Theoretical Evaluation of Novel Thermolysin Inhibitors from Bacillus thermoproteolyticus. Possible Antibacterial Agents

Lamazares, E.
MacLeod-Carey, D.
Miranda, F.P.
Mena-Ulecia, K.

Abstract
The search for new antibacterial agents that could decrease bacterial resistance is a subject in continuous development. Gram-negative and Gram-positive bacteria possess a group of metalloproteins belonging to the MEROPS peptidase (M4) family, which is the main virulence factor of these bacteria. In this work, we used the previous results of a computational biochemistry protocol of a series of ligands designed in silico using thermolysin as a model for the search of antihypertensive agents. Here, thermolysin from Bacillus thermoproteolyticus, a metalloprotein of the M4 family, was used to determine the most promising candidate as an antibacterial agent. Our results from docking, molecular dynamics simulation, molecular mechanics Poisson-Boltzmann (MM-PBSA) method, ligand efficiency, and ADME-Tox properties (Absorption, Distribution, Metabolism, Excretion, and Toxicity) indicate that the designed ligands were adequately oriented in the thermolysin active site. The Lig783, Lig2177, and Lig3444 compounds showed the best dynamic behavior; however, from the ADME-Tox calculated properties, Lig783 was selected as the unique antibacterial agent candidate amongst the designed ligands.

Author keywords
ADME-Tox
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