RESEARCH PAPER

Molecular Docking Analysis of Gedunin as a Potential Inhibitor of Penicillin-Binding Protein 2a (PBP2a) in Methicillin-Resistant *Staphylococcus aureus*

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ABSTRACT

Methicillin-resistant Staphylococcus aureus (MRSA) is a major cause of antibiotic-resistant infections worldwide, primarily due to the presence of Penicillin-Binding Protein 2a (PBP2a), which reduces the effectiveness of β-lactam antibiotics. This study investigated the binding potential of Gedunin, a natural limonoid from Azadirachta indica (neem), against PBP2a using molecular docking and computational pharmacokinetic analysis. Docking was performed with AutoDock Vina against both the active and allosteric sites of PBP2a. Re-docking validation of the co-crystallised ligand yielded an RMSD of 0.537 Å, confirming the reliability of the docking protocol. Gedunin showed favourable binding affinities at both the active site (−6.935 kcal/mol) and the allosteric site (−6.912 kcal/mol). Interaction analysis revealed hydrogen bonds, hydrophobic interactions, π-stacking, and salt bridges with key amino acid residues within the binding pockets. Comparative docking with oxacillin and ceftaroline suggested that Gedunin can effectively interact with functionally significant regions of PBP2a. In addition, ADMET analysis using SwissADME and pkCSM indicated favourable drug-like properties, including high gastrointestinal absorption, low cardiotoxicity risk, and absence of major CYP450 inhibition. Overall, the findings suggest that Gedunin may serve as a promising natural-product scaffold for developing new anti-MRSA agents targeting PBP2a. Further experimental studies are required to validate these computational findings.

Keywords: Gedunin; PBP2a; MRSA; molecular docking; antimicrobial resistance; AutoDock Vina; natural products; beta-lactam resistance

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1. INTRODUCTION

Antimicrobial resistance has emerged as one of the defining public health crises of the twenty-first century. The World Health Organisation (WHO) has identified AMR as among the top ten global threats to human health, estimating that drug-resistant infections directly caused 1.27 million deaths worldwide in 2019 and contributed to approximately 4.95 million deaths (Murray et al., 2022). Without concerted intervention, projections suggest AMR-related mortality could reach 10 million deaths annually by 2050 (O'Neill, 2016).

Among the priority pathogens identified by the WHO, methicillin-resistant *Staphylococcus aureus* (MRSA) occupies a critical tier, accounting for a disproportionate burden of hospital-acquired and community-onset infections, including bacteraemia, endocarditis, pneumonia, and skin and soft tissue infections (Tong et al., 2015). MRSA is estimated to cause over 100,000 deaths annually in the United States and the European Union combined (European Centre for Disease Prevention and Control, 2023). The predominant mechanism underlying MRSA resistance to beta-lactam antibiotics is the acquisition and expression of the *mecA* gene (Llarrull et al., 2009). The *mecA* gene encodes Penicillin-Binding Protein 2a (PBP2a), a bifunctional transpeptidase and transglycosylase (Peacock & Paterson, 2015). Unlike native PBPs, PBP2a maintains a closed active site conformation with low affinity for beta-lactam compounds, effectively rendering this entire antibiotic class clinically ineffective against MRSA strains carrying this determinant (Lim & Strynadka, 2002). Structural studies have further demonstrated that PBP2a possesses a distal allosteric site whose occupancy induces conformational changes that transiently open the active site, a mechanism with significant implications for drug design (Otero et al., 2013).

Current therapeutic options for MRSA infections, including vancomycin, daptomycin, linezolid, and the fifth-generation cephalosporin ceftaroline, are associated with limitations including nephrotoxicity, emergence of tolerance or resistance, poor oral bioavailability, and high treatment costs (van Hal & Fowler, 2013; Dhand & Sakoulas, 2014). Ceftaroline is the only beta-lactam approved for MRSA by exploiting affinity for both the active and allosteric sites of PBP2a; however, ceftaroline-resistant MRSA isolates have been reported (Long et al., 2014). This underscores the urgent necessity for the identification of novel scaffolds with alternative binding mechanisms. Natural products have historically contributed the majority of clinically approved antibiotics and continue to represent a prolific source of lead compounds (Newman & Cragg, 2020).

Gedunin (CAS: 2753-30-2), a tetranortriterpenoid limonoid

isolated primarily from *Azadirachta indica* (neem) and *Entandrophragma* species, has demonstrated a broad spectrum of biological activities, including antibacterial, antifungal, anti-inflammatory, antiplasmodial, and anticancer properties (Alzohairy, 2016; Yadav et al., 2021). Gedunin has shown inhibitory activity against *S. aureus* in minimum inhibitory concentration (MIC) assays and has been identified as an inhibitor of HSP90 disrupting biofilm formation (Rao et al., 2019). Despite this promising biological profile, the molecular basis of Gedunin's antibacterial activity, specifically its potential interaction with PBP2a, has not been elucidated computationally.

Molecular docking is a well-established and widely validated in silico technique that predicts the preferred binding orientation and affinity of a small molecule within a protein active site, enabling rapid and cost-effective prioritisation of drug candidates before experimental screening (Meng et al., 2011). AutoDock Vina, in particular, has been extensively benchmarked and is among the most widely employed docking platforms in medicinal chemistry and antimicrobial drug discovery (Trott & Olson, 2010).

