentially effective anti-tuberculosis agents.

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