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Molecular Docking Analysis of Sesquiterpenes Hydrocarbons from Merauke Agarwood (Aquilaria malaccensis) Targeting Penicillin-Binding Proteins in Acinetobacter baumanni

Analisis Penambatan Molekuler Hidrokarbon Seskuiterpen Gaharu Merauke terhadap protein pengikat penisilin pada Acinetobacter baumanii

Yulianto Ade Prasetya[1], Arif Luqman[2*]

[1]Diploma of Medical Laboratory Technology Study Program, Faculty of Health Science, Universitas Anwar Medika, Sidoarjo, Indonesia

[2]Department of Biology, Institut Teknologi Sepuluh Nopember, Surabaya, Indonesia

*Email: arif.luqman@its.ac.id

ABSTRACT

Background: *Acinetobacter baumannii is a critical nosocomial pathogen associated with a high level of antibiotic resistance, necessitating the exploration of alternative antibacterial candidates from natural sources. Merauke agarwood (Aquilaria malaccensis) essential oil contains various sesquiterpenes; however, molecular-level evidence targeting A. baumannii penicillin-binding proteins (PBPs) remains limited.*

Objective: *This study evaluated the interactions of selected sesquiterpene hydrocarbons, γ-cadinene, kessane, and α-gurjunene, from Merauke agarwood using an in silico approach.*

Methods: *Drug-likeness and ADMET properties were predicted using* ADMETLab 3.0*, while potential biological activities were assessed with PASS Online. Molecular docking was performed against A. baumannii PBP1a (3UE3) and PBP3 (3UDF) using CB-Dock2, followed by protein–ligand interaction analysis with PLIP.*

Results: *All compounds complied with Lipinski's rule and showed moderate quantitative estimates of drug-likeness, although high lipophilicity and plasma protein binding were predicted. Docking analysis revealed moderate binding affinities toward both PBPs (−6.2 to −6.7 kcal/mol) and identified conserved hydrophobic interaction regions involving recurrent amino acid residues within each protein. PASS predictions indicated higher probabilities of antibacterial-related activity than inactivity for all ligands*

Conclusions: *These sesquiterpene hydrocarbons from agarwood form stable interactions with A. baumannii PBPs, providing a structural basis for lead scaffolds in structure-based screening. Further studies on oxygenated derivatives, formulation strategies, and experimental validation are recommended. These sesquiterpene hydrocarbons from agarwood form stable interactions with A. baumannii PBPs, providing a structural basis for lead scaffolds in structure-based screening. Further studies on oxygenated derivatives, formulation strategies, and experimental validation are recommended.*

Keywords: *Acinetobacter baumannii, Aquillaria malaccensis, Merauke agarwood, Sesquiterpene hydrocarbons*

ABSTRAK

Latar Belakang: *Acinetobacter baumannii* merupakan patogen nosokomial kritis yang dengan tingkat resistensi antibiotik yang tinggi, sehingga diperlukan eksplorasi kandidat antibakteri alternatif dari sumber alam. Minyak atsiri gaharu Merauke dari *Aquilaria malaccensis* kaya akan hidrokarbon seskuiterpena, bukti interaksi molekuler dengan penicillin-binding protein (PBP) pada *A. baumannii* masih terbatas.

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Tujuan: Penelitian ini bertujuan untuk mengevaluasi interaksi senyawa sesquiterpene hydrocarbons terpilih γ-cadinene, kessane, dan α-gurjunene—dari gaharu Merauke menggunakan pendekatan *in silico*.
Metode: Prediksi drug-likeness dan ADMET dilakukan dengan ADMETLab 3.0, sedangkan potensi aktivitas biologis diprediksi melalui PASS Online. Molecular docking dilakukan terhadap PBP1a (3UE3) dan PBP3 (3UDF) *A. baumannii* menggunakan CB-Dock2, diikuti analisis interaksi protein–ligan menggunakan PLIP.
Hasil: Seluruh senyawa memenuhi aturan Lipinski dan menunjukkan estimasi kuantitatif drug-likeness yang sedang, meskipun diprediksi memiliki lipofilisitas dan ikatan protein plasma yang tinggi. Analisis docking menunjukkan afinitas ikatan sedang terhadap kedua PBP (−6,2 hingga −6,7 kcal/mol) serta mengidentifikasi daerah interaksi hidrofobik konservatif yang melibatkan residu asam amino berulang pada masing-masing protein. Prediksi PASS menunjukkan probabilitas aktivitas terkait antibakteri yang lebih tinggi dibandingkan probabilitas inaktivitas pada seluruh ligan.
Kesimpulan: Senyawa hidrokarbon seskuiterpena dari gaharu membentuk interaksi yang stabil dengan PBP A. baumannii, sehingga berpotensi menjadi kerangka awal (lead scaffold) dalam structure-based screening. Penelitian lanjutan terkait derivat teroksigenasi, strategi formulasi, dan validasi eksperimental masih diperlukan.