The present study aims to evaluate the binding affinity of Gedunin against both the active and allosteric sites of PBP2a using molecular docking and characterise the key protein-ligand interactions at the atomic level. It also aims to compare predicted binding affinity with the clinically established PBP2a-targeting compounds oxacillin and ceftaroline and assess the drug-likeness and ADMET profile of Gedunin to evaluate its potential as a drug candidate for anti-MRSA therapy.

2. MATERIALS AND METHODS

2.1 Protein Structure Retrieval and Preparation

The three-dimensional crystal structure of PBP2a from MRSA was retrieved from the RCSB Protein Data Bank (rcsb.org) in PDB format. Two structures were employed: PDB ID 1VQQ (apo form, resolution 1.80 Å) for primary docking experiments, and PDB ID 4CJN (co-crystallised form, resolution 2.20 Å) for re-docking validation (Berman et al., 2000). Protein preparation was performed in AutoDockTools (ADT) version 1.5.7 (Scripps Research Institute). Crystallographic water molecules and non-essential HETATM records were removed. Polar hydrogen atoms were added, and Gasteiger partial charges were assigned to all atoms. The prepared protein coordinates were saved in PDBQT format for compatibility with AutoDock Vina.

2.2 Binding Site Identification

Druggable binding pockets on the PBP2a structure were identified using two independent computational tools: CASTp 3.0 (Computed Atlas of Surface Topography of Proteins; sts.bioe.uic.edu/castp) and DoGSiteScorer (dogsite.zbh.uni-hamburg.de) (Tian et al., 2018; Volkamer et al., 2012). Based on consensus pocket prediction and corroboration with the published structural literature, two sites were selected for docking. The transpeptidase active site, centred on the catalytic residue Ser403, with key surrounding residues Lys406 and Thr600. The allosteric site near residue Trp374, whose occupancy is associated with conformational opening of the active site (Fishovitz et al., 2014). Grid boxes of 25 × 25 × 25 Å were defined for each site using the centre-of-mass coordinates of the respective pocket residues.

2.3 Ligand Preparation

The three-dimensional structure of Gedunin (PubChem CID: 122767; molecular formula C28H34O7; molecular weight: 482.55 g/mol) was retrieved from the PubChem Compound Database in SDF format (Kim et al., 2021). Structural conversion and energy minimisation were performed using Open Babel version 3.1.1 with the MMFF94 force field (O'Boyle et al., 2011). Rotatable bonds were assigned automatically in AutoDockTools, and Gasteiger charges were computed. The prepared ligand was saved in PDBQT format. Reference compounds oxacillin (PubChem CID: 6196) and ceftaroline (PubChem CID: 16007562) were prepared using an identical workflow for comparative docking.

2.4 Molecular Docking

All docking simulations were conducted using AutoDock Vina version 1.1.2 (Trott & Olson, 2010). Docking was performed with an exhaustiveness parameter of 16, generating ten output binding poses for each compound-site combination. All compounds (Gedunin, oxacillin, ceftaroline) were docked against both the active site and the allosteric site of PBP2a under identical conditions to enable direct comparisons. Binding affinity was expressed as the predicted free energy of binding (kcal/mol), where more negative values indicate stronger predicted binding. The top-ranked pose (lowest binding affinity) was selected for subsequent interaction analysis.

2.5 Re-Docking Validation

To validate the docking protocol, the co-crystallised ligand was extracted from PDB structure 4CJN and re-docked into the prepared apo-form receptor under identical conditions. The root mean square deviation (RMSD) between the re-docked pose and the original crystallographic ligand position was calculated using PyMOL version 2.5 (Schrödinger LLC). An RMSD threshold of 2.0 Å was applied as the criterion for protocol validity, consistent with established standards in the field (Warren et al., 2006).

2.6 Protein-Ligand Interaction Analysis

Protein-ligand interactions for the best-ranked Gedunin pose were characterised using the Protein-Ligand Interaction Profiler (PLIP; plip-tool.biotec.tu-dresden.de) which identifies and quantifies hydrogen bonds, hydrophobic contacts, pi-stacking interactions, pi-cation interactions, and salt bridges with precise bond geometry parameters (Salentin et al., 2015). Two-dimensional schematic interaction diagrams were generated using LigPlot+ version 2.2 (EMBL-EBI) (Laskowski & Swindells, 2011). Three-dimensional visualisations of binding poses and protein surface representations were rendered in PyMOL version 2.5.

2.7 ADMET Analysis

Drug-likeness and pharmacokinetic profiling of Gedunin and reference compounds were evaluated using two established web-based platforms. SwissADME (swissadme.ch) was used to predict physicochemical properties (molecular weight, LogP, hydrogen bond donors and acceptors, topological polar surface area, and rotatable bonds), lipophilicity, water solubility, and compliance with Lipinski's Rule of Five (Daina et al., 2017). Absorption, distribution, metabolism, elimination, and toxicity (ADMET) parameters, including intestinal permeability (Caco-2), blood-brain barrier (BBB) penetration, CYP450 isoform inhibition, hERG cardiotoxicity, and AMES mutagenicity were assessed using pkCSM (biosig.unimelb.edu.au/pkcsm) (Pires et al., 2015).

