DRUG-LIKE INHIBITORS TARGETING BACTERIAL PROTEINS FOR TREATING BACTERIAL INFECTIONS OF ANIMAL FEEDS

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I. INTRODUCTION

There is an increasing threat of communicable diseases, particularly those of bacterial origin, due to the emergence of drug-resistant strains. It emphasizes the need for novel antibacterial agents, with a focus on natural products like *Rheum palmatum*, known for its various medicinal properties, including antibacterial effects. While the antibacterial activity of *R. palmatum* extracts is known [1], information on specific active constituents and their mechanisms of action is limited. To this end, development of structure-based drug discovery platforms is necessary, particularly computer-aided drug design (CADD), to screen phytoconstituents and assess their inhibitory effects against various bacterial protein targets, including penicillin-binding proteins (PBPs), peptide deformylase (PDF), topoisomerase IV, and methyl-coenzyme M reductase [2]. These proteins are essential for bacterial growth or replication and are potential targets for novel antibiotics. Therefore, the study aims to evaluate the binding energies of compounds from *R. palmatum* root extract with these protein targets using PyRx, a set of Autodock programs, to identify potential antibacterial agents, as well as to assess the drug-likeness of these hits based on Lipinski's Rule of Five and ADMET property analysis.

II. MATERIALS AND METHODS

Various bioinformatic tools such as PyRx 0.8, AutoDock, AutoDock Vina, FAFDrugs3 web server, ProTox, and the Protein Data Bank (PDB) were used for molecular docking and virtual screening. Small molecules from *Rheum palmatum* root extract were identified through GC-MS analysis, with compounds selected for docking experiments after energy minimization. Crystal structures of target proteins, including Penicillin binding proteins, Peptide deformylase, Topoisomerase IV inhibitors, and Methyl-coenzyme reductase, were retrieved from the PDB. Molecular docking simulations were conducted using AutoDock and AutoDock Vina in PyRx 0.8, employing the Lamarckian Genetic Algorithm for scoring function calculation. The grid map for docking calculations was centered on the target proteins, and the best drug-like compounds were selected based on higher scoring functions and interactions with the protein models. Visualization of structures was performed using PyMol. In silico ADMET prediction was carried out to assess drug likeness and pharmacokinetic properties, utilizing FAFDrugs3 web server for ADME parameter evaluation and ProTox server for oral toxicity assessment of the finalized compounds.

III. RESULTS AND DISCUSSION

This study focuses on virtual screening and molecular docking as a strategy for drug discovery, particularly targeting bacterial enzymes essential for pathogen survival. By screening compounds from *Rheum palmatum* root extract against four bacterial proteins crucial for infection, three potent drug-like molecules were identified: Ligand 29, Ligand 31, and Ligand 33. These compounds exhibited strong binding affinities to their respective target proteins, as indicated by their low binding energy scores. Molecular interactions between the ligands and proteins were analyzed, revealing hydrogen bonds and hydrophobic interactions crucial for inhibition. Furthermore, the drug-like properties of the selected ligands were assessed using computational tools, indicating good bioavailability, solubility,

and low toxicity. These compounds adhere to Lipinski's rule of five, suggesting potential oral drug delivery.

Table 1. Properties of ligands analyzed by FAFDrugs3 and ProTox server.

Ligand	MW	Oral bioavailability	Rotatable bonds	Flexibility	logP	HBD	HBA	Rings	Lipinski Violations	Solubility (mg/l)	Stereo centers
Lig 29	254.24	Good	0	0	3.53	2	4	1	0	4913.02	0
Lig 31	474.72	Good	23	0.74	10.21	0	4	1	1	204.40	0
Lig 33	390.56	Good	16	0.67	8.41	0	4	1	1	546.92	0

The study underscores the importance of computational approaches in drug discovery, especially in addressing challenges posed by antibiotic resistance. While the development of novel drugs from natural sources faces limitations in scalability and downstream processing, the compounds identified in this study show promise in inhibiting bacterial enzymes, offering potential for treating infectious diseases of bacterial origin.

IV. CONCLUSION

The study aimed to address emerging bacterial infections caused by antibiotic resistance by identifying new natural compounds with drug-like and antibacterial properties. Through computational screening of compounds from *R. palmatum*, three promising ligands were identified for their potential to inhibit bacterial enzymes. These ligands showed minimal toxicity and good bioavailability, indicating their suitability as novel inhibitors against bacterial infections. Further validation through in vitro and in vivo studies is needed to confirm their efficacy in treating bacterial diseases caused by drug-resistant strains.

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