Kata kunci: *Acinetobacter baumannii, Agarwood Merauke, Aquillaria malaccensis, Hidrokarbon Seskuiterpen*

INTRODUCTION

Acinetobacter baumannii is a Gram-negative, non-fermentative, aerobic coccobacillus that has emerged as one of the most problematic pathogens associated with hospital-acquired (nosocomial) infections worldwide.[1,2] These characteristics, combined with its remarkable ability to acquire resistance determinants, have positioned *A. baumannii* as a critical threat to global public health.[3] Clinically, *Acinetobacter baumannii* is frequently associated with ventilator- associated pneumonia, bloodstream infections, urinary tract infections, and wound infections, particularly among critically ill patients in intensive care units (ICUs).[3] The World Health Organization (WHO) has classified carbapenem-resistant *A. baumannii* as a Priority 1 (Critical) pathogen, highlighting the urgent need for new therapeutic strategies.[4] Globally, the prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *A. baumannii* has increased dramatically over the past two decades, with reported resistance rates exceeding 50% in several regions of Asia, the Middle East, Southern Europe, and Latin America.[5]

In Indonesia, *A. baumannii* is consistently reported as one of the dominant causes of nosocomial infections, particularly in tertiary hospitals.[6] Surveillance studies from Indonesian referral hospitals have demonstrated high resistance rates to β-lactams, aminoglycosides, and fluoroquinolones, with carbapenem resistance becoming increasingly prevalent[3]. This alarming trend underscores the importance of exploring alternative antibacterial sources, including bioactive compounds derived from medicinal plants.

Natural products are a key source of structurally diverse bioactive compounds[7]. Agarwood Merauke (*Aquilaria malaccensis*) is notable for its rich phytochemical profile, formed through plant defense responses that produce resinous compounds9. Its essential oil is dominated by sesquiterpenes and chromone derivatives.[8,9] Chemically, agarwood essential oil is characterized by a complex mixture of sesquiterpenes and chromone derivatives, with sesquiterpenes constituting the dominant fraction.[10]

These compounds are classified as sesquiterpene hydrocarbons and oxygenated sesquiterpenes, both contributing to agarwood bioactivityl.[11] Merauke agarwood (Papua, Indonesia) remains underexplored, with studies reporting unique sesquiterpenes such

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as γ-cadinene, kessane, and α-gurjunenes.[12] Despite traditional medicinal use, scientific evaluation—especially against nosocomial pathogens—is still limited, highlighting its potential for developing local antibacterial agents.[13]

Penicillin-binding proteins (PBPs) are key antibacterial targets involved in peptidoglycan synthesis, particularly transpeptidation and transglycosylation14. In *A. baumannii*, PBP alterations contribute to β-lactam resistance, highlighting their relevance for novel drug discovery. Available structures (PDB: 3UE3 and 3UDF) support structure-based approaches.In silico molecular docking is widely used to evaluate ligand–protein interactions and screen antibacterial candidates prior to experimental studies. Previous works have applied docking to plant-derived sesquiterpenes against PBPs, DNA gyrase, and other targets with promising results.[15,16]

This study investigates binding of γ-cadinene, kessane, and α-gurjunene from Merauke *Aquilaria malaccensis* with *A. baumannii* PBP1a (PDB: 3UE3) and PBP3 (3UDF) using CB-Dock2 docking. The findings of this study are expected to provide molecular-level insights into the antibacterial potential of Merauke agarwood constituents and to support further experimental validation and formulation development, including future nanoemulsion-based antibacterial applications.