3. RESULTS

3.1 Re-Docking Validation

To confirm the reliability of the docking protocol before the primary experiments, QNZ (co-crystallised ligand) extracted from PDB structure 4CJN was re-docked into the prepared PBP2a receptor. The re-docked pose achieved an RMSD of 0.537 Å relative to the original crystallographic binding mode, which is below the 2.0 Å threshold accepted as indicative of a valid docking protocol. The superimposition of the re-docked and crystal poses demonstrated high positional concordance with retention of critical interactions at the active site (Figure 1).

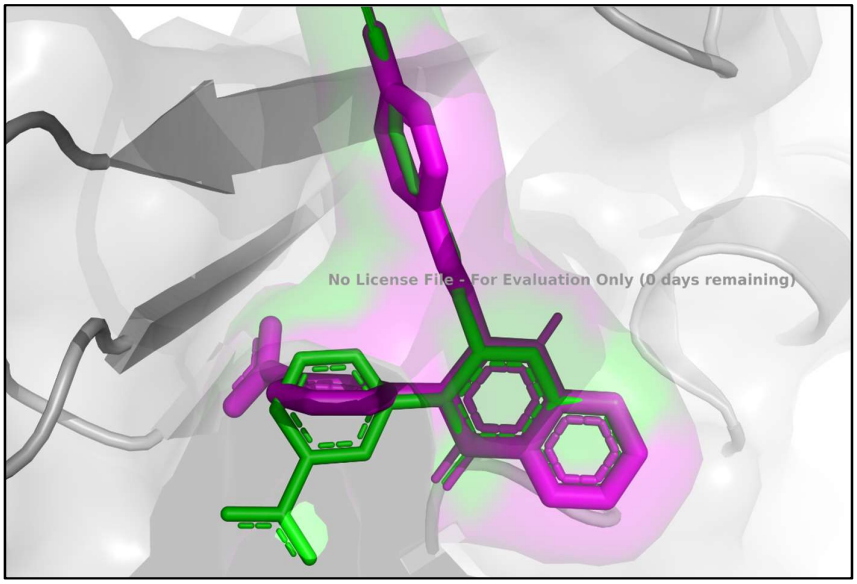

Figure 1. Re-docking validation of the molecular docking protocol. The co-crystallized ligand extracted from PDB 4CJN (green sticks) is superimposed with the top-ranked re-docked pose (purple sticks) within the PBP2a active site (grey cartoon).

3.2 Binding Affinity of Gedunin Against PBP2a

Gedunin demonstrated favourable predicted binding affinity against both the active site and allosteric site of PBP2a. At the active site (centred on Ser403), the best-ranked docking pose yielded a binding affinity of -6.935 kcal/mol, with a mean affinity of -6.935 kcal/mol across ten poses, indicating consistent convergence. At the allosteric site (centred on Trp374), Gedunin achieved a binding affinity of -6.912 kcal/mol. Comparatively, the active site exhibited a marginally stronger binding affinity than the allosteric site, suggesting that Gedunin may preferentially interact with the catalytic region of PBP2a while still retaining the potential to modulate protein function through allosteric interactions.

Table 1. Predicted binding affinities (AutoDock Vina) of Gedunin, oxacillin, and ceftaroline against the active site and allosteric site of PBP2a.

Compound	Binding Site	Best Affinity (kcal/mol)	Mean Affinity (kcal/mol)
Gedunin	Active site (Ser403)	-6.935	-6.607
Gedunin	Allosteric site (Trp374)	-6.912	-6.656
Oxacillin	Active site	-7.455	-6.618
Oxacillin	Allosteric site	-7.377	-6.773
Ceftaroline	Active site	-7.48	-6.777
Ceftaroline	Allosteric site	-8.652	-7.526

3.3 Comparative Docking with Reference Compounds

The predicted affinity of Gedunin, PBP2a-targeting compounds like oxacillin and ceftaroline were docked under identical conditions (Table 1).

Gedunin demonstrated slightly weaker docking affinity than oxacillin at both the active and allosteric sites of PBP2a. However, the comparable interaction profile observed for gedunin may still indicate its ability to associate with functionally relevant regions of PBP2a, because of the known reduced effectiveness of oxacillin against the conformationally restricted active site of the protein (Figure 2).

In comparison with ceftaroline, Gedunin exhibited lower binding affinity at both binding pockets, particularly at the allosteric site. Nevertheless, the ability of gedunin to dock within the allosteric region suggests a possible interaction with regulatory residues of PBP2a. This, however remains a subject of further experimental validation.

