Interaction of mutant PBP2a and bioactive compounds from Streptomyces with anti-MRSA activities

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Abstract	Methicillin-Resistant Staphylococcus aureus (MRSA) is the leading cause of nosocomial infections in hospitals. Treatment of MRSA infection using ceftaroline has been reported to be resistant due to mutations in the Penicillin Binding Protein (PBP)2a. In silico's approach through virtual screening can analyze the bioactive compounds that can bind effectively to mutant PBP2a. The potential source of bioactive compounds with anti-MRSA activities is Streptomyces, which is the main antibiotic-producing bacteria. Thus, the study aimed to analyze the interactions of PBP2a/mutant PBP2a against ceftaroline and the interactions between mutant PBP2a against bioactive compounds from Streptomyces. The protein receptors were PBP2a (PDB 3ZG0) and mutant PBP2a (PDB 4CPK). The ligands used were ceftaroline (CID 9852981) as control and nine bioactive compounds produced by Streptomyces. Protein preparation and visualization used Discovery Studio, ligand preparation used Marvin, and molecular docking used Autodock4. The alignment results showed that mutant PBP2a has a more extended amino acid sequence (643 amino acids) than PBP2a (641 amino acids). The mutations that occurred in mutant PBP2a caused conformation changes in the active site of mutant PBP2a so that the interaction between ceftaroline and mutant PBP2a decreased. The virtual screening results indicated that 1-acetyl-beta-carboline was the most potent compound as anti-MRSA with the lowest binding energy (-7.12 Kcal /mol) compared to ceftaroline (-6.32 Kcal/mol). The amino acids involved in the binding of 1- acetyl-beta-carboline with PBP2a mutant were Ser403, Ser461, Asn464, Thr600; Ser462, Tyr446, and Ala642. This result suggests that 1-acetyl-beta-carboline has better interaction with mutant PBP2a, hence might serve as a potential anti-MRSA compound.
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