METHODS

Study Design and Computational Platform

This study employed a structure-based *in silico* approach to evaluate interactions between sesquiterpene hydrocarbons from Merauke agarwood and PBPs of *Acinetobacter baumannii*. The workflow integrated molecular docking, interaction profiling, and ADMETlab 3.0 prediction to assess antibacterial potential prior to experimental validation.

The study was conducted from July to September 2025 at the Laboratory of Microbiology and Biotechnology, Universitas Anwar Medika. Computational analyses were performed using web-based tools to ensure reproducibility. A sequential workflow was applied, including ligand–protein preparation, drug-likeness and ADMET prediction, activity estimation, molecular docking, and interaction analysis, enabling systematic and comparative evaluation of ligand–PBP interactions.

Data Source and Sampling Procedure

The selected ligands, including γ-cadinene, kessane, and α-gurjunene, were obtained from PubChem and verified using molecular formulas and canonical SMILES[10]. Ligands were standardized and geometry-optimized using Open Babel, then maintained in neutral form due to their non-polar nature.[17] The target proteins were PBP1a and PBP3 of *A. baumannii*, retrieved from the RCSB Protein Data Bank as PDB IDs 3UE3 and 3UDF.[17,18] Meropenem was used as a reference control ligand and processed using the same protocol.

Variables of the Study

The independent variables were the tested ligands and meropenem as control. The dependent variables were binding energy, binding cavity, interacting amino acid residues, interaction type, ADMET properties, predicted biological activity, and RMSD values from docking validation.

Measurenment and Instruments

Drug-likeness and ADMET properties were predicted using ADMETlab 3.0 based on canonical SMILES.[19] The evaluated parameters included molecular weight, LogP, hydrogen bond donors and acceptors, TPSA, absorption, distribution, and rule-based drug-likeness compliance.[20] Biological activity was predicted using PASS Online by comparing Pa and Pi values, with Pa > Pi indicating probable activity.[21,22,23] Antibacterial and enzyme inhibition activities were prioritized. These predictions complemented

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docking results and provided preliminary insight prior to experimental validation. Molecular docking was performed using CB-Dock2 (https://cadd.labshare.cn/cb-dock2)[24], which integrates cavity detection and docking. Protein structures (3UE3, 3UDF) and optimized ligands were submitted for analysis.

Docking was conducted in blind mode, allowing automatic identification of binding cavities, with poses ranked by binding energy.[25] The best pose was selected based on the lowest energy and relevance to the PBP active site. All procedures were applied consistently for comparative analysis. To ensure biological relevance, the detected docking cavities were further examined to confirm their correspondence with the catalytic sites of the penicillin-binding proteins. The positions of the docked ligands were evaluated relative to the conserved catalytic serine residues and compared with the known β-lactam binding pocket reported for PBP structures.

For provide a comparative reference for docking affinity, Meropenem, were included as control ligands. The antibiotic structures were obtained from the PubChem database and subjected to the same docking protocol as the investigated sesquiterpene compounds against PBP1a (3UE3) and PBP3 (3UDF). This comparison allowed the binding affinities of the natural compounds to be interpreted relative to established PBP inhibitors.[21]

Data Collection

Ligand structures were collected from PubChem, while protein structures were retrieved from the RCSB Protein Data Bank. The prepared ligands and proteins were submitted to CB-Dock2 for blind docking. Native ligands from 3UE3 and 3UDF were re-docked into their respective binding sites to validate the docking protocol. RMSD values below 2.0 Å were considered acceptable.

Ethical Considerations

This study did not involve human participants, animal subjects, clinical specimens, or identifiable personal data. Therefore, ethical clearance was not required. All data were obtained from publicly available databases.

Data Analysis

Docking results were analyzed descriptively by comparing binding energy, predicted cavity, interaction residues, and interaction types. Ligand positions were evaluated relative to the conserved catalytic serine residues and β-lactam binding pocket of PBPs. ADMET and PASS results were used as supporting data to identify compounds with the most promising antibacterial potential.