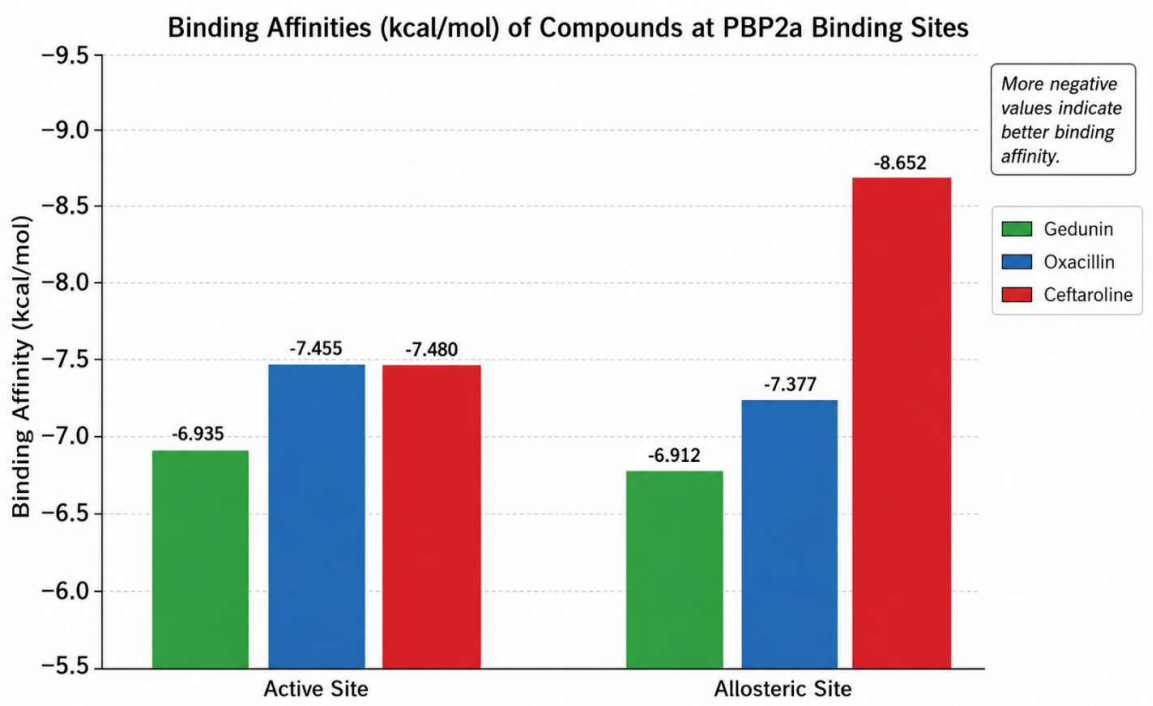

Figure 2. Comparative binding affinities of Gedunin, oxacillin, and ceftaroline against the PBP2a active site and allosteric site as predicted by AutoDock Vina. Values represent the best-ranked pose for each compound-site combination. More negative values indicate stronger predicted binding affinity.

3.4 Protein-Ligand Interaction Analysis

Detailed analysis of the top-ranked Gedunin pose at the PBP2a active site using PLIP revealed 5 key interactions, comprising 1 hydrogen bond, 3 hydrophobic contacts, and 1 π-stacking interaction (Table 2). Notably, Gedunin formed a hydrogen bond with ASN146B (H–A distance: 2.27 Å). Hydrophobic interactions were observed with THR308A, ILE309A, and ASN146B, contributing to the stabilisation of the ligand within the binding cavity. In addition, a π-stacking interaction with TRP205B further enhanced binding stability. These interactions are illustrated in the three-dimensional binding pose (Figure 3) and the two-dimensional schematic interaction map (Figure 4).

Table 2. Protein-ligand interactions between Gedunin and PBP2a active-site residues, as identified by PLIP. Bond distances are given in Angstroms (Å).

Residue	Interaction Type	Bond Distance (Å)	Atom (Gedunin)	Atom (Residue)
ASN146B	Hydrogen bond	2.91	O2	ND2
ASN146B	Hydrophobic contact	3.46	C22	Side-chain carbon atoms
THR308A	Hydrophobic contact	3.41	C14	Side-chain carbon atoms
ILE309A	Hydrophobic contact	3.69	C28	Side-chain carbon atoms
TRP205B	π-Stacking interaction	4.25	Aromatic ring atoms (23,24,25,26,33)	Indole ring of TRP205B

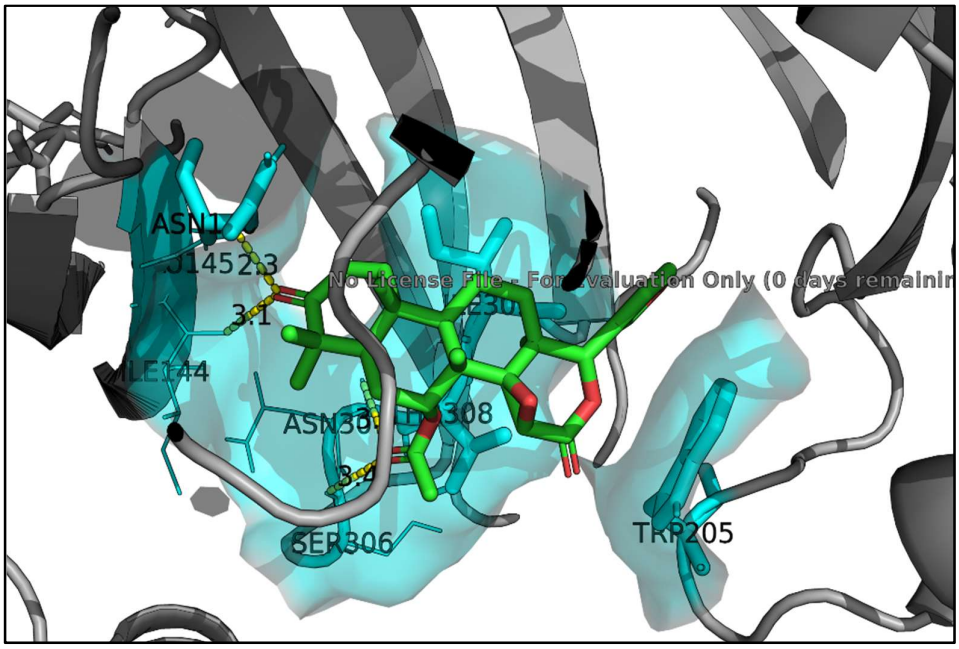

Figure 3. Three-dimensional binding pose of Gedunin within the active site of PBP2a. Gedunin is shown as green sticks within the cyan semi-transparent binding pocket surface, while the protein backbone is represented as a grey cartoon. Key interacting residues including ASN223, ILE144, ASN308, SER306, and TRP205 are labelled. Hydrogen bond interactions are depicted as yellow dashed lines with bond distances indicated in Å. The figure was rendered using PyMOL version 2.5.

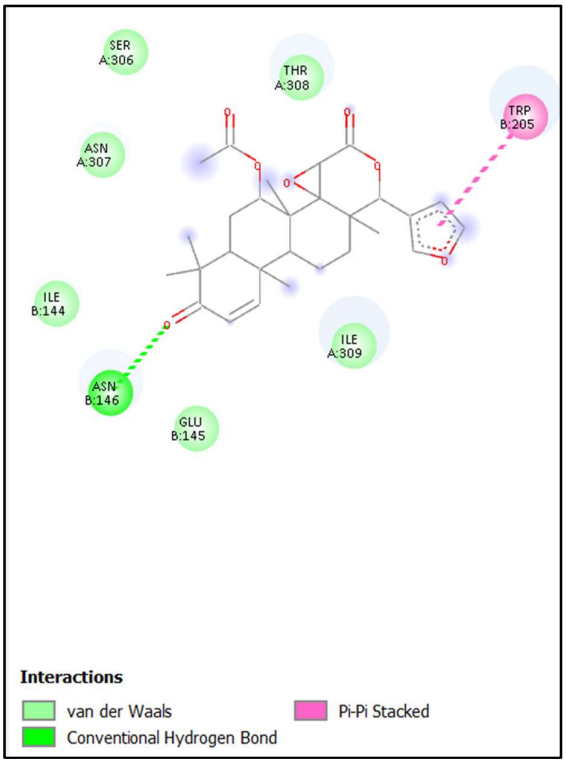

Figure 4. Two-dimensional schematic diagram showing the binding interactions between Gedunin and active-site residues of PBP2a, generated using Discovery Studio Visualizer. Conventional hydrogen bonds are depicted as green dashed lines, π–π stacking interactions as magenta dashed lines, and van der Waals contacts as light green circles.

Detailed analysis of the Gedunin pose at the PBP2a allosteric site using PLIP revealed 4 key interactions, comprising 3 hydrophobic contacts and 1 salt bridge interaction (Table 3). Hydrophobic interactions were observed with LYS318A, ASP320A, and LYS322A, with interaction distances ranging from 3.57–3.93 Å, contributing to stabilisation of the ligand within the allosteric binding cavity. In addition, Gedunin formed a salt bridge interaction with LYS317A (5.29 Å), which may further enhance electrostatic stabilisation of the ligand–protein complex. These interactions are illustrated in the three-dimensional binding pose (Figure 5) and the two-dimensional schematic interaction map (Figure 6).

Table 3. Protein-ligand interactions between Gedunin and PBP2a allosteric-site residues, as identified by PLIP. Bond distances are given in Angstroms (Å).

Residue	Interaction Type	Bond Distance (Å)	Atom (Gedunin)	Atom (Residue)
LYS318A	Hydrophobic contact	3.69	Atom 24	Side-chain carbon atoms
ASP320A	Hydrophobic contact	3.93	Atom 8	Side-chain carbon atoms
LYS322A	Hydrophobic contact	3.47	Atom 22	Side-chain carbon atoms
LYS317A	Salt bridge	5.29	Carboxylate atoms (30,31)	NZ atom of Lys317

