

COMPARATIVE STUDY OF MOLECULAR DOCKING WITH BIOACTIVE PHYTOCHEMICALS FROM VOLKAMERIA INERMIS AND BUTEA MONOSPERMA AGAINST BACTERIAL DNA GYRASE B

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ABSTRACT

Antimicrobial resistance has increased the need for antibacterial candidates with novel molecular targets. The present in silico study comparatively evaluated selected phytoconstituents reported from Volkameria inermis and Butea monosperma against bacterial DNA Gyrase B (GyrB), an essential enzyme involved in bacterial DNA topology. Three compounds from each plant were selected from the GC–MS-derived constituent list and screened by molecular docking using AutoDock Vina against the Staphylococcus aureus GyrB structure PDB ID 3TTZ (1.63 Å). Dodecane, 2,3-anhydro-D-mannosan and heptadecanoic acid from V. inermis showed docking scores of –7.2, –7.4 and –8.5 kcal/mol, respectively. The B. monosperma compounds 4morpholinecarbonitrile, triamcinolone acetonide and 2-acetyl-5-methylfuran showed –4.7, –5.9 and –4.4 kcal/mol, respectively. Heptadecanoic acid showed the most favourable predicted binding among the six compounds. Interaction analysis indicated hydrogen-bond/polar and hydrophobic contacts for the V. inermis compounds, whereas the B. monosperma compounds mainly showed van der Waals and conventional hydrogen-bond interactions. The findings prioritize V. inermis-derived compounds, particularly heptadecanoic acid and 2,3-anhydro-D-mannosan, for further experimental validation. However, the docking and toxicity findings are computational predictions and require laboratory confirmation.

KEYWORDS

Volkameria inermis; Butea monosperma; DNA Gyrase B; molecular docking; AutoDock Vina; phytochemicals; antibacterial drug discovery; antimicrobial resistance.

1. INTRODUCTION

Drug discovery integrates biology, chemistry and pharmacology to identify and optimize candidate molecules. Computational approaches have become important in early drug discovery because virtual screening can reduce the time and cost associated with experimental screening. Molecular docking is a structure-based technique used to predict the orientation of a ligand in a protein binding site and to estimate its binding affinity. The approach therefore provides a useful preliminary method for prioritizing compounds for subsequent laboratory evaluation.

Antibiotic resistance is a major public-health challenge and has increased interest in alternative sources of antibacterial molecules. Medicinal plants contain structurally diverse secondary metabolites, including flavonoids, phenolics, terpenoids, steroids and glycosides. V. inermis is a medicinal coastal shrub reported to contain diverse bioactive constituents, while B. monosperma is a traditionally used plant known for flavonoids, chalcones and other secondary metabolites.

DNA gyrase is a bacterial type II topoisomerase that uses ATP to manage DNA supercoiling. GyrB contains the ATPase region and is therefore an attractive antibacterial target. The present study compares selected phytoconstituents from V. inermis and B. monosperma against the same GyrB target to identify compounds with comparatively favourable predicted binding.

2. AIM

To comparatively evaluate selected bioactive phytochemicals from Volkameria inermis and Butea monosperma against bacterial DNA Gyrase B using molecular docking and preliminary computational safety assessment.

3. OBJECTIVES

To select reported phytoconstituents, retrieve their structures from PubChem, prepare the bacterial GyrB target from the Protein Data Bank, perform AutoDock Vina docking, analyse protein–ligand interactions, compare the two plants, and prioritize promising compounds for further antibacterial investigation.

4. MATERIALS AND METHODS

4.1 STUDY DESIGN

The study was performed as an in silico molecular docking investigation. The workflow comprised plant and phytochemical selection, ligand retrieval and preparation, target protein selection and preparation, binding-site identification, docking, interaction analysis, comparative evaluation and preliminary toxicity interpretation.

4.2 SELECTION OF MEDICINAL PLANTS AND COMPOUNDS

V. inermis and *B. monosperma* were selected on the basis of their traditional medicinal use and reported phytochemical diversity. The project document reports GC–MS analysis of the plant extracts and provides lists of detected constituents. Three compounds from each plant were shortlisted for docking based on their reported presence and availability of molecular structure information.

Plant	Selected compounds	Docking score (kcal/mol)
<i>V. inermis</i>	Dodecane	−7.2
<i>V. inermis</i>	2,3-Anhydro-D-mannosan	−7.4
<i>V. inermis</i>	Heptadecanoic acid	−8.5
<i>B. monosperma</i>	4-Morpholinecarbonitrile	−4.7
<i>B. monosperma</i>	Triamcinolone acetonide	−5.9
<i>B. monosperma</i>	2-Acetyl-5-methylfuran	−4.4

4.3 LIGAND RETRIEVAL AND PREPARATION

Ligand structures were obtained from PubChem. Compound name, PubChem CID, molecular formula, molecular weight and structural identifiers were recorded. The structures were checked, hydrogen atoms and appropriate charges were considered, rotatable bonds were defined and the ligands were converted into a docking-compatible PDBQT format.

4.4 TARGET PROTEIN SELECTION AND PREPARATION

Bacterial DNA Gyrase B was selected as the target because of its essential role in bacterial DNA topology and its ATP-binding region. The project used PDB ID 3TTZ from *Staphylococcus aureus*, reported at 1.63 Å resolution, with chain A selected for preparation. The structure contained a co-crystallized ligand and magnesium ions. Protein preparation included selection of the relevant chain, removal of unnecessary molecules/waters where appropriate, addition of hydrogens, charge assignment and conversion to PDBQT.

4.5 BINDING-SITE AND GRID PREPARATION

The binding pocket was identified using structural information and the position of the co-crystallized ligand. A grid box was defined around the selected binding region, and the same docking region was maintained for all test compounds to support a fair comparison.

4.6 MOLECULAR DOCKING

Docking was performed using AutoDock Vina. Each prepared ligand was docked individually into the selected GyrB binding site. Docking poses were ranked by predicted binding affinity, expressed in kcal/mol. Under identical docking conditions, a more negative score indicates a more favourable predicted interaction.

4.7 INTERACTION ANALYSIS

The docked complexes were examined using molecular-visualization tools. Hydrogen bonds, hydrophobic contacts, van der Waals contacts, π -related interactions and important amino-acid residues were considered. Novobiocin was identified in the project as a suitable GyrB-focused reference inhibitor.

5. RESULTS

5.1 DOCKING SCORE COMPARISON

Rank	Plant	Compound	Binding affinity (kcal/mol)
1	V. inermis	Heptadecanoic acid	-8.5
2	V. inermis	2,3-Anhydro-D-mannosan	-7.4
3	V. inermis	Dodecane	-7.2
4	B. monosperma	Triamcinolone acetonide	-5.9
5	B. monosperma	4-Morpholinecarbonitrile	-4.7
6	B. monosperma	2-Acetyl-5-methylfuran	-4.4

The three V. inermis compounds showed stronger predicted binding than the three B. monosperma compounds under the reported docking conditions. Heptadecanoic acid produced the lowest docking score (-8.5 kcal/mol), followed by 2,3-anhydroD-mannosan (-7.4 kcal/mol) and dodecane (-7.2 kcal/mol). The B. monosperma compounds ranged from -4.4 to -5.9 kcal/mol.

5.2 PROTEIN-LIGAND INTERACTIONS

Plant/compound	Interaction pattern	Reported residues
V. inermis – Dodecane	Hydrophobic	VAL349, LEU352, SER353, TYR355, PHE357, LEU359, PHE381, LEU384, TYR385, TRP387
V. inermis – 2,3-Anhydro-D-mannosan	H-bond/polar/hydrophobic	TYR115, VAL116, LEU117, SER119, ARG120, TYR122, ILE345, TYR348, VAL349
V. inermis – Heptadecanoic acid	H-bond/polar/hydrophobic	ARG44, GLY45, GLU46, CYS47, MET48; TRP323, GLN327, PHE371, TYR373, GLN374
B. monosperma – 4-Morpholinecarbonitrile	van der Waals + H-bond	ILE A:722, VAL A:767, CYS A:721, LEU A:755, ILE A:744, VAL A:836, THR A:768, LYS A:723; LEU A:766, ASP A:833, PHE A:834
B. monosperma – Triamcinolone acetonide	van der Waals + H-bond + alkyl	VAL A:753, GLN A:769, LEU A:771, GLY A:774, ASP A:833; THR A:768, CYS A:721; VAL A:704, ALA A:723, LEU A:822
B. monosperma – 2-Acetyl-5-methylfuran	van der Waals + H-bond + alkyl	ALA A:832, VAL A:753, ASP A:833, LYS A:723, LEU A:766; THR A:768; PHE A:834

5.3 TOXICITY INTERPRETATION

The project document did not contain complete numerical ProTox outputs. Instead, the listed toxicity interpretation was based on structural class/read-across. The three V. inermis compounds were described as having low predicted toxicity in the project, while the three B. monosperma compounds were described as moderate, with structural or pharmacological concerns noted. These observations should not be treated as experimentally validated toxicity results.

5.4 COMPARATIVE OUTCOME

Overall, V. inermis demonstrated a more favourable docking profile than B. monosperma in this six-compound screening set. The difference was consistent across all three compounds from each plant, with the strongest B. monosperma score (-5.9 kcal/mol) remaining less negative than the weakest V. inermis score (-7.2 kcal/mol).

6. DISCUSSION

The present computational comparison suggests that selected phytoconstituents of *V. inermis* may have greater predicted affinity toward bacterial DNA Gyrase B than the selected *B. monosperma* constituents. This result is notable because GyrB contains an ATP-binding region that can be exploited for antibacterial drug discovery. The consistent ranking of the *V. inermis* compounds indicates that the plant deserves further investigation as a source of candidate molecules for GyrB-focused screening.

Heptadecanoic acid produced the best docking score of -8.5 kcal/mol. Its interaction pattern included hydrogen-bond/polar and hydrophobic contacts involving residues reported in the project. 2,3-Anhydro-D-mannosan also showed a favourable score of -7.4 kcal/mol and combined hydrogen-bond/polar and hydrophobic interactions. Dodecane showed a -7.2 kcal/mol score and was characterized mainly by hydrophobic interactions.

In comparison, triamcinolone acetonide was the strongest of the *B. monosperma* compounds at -5.9 kcal/mol, followed by 4-morpholinecarbonitrile (-4.7 kcal/mol) and 2-acetyl-5-methylfuran (-4.4 kcal/mol). Their reported interactions were dominated by van der Waals and conventional hydrogen-bond contacts, with alkyl contacts additionally reported for the latter two compounds.

The findings should be interpreted as a prioritization exercise rather than proof of antibacterial efficacy. Docking scores are model-dependent and do not by themselves establish inhibition of GyrB in a biological system. The project also notes that actual numerical outputs from SwissADME and ProTox were not generated in the supplied document. Therefore, the toxicity and pharmacokinetic discussion remains preliminary and should be replaced or supplemented with actual computational outputs before journal submission.

The choice of GyrB is mechanistically relevant because this subunit participates in the ATP-dependent function of DNA gyrase. Novobiocin was identified as a GyrB-focused reference inhibitor in the project. Ciprofloxacin, while relevant to the gyrase enzyme system, mainly acts through GyrA/topoisomerase IV rather than the ATP-binding site of GyrB; therefore it should be considered a mechanistic comparator rather than a direct GyrB docking control.

7. LIMITATIONS

The study is limited by the small number of docked compounds, reliance on a single protein structure and computational predictions. The supplied project document also contains incomplete direct toxicity-platform outputs. In addition, the GC-MS compound identities should be verified carefully because some reported hits may require analytical confirmation before being treated as definitive plant metabolites.

8. FUTURE PERSPECTIVES

The prioritized compounds should undergo confirmatory in vitro antibacterial assays, followed by GyrB enzyme inhibition studies where feasible. Redocking/validation using the co-crystallized ligand, repeated docking with standardized parameters, molecular-dynamics simulation and free-energy calculations could strengthen the computational evidence. Actual SwissADME and ProTox outputs should also be generated from verified SMILES structures before final publication.

9. CONCLUSION

Comparative molecular docking identified *V. inermis* as the stronger-performing plant in the present six-compound screening study. Heptadecanoic acid (-8.5 kcal/mol) and 2,3-anhydro-D-mannosan (-7.4 kcal/mol) were the leading predicted binders against *S. aureus* DNA Gyrase B (PDB 3TTZ). These compounds may be considered preliminary lead candidates for further antibacterial investigation. Nevertheless, the findings remain computational and require experimental validation before any therapeutic conclusions are made.

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Key reported docking data and interactions were taken from the supplied project results. □filecite □turn1file0 □ L13-L24 □filecite turn1file0 □ L28-L80

The supplied document explicitly notes that complete ProTox numerical outputs were not generated; therefore toxicity statements should be verified before submission. filecite turn2file0 L40-L45 □