RESULTS

Three-Dimensional Structure of Major Sesquiterpen Hydrocarbons in Merauke Agarwood Oil

Figure 1 shows the 3D structures of γ-cadinene, kessane, and α-gurjunene ($C_{15}H_{24}$), classified as non-oxygenated sesquiterpenes. γ-cadinene is more flexible (bicyclic), while kessane and α-gurjunene are more rigid (polycyclic), influencing binding compatibility. Their non-polar nature indicates interactions are dominated by hydrophobic and van der Waals forces. These compounds are typical constituents of agarwood oil and are suitable as ligands for in silico studies targeting *A. baumannii* PBPs.[28]

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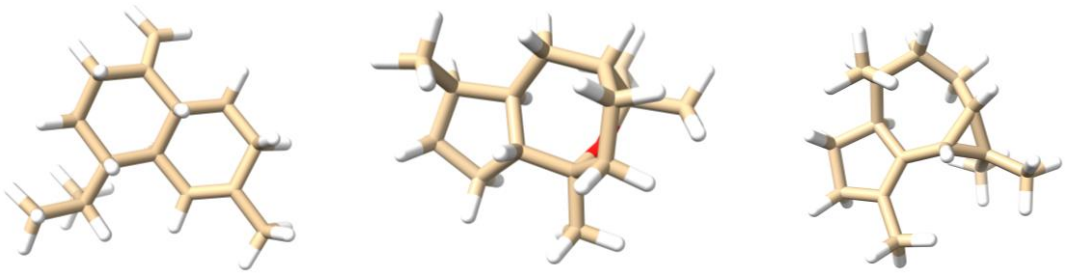

γ-cadinene Kessane α-gurjunene

Figure 1. Three-dimensional structure of the hydrocarbons sesquiterpens from *Aquilaria malaccencis*

Drug- Likeness and ADMET Profile

Table 1 summarizes the drug-likeness and ADMET properties of γ-cadinene, kessane, and α-gurjunene predicted using ADMETlab 3.0. All compounds show low molecular weight and high lipophilicity, reflecting typical hydrophobic sesquiterpene characteristics.[20] Low TPSA indicates limited polarity but favorable membrane permeability, and all comply with Lipinski's rule with moderate drug-likeness. Absorption is moderate with strong P-glycoprotein inhibition. High plasma protein binding (>95%) suggests wide distribution but low free drug fraction, while kessane shows higher BBB penetration. The compounds may interact with CYP450 enzymes and display high metabolic stability, with rapid clearance and short half-lives (<1.2 h). Toxicity risks are moderate, with no high-risk indications.

Table 1. Predicted physicochemical, pharmacokinetic (ADMET), and drug-likeness profile of Hydrocarbons sesquiterpenes from *Aquilaria malaccensis* using ADMETlab 3.0

Category		γ- cadinene	Kessane	α- Gurjunene
Compund Identity	MW (g/mol)	204.19	222.2	204.19
	LogP	4.59	4.472	5.358
	TPSA (Å²)	0.0	9.23	0.0
	Lipinski's Rule	Accepted	Accepted	Accepted
Drug-likeness	QED	0.548	0.601	0.513
	SAscore	1.0	1.0	1.0
	Fsp^3	0.733	1.0	0.867
Absorption	Caco-2 Permeabilty (×10⁻⁶ cm/s)	-4.541	-4.567	-4.722
	MDCK Permeability (×10⁻⁶ cm/s)	0.0	0.0	0.0
	P-gp inhibitor (μM)	+++	++	+++
	HIA (%)	---	---	---
Distribution	PPB (%)	96.9	95.6	96.1
	BBB Permeability	---	+++	- ---
	VDss (L/kg)	3.3	3.014	1.705
	CYP2C19 inhibitor (μM)	+++	+	+++
Metabolism	CYP3A4 subtrate	-	+++	++
	CYP2C9 Inhibitor	--	+	+
	HLM Stability (μL/min/mg)	+++	+++	+++

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	Category	γ- cadinene	Kessane	α- Gurjunene
Excretion	Cl_{plasma} μL/min/kg	11.528	10.674	11.78
	Half-life (T1/2) (jam)	1.011	1.187	0.901
	hERG Blockers (10 mM)	0.433	0.529	0.307
	Human Hepatotoxicity	0.597	0.449	0.597
Toxicity	Ames Toxicity	0.203	0.571	0.468
	Carcinogenicity	0.644	0.753	0.852
	Neurotoxicity	0.45	0.544	0.126
	Hematotoxicity	0.601	0.412	0.679

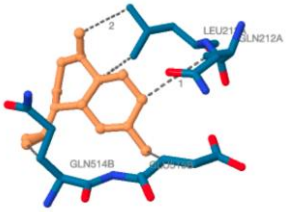
Protein-Ligand Docking Interaction

For validate the docking protocol, native co-crystallized ligands were re-docked into PBP binding sites, and RMSD between crystallographic and predicted poses was calculated. RMSD values of 1.76 Å (PBP1a, 3UE3) and 1.52 Å (PBP3, 3UDF) were below the 2.0 Å threshold, confirming reliable reproduction of experimental binding modes. Docking protocol validation was performed by re-docking native ligands into PBP1a (3UE3) and PBP3 (3UDF). RMSD values of 1.76 Å and 1.52 Å (<2.0 Å) confirm reliable reproduction of experimental binding modes. The validated protocol was then applied to γ-cadinene, kessane, and α-gurjunene against A. baumannii PBPs.

Figure 2 shows that all ligands occupy the binding pockets and interact mainly through hydrophobic and van der Waals interactions with residues such as GLN514, GLN212, LEU213 (PBP3), and LEU372, TYR539 (PBP1a). The predicted binding sites correspond to the catalytic pocket containing the conserved SXXK motif and catalytic serine responsible for β-lactam acylation. The docked ligands are positioned in proximity to this catalytic serine and overlap with the reported β-lactam binding pocket, suggesting that the interactions occur within the functional active site rather than a non-functional hydrophobic cavity.

Comparative Docking Energies

Table 2 summarizes the docking results of γ-cadinene, kessane, and α-gurjunene against PBP1a and PBP3 of Acinetobacter baumannii. All ligands showed comparable binding energies (−6.2 to −6.7 kcal/mol). For PBP1a, similar affinities (−6.3 to −6.4 kcal/mol) were observed, with shared interactions involving GLN212A, LEU213A, and GLN514B. For PBP3, kessane and α-gurjunene exhibited the strongest binding (−6.7 kcal/mol), with consistent interactions at TYR450A, HIS530A, and TYR539A. PASS predictions indicated moderate activity (Pa: 0.459–0.548) with low inactivity probabilities. Overall, the ligands demonstrated comparable binding affinities and shared key interacting residues across both targets.



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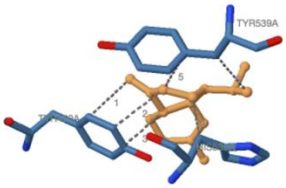

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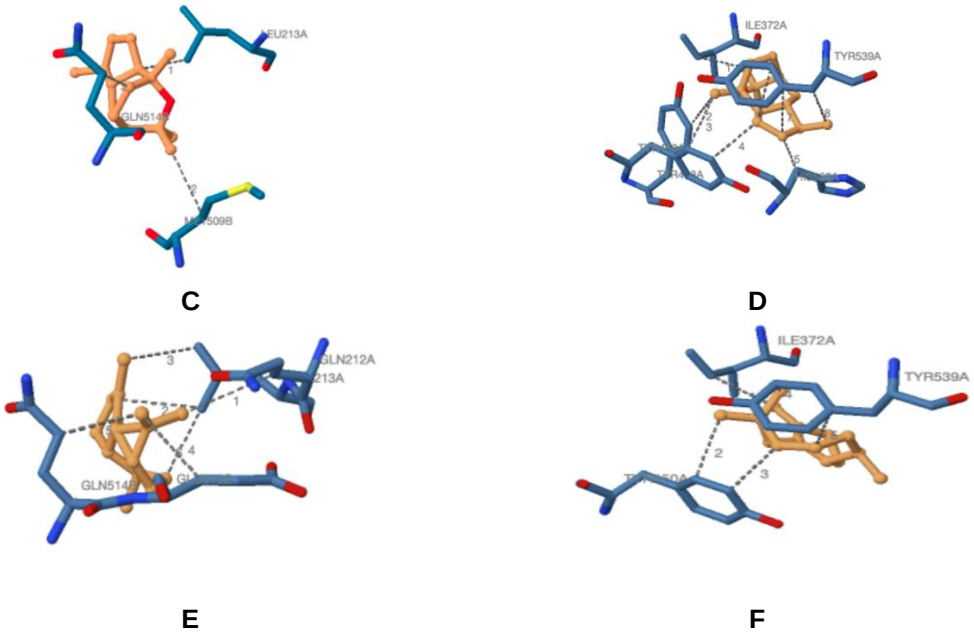

Figure 2. Predicted docking interactions of sesquiterpenes hydrocarbons with *Acinetobacter baumannii* PBP3 (3UDF, left) and PBP1a (3UE3, right). γ- cadinene (A, B); (C, D) Kessane; (E, F) α-gurjunene. Dashed lines indicated close-contact interactions between the ligands (orange) and surrounding amino acid residues (blue), primarily respresenting hydrophobic and van der Waals interactions within the predicted binding pockets

Table 2. Summary of docking and PASS Online results of three hydrocarbon sesquiterpenes on PBP1a and PBP3 of *Acinetobacter baumanni*

Compound	Receptor	Binding Energi (ΔG, kcal/mol)	Key Interacting Amino Acids	Pa	Pi
γ-cadinene	PBP1a	-6.3	Hydrophobic interactions: 212A (GLN); 213A (LEU); 514B (GLN); 515B (GLU)	0.505	0,021
	PBP3	-6.2	Hydrophobic interactions: 450A (TYR);530A (HIS); 539A (TYR)		
Kessane	PBP1a	-6.3	Hydrophobic interactions: 213A (LEU); 509B (MET); 514B (GLN)	0.459	0,032
	PBP3	-6.7	Hydrophobic interactions: 372A (ILE); 448A (TYR); 450A (TYR); 530 A (HIS); 539A (TYR)		
α-gurjunene	PBP1a	-6.4	Hydrophobic interactions: 212A (GLN); 213A (LEU); 514B (GLN), 515B (GLU)	0.548	0,014
	PBP3	-7	Hydrophobic interactions: 372A (ILE); 450A (TYR); 539A (TYR)		
Meropenem	PBP 1a	-8.4	Interaction with catalytic pocket residues: 370A(SER) 373A(LYS); 526A(THR); 539A (TYR)	0.953	0,000
	PBP3	-8.7	Interaction with catalytic pocket residues: 336A (SER); 339A (LYS); 528A (THR); 532A (TYR)		

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DISCUSSION

The three-dimensional structures of γ-cadinene, kessane, and α-gurjunene represent typical sesquiterpene hydrocarbons in agarwood (Aquilaria malaccensis), characterized by a C_{15} backbone and absence of oxygenated functional groups, distinguishing them from more reactive oxygenated sesquiterpenes.[29]

Despite sharing the same molecular class, γ-cadinene, kessane, and α-gurjunene exhibit distinct conformations, with γ-cadinene being more flexible and the others more rigid.[30] This structural variation, along with high sp^3 character, may enhance adaptability and influence binding within protein pockets. The absence of polar groups indicates that interactions are mainly driven by hydrophobic forces rather than hydrogen bonding.[31] This is typical in terpene–protein complexes and may support stable binding within hydrophobic regions of penicillin-binding proteins without directly competing with β-lactam antibiotics.[4] From a phytochemical perspective, γ-cadinene, kessane, and α-gurjunene are consistent with reported major sesquiterpene hydrocarbons in agarwood essential oil.[32] Although less bioactive than oxygenated counterparts, their abundance and stability make them suitable for comparative in silico studies on bacterial targets. The structural features in Figure 1 support the selection of these compounds as model sesquiterpenes for docking studies. Their distinct conformations enable comparison of how structural differences influence binding orientation and interactions with *Acinetobacter baumannii* penicillin-binding proteins.

The ADMETlab 3.0 profiles indicate that γ-cadinene, kessane, and α-gurjunene exhibit typical sesquiterpene pharmacokinetics, with low molecular weights (204–222 g/mol) and compliance with Lipinski's rule. Their high lipophilicity (LogP 4.47–5.36) reflects a strong hydrophobic character common in non-oxygenated terpenoid.[33] The high lipophilicity (LogP up to 5.36), near-zero TPSA values, and strong plasma protein binding (>95%) further suggest limited aqueous solubility and a reduced free drug fraction in systemic circulation. These properties may pose challenges for oral bioavailability and highlight the need for formulation strategies or structural modification in future studies.

Low TPSA values indicate limited polarity and hydrogen-bonding capacity, suggesting poor aqueous solubility but favorable membrane diffusion. Moderate QED (0.51–0.60) and high Fsp^3 values support structural saturation and adaptability within hydrophobic binding pockets.[34] Absorption predictions indicate limited intestinal permeability and strong P-glycoprotein inhibition, which may enhance intracellular accumulation but raise drug–drug interaction concerns. The absence of predicted human intestinal absorption highlights uncertainty in oral bioavailability, a common limitation of lipophilic terpenes.[20]

Distribution analysis shows high plasma protein binding (>95%), indicating reduced free drug fraction but prolonged systemic presence. Kessane is predicted to cross the blood–brain barrier, while γ-cadinene and α-gurjunene show limited penetration, with moderate to extensive tissue distribution.[35] Metabolism predictions indicate potential interactions with cytochrome P450 enzymes, where γ-cadinene and α-gurjunene may inhibit CYP2C19, and kessane may act as a CYP3A4 substrate. All compounds exhibit high metabolic stability. Excretion profiles suggest rapid clearance and short half-lives, consistent with small, lipophilic molecules undergoing hepatic metabolism.[36]

Toxicity predictions indicate moderate risks for hERG inhibition, hepatotoxicity, and genotoxicity, without extreme values, although variability in carcinogenicity and neurotoxicity highlights the need for experimental validation. Overall, the profiles are acceptable for early-stage in silico screening. Docking results show that γ-cadinene, kessane, and α-gurjunene bind to PBP1a (3UE3) and PBP3 (3UDF) with similar affinities (−6.2 to −6.7 kcal/mol), indicating comparable binding strength37. Shared interacting

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residues were observed, including GLN212A, LEU213A, and GLN514B in PBP1a, and TYR450A, HIS530A, and TYR539A in PBP3, suggesting conserved binding regions.[37] The interaction pattern is consistent with the hydrophobic nature of these sesquiterpenes, where binding is mainly driven by hydrophobic and van der Waals interactions rather than hydrogen bonding. Residues such as leucine, isoleucine, tyrosine, histidine, and glutamine support a mixed hydrophobic–polar environment within the binding pocket.

Comparable studies show essential-oil terpenes bind PBPs with moderate affinity via hydrophobic interactions, supporting their use in early-stage screening of *A. baumannii* targets. γ-cadinene-type compounds also have reported antibacterial activity, reinforcing their relevance.The consistent binding to 3UE3 and 3UDF, shared residue interactions, and favorable activity signals (Pa > Pi) support prioritization of these sesquiterpenes for further structural and experimental validation.
Hydrophobic interactions dominate, consistent with the lipophilic, non-polar nature of sesquiterpenes.

These compounds typically bind PBPs with moderate affinity via hydrophobic complementarity rather than hydrogen bonding, unlike β-lactam antibiotics that rely on strong polar interactions.[39] The predicted PASS activity values indicate that the investigated ligands may possess moderate antibacterial potential, as all three compounds showed Pa values higher than Pi values. Among them, α-gurjunene exhibited the highest Pa value, which is consistent with its slightly stronger docking affinity toward both PBP targets. However, the Pa values fall within a borderline to moderate range, and therefore the PASS predictions should be interpreted cautiously as preliminary indications rