Dieckol as a Multi-Target Inhibitor of Methicillin-Resistant *Staphylococcus aureus* Virulence and Resistance Proteins: An *In Silico* Molecular Docking Investigation

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Abstract

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a significant worldwide concern due to resistance to β-lactam and non-β-lactam antibiotics, and its persistence in healthcare and community settings. This requires new approaches focusing on virulence factors rather than bactericidal properties, with marine phlorotannin dieckol, rich in hydroxyl groups, providing multi-target potential through H-bonding and π-interactions. Aim: To evaluate the binding of dieckol to MRSA proteins Sortase A (1T2W, virulence), PBP2a (1VQQ, resistance), and α-hemolysin (4YHD, toxin) by molecular docking. **Methodology:** UCSF Chimera was used for protein preparation, and dieckol (PubChem 3008868) was prepared in AutoDockTools. Docking was performed using PyRx-AutoDock Vina, and results were analyzed in Discovery Studio 2025. **Results:** Molecular docking studies revealed high binding affinities of dieckol to MRSA targets with -9.6 kcal/mol binding energy for PBP2a (PDB: 1VQQ; H-bonds: ARG151, THR165, SER240, THR216; π-cation: HIS293; π-alkyl: VAL256, VAL277), -8.5 kcal/mol for Sortase A (PDB: 1T2W; H-bonds: SER109, ASP111, ASP112, GLU108; π-anion/π-alkyl: ILE65), and -6.6 kcal/mol for α-hemolysin (PDB: 4YHD; H-bonds: LYS58, GLY59, GLY223, SER225; π-cation: LYS37; π-alkyl ILE5, ALA35, VAL149). These non-covalent interactions, namely the hydrogen bonding between the polyhydroxyl groups of dieckol, π-stacking, and hydrophobic interactions, do confirm the presence of stable complexes, thus validating polypharmacology. **Conclusion:** Dieckol does possess polypharmacological potential against the virulence/resistance of MRSA, thus making it at the cutting edge of green, marine-derived one health oriented anti-infectives pending in vitro validation..

Key words: Binding affinity, good health, hydrogen bonding, phlorotannin, polypharmacology, virulence factors, well-being