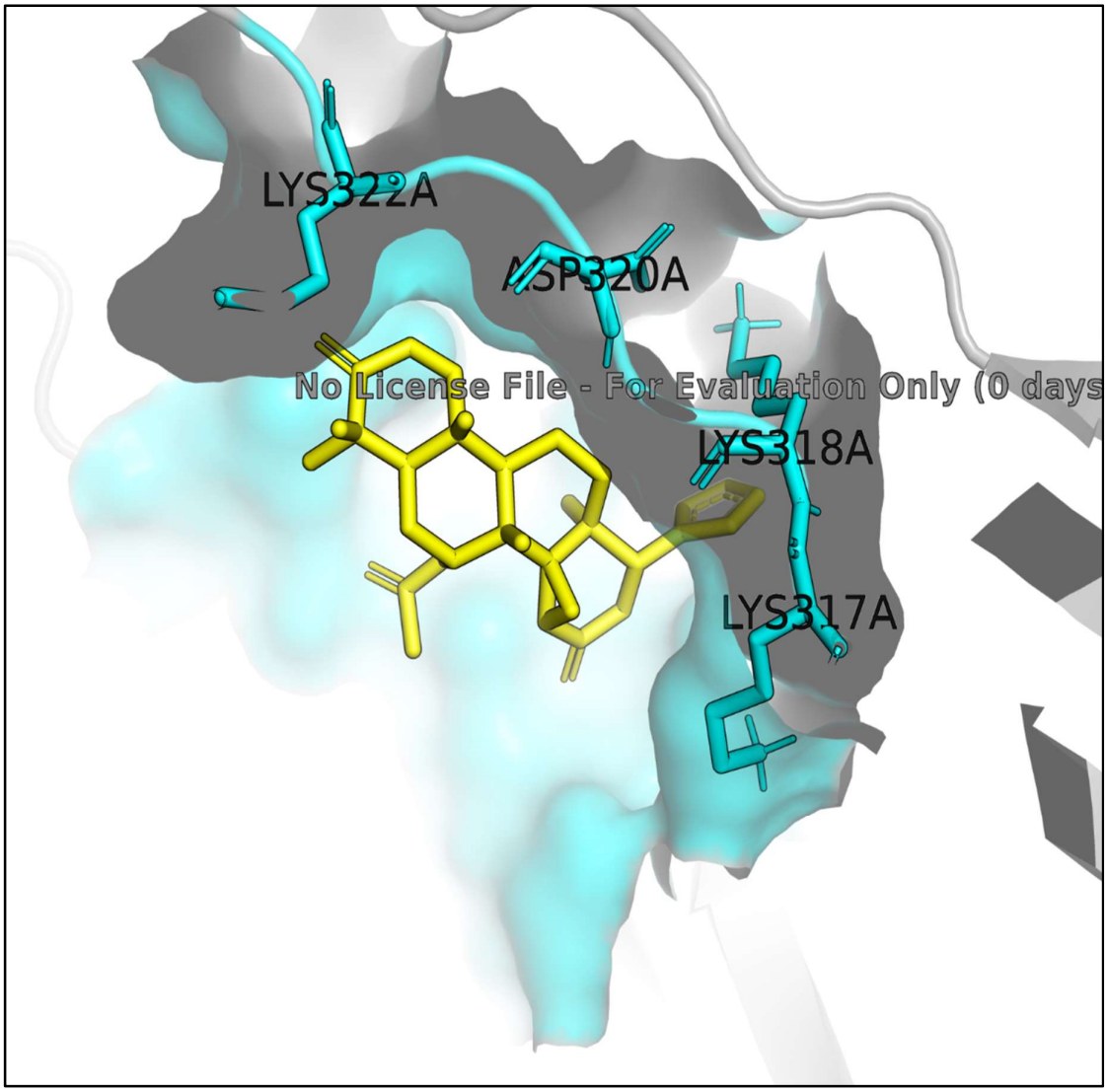

Figure 5. Three-dimensional binding pose of Gedunin within the allosteric site of PBP2a. Gedunin is shown as yellow sticks within the cyan semi-transparent binding pocket surface, while the protein backbone is represented as a grey cartoon. Key interacting residues including ASN223, ILE144, ASN308, SER306, and TRP205 are labelled. The figure was rendered using PyMOL version 2.5.

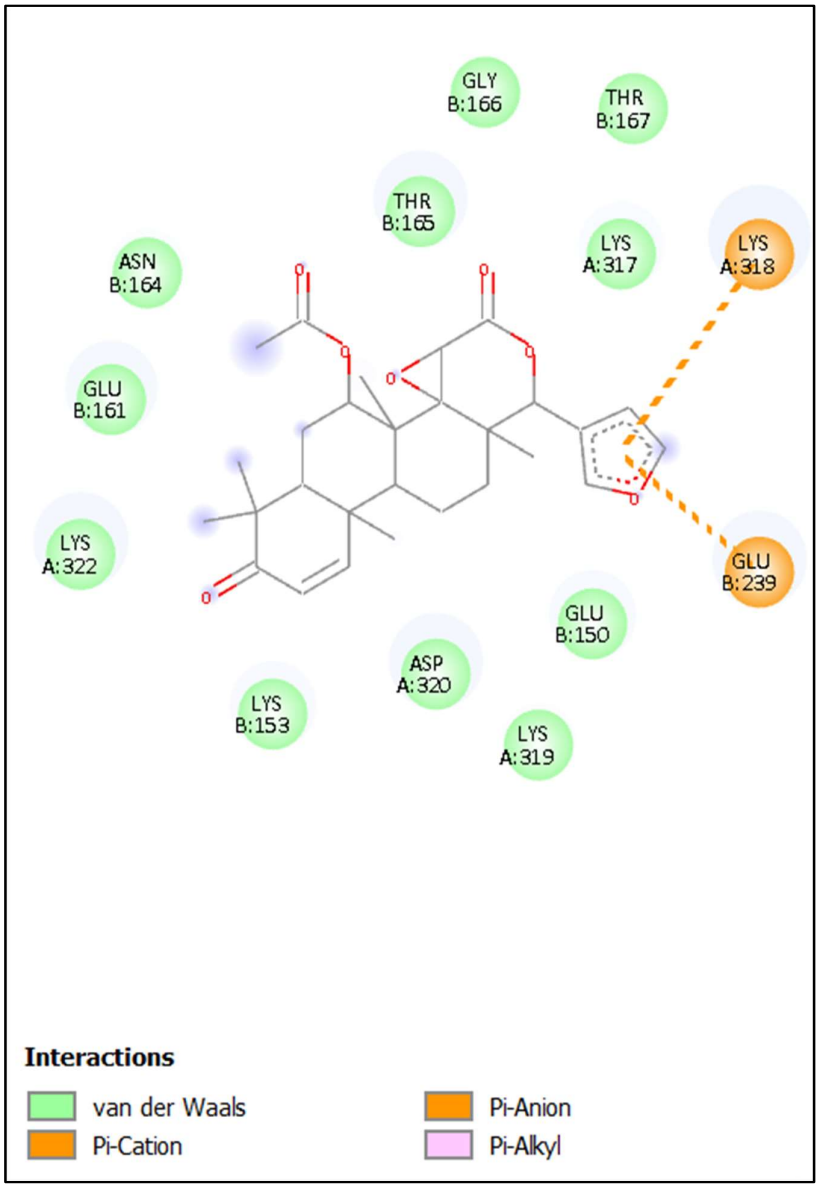

Figure 6. Two-dimensional schematic diagram showing the binding interactions between Gedunin and allosteric-site residues of PBP2a, generated using Discovery Studio Visualizer. π-anion and π -cation interactions appear orange and van der Waals contacts as light green circles.

3.5 ADMET Pharmacokinetic Profile

The physicochemical and pharmacokinetic properties of Gedunin, as predicted by SwissADME and pkCSM, are presented in Table 3 and Table 4 alongside the reference compounds. Gedunin has a molecular weight of 482.55 g/mol, which is within the commonly cited drug-like range (< 500 g/mol) according to Lipinski's Rule of Five. Gedunin exhibited zero Lipinski violations, indicating favourable drug-likeness and suitability for oral administration. GI absorption was predicted to be high, while BBB penetration was predicted to be absent, suggesting limited central nervous system exposure. Gedunin was predicted not to inhibit the key CYP450 isoforms CYP3A4 and CYP2D6, indicating a low potential for CYP-mediated drug–drug interactions. The compound was also predicted to be non-substrate for P-glycoprotein, which may support improved intracellular retention. Furthermore, Gedunin demonstrated acceptable aqueous solubility and moderate lipophilicity (consensus Log P = 2.50), supporting favourable absorption characteristics. No PAINS alerts were detected, indicating a low probability of assay interference. However, three Brenk alerts associated with reactive functional groups were identified, suggesting possible concerns regarding chemical reactivity or metabolic instability. The bioavailability score of Gedunin was predicted to be 0.55, indicating moderate oral bioavailability potential.

Table 3. Comparative physicochemical properties of Gedunin, oxacillin, and ceftaroline as predicted by SwissADME.

Property	Gedunin	Oxacillin	Ceftaroline
Molecular Weight (g/mol)	482.55	401.44	684.74
LogP	2.50	2.41	2.30
H-bond Donors	0	2	4
H-bond Acceptors	6	6	17
TPSA (Å²)	86.74	138.04	330
Rotatable Bonds	2	4	10
GI Absorption	High	High	Low
BBB Permeability	No	No	No
P-gp Substrate	No	Yes	Yes
CYP3A4 Inhibition	No	No	No
CYP2D6 Inhibition	No	No	No
Lipinski Violations	0	0	3
Water Solubility	Soluble / Moderately soluble	Soluble	Highly soluble
Bioavailability Score	0.55	0.55	0.17
PAINS Alerts	0	0	0
Brenk Alerts	3	1	2
Lead-likeness	No	Yes	No
Synthetic Accessibility	4.39	4.01	6.12

ADMET profiling indicated that Gedunin possesses favourable pharmacokinetic and safety properties (Table 4). It showed high Caco-2 permeability, no BBB penetration, and no inhibition of CYP3A4 or CYP2D6 enzymes. Gedunin was also predicted to be non-mutagenic with low hERG toxicity risk, although moderate oral toxicity was observed. Overall, these findings support its potential as a promising therapeutic candidate (Figure 5).

Table 4. Comparative ADMET properties of Gedunin, oxacillin, and ceftaroline as predicted by pkCSM.

ADMET Parameter	Gedunin	Oxacillin	Ceftaroline
Caco-2 Permeability	High permeability predicted	Moderate permeability	Low permeability
BBB Penetration	No	No	No
CYP450 Inhibition	No inhibition of CYP3A4/CYP2D6	Minimal inhibition predicted	Minimal inhibition predicted
hERG Toxicity	Low risk	Low risk	Low risk
AMES Toxicity	Negative (non-mutagenic)	Negative	Negative
Oral LD50 (mg/kg)	Moderate toxicity	Low toxicity	Low toxicity

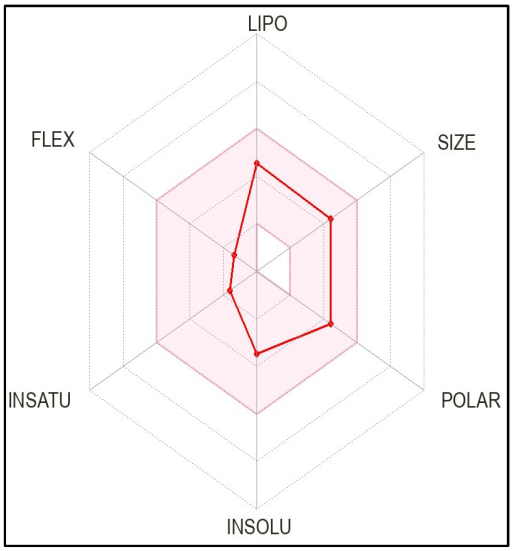

Figure 5. SwissADME bioavailability radar of Gedunin showing predicted drug-likeness properties including lipophilicity, size, polarity, flexibility, insolubility, and saturation. The pink region represents the optimal physicochemical space for oral bioavailability.

4. DISCUSSION

The present study explored the potential of Gedunin as an inhibitor of Penicillin-Binding Protein 2a (PBP2a), which plays a major role in methicillin resistance in MRSA. Using molecular docking In the analysis, Gedunin was observed to interact positively with both the active and allosteric sites of PBP2a, suggesting that it interferes with the normal functioning of the protein. Since PBP2a is responsible for the reduced effectiveness of β-lactam antibiotics in MRSA, the ability of Gedunin to bind with this protein is important for the development of new therapeutic strategies against resistant bacterial infections.

Before the main docking experiments, a test docking protocol was validated through re-docking of the co-crystallised ligand. The RMSD value obtained (0.537 Å) was well below the accepted threshold of 2.0 Å, indicating that the docking procedure used in this study was reliable and accurately reproduced ligand-binding poses. This provided confidence in the predicted binding interactions and docking scores obtained for Gedunin and the reference compounds.

Gedunin showed favourable binding affinity at both binding sites of PBP2a, with slightly stronger interaction observed at the active site. Although its docking scores were lower than those of oxacillin and ceftaroline, Gedunin was able to demonstrate meaningful interactions with residues located within functionally important regions of the protein. Protein–ligand interaction analysis have further supported the docking results. Gedunin formed hydrogen bonds, hydrophobic interactions, π-stacking interactions, and salt bridge interactions with several amino acid residues within the binding pockets. These interactions with residues are important because they contribute to the stability of the ligand–protein complex. Hydrophobic contacts observed with residues such as THR308A and ILE309A, along with π-stacking interaction with TRP205B, helps stabilise Gedunin within the active site cavity. Similarly, interactions at the allosteric site involving LYS317A, LYS318A, and ASP320A ensure that Gedunin can effectively occupy the regulatory pocket of PBP2a.

The ADMET analysis indicate promising drug-like properties for Gedunin. The compound followed Lipinski's Rule of Five without any violations and showed high predicted gastrointestinal absorption, suggesting good oral bioavailability potential. Additionally, Gedunin had low cardiotoxicity risk and no major inhibition of CYP450 enzymes, indicating a relatively favourable safety and pharmacokinetic profile. However, the presence of Brenk alerts and moderate oral toxicity suggests that structural optimisation and further pharmacological studies may still be required before considering therapeutic application.

Overall, the findings suggest that Gedunin possesses promising characteristics as a natural-product scaffold targeting PBP2a. However the present study has certain limited to a theoretical prediction of ligand binding and does not fully account for protein flexibility or dynamic conformational changes that occur under physiological conditions. In addition, the results obtained are computational predictions and therefore require experimental validation through in vitro antibacterial assays, MIC studies, enzyme inhibition experiments, and molecular dynamics simulations. Such studies would provide deeper insight into the stability, efficacy, and mechanism of action of Gedunin against MRSA.

5. CONCLUSION

Overall, this study highlights the potential of Gedunin as a candidate for future drug development against antibiotic-resistant *Staphylococcus aureus,* because it has promising binding potential against Penicillin-Binding Protein 2a (PBP2a), which is a key protein responsible for methicillin resistance. The molecular docking analysis showed that Gedunin can interact favourably with both the active and allosteric sites of PBP2a through hydrogen bonding, hydrophobic interactions, π-stacking, and salt bridge interactions. Although its binding affinity was slightly lower than that of the reference compounds oxacillin and ceftaroline, Gedunin was still able to occupy functionally important regions of the protein, indicating its potential as a natural inhibitor of PBP2a. Additionally, ADMET analysis showed favourable drug-like and pharmacokinetic properties, including high gastrointestinal absorption, low cardiotoxicity risk, and absence of major CYP450 inhibition. These results suggest that Gedunin can serve as a promising natural-product scaffold for the development of new anti-MRSA therapeutics. However, since the present work is entirely computational, further validation through in vitro antibacterial studies, enzyme inhibition assays, molecular dynamics simulations, and in vivo investigations is necessary to confirm the biological activity and therapeutic potential of Gedunin.

DECLARATIONS

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The author(s) declare no conflict of interest.

Data Availability

All protein structures used in this study are publicly available from the RCSB Protein Data Bank (rcsb.org). Ligand structures are available from PubChem (pubchem.ncbi.nlm.nih.gov). Docking configuration files and output poses are available from the corresponding author upon reasonable request.

Ethical Approval

This study is entirely computational and did not involve human participants, animal subjects, or biological samples. Ethical approval was not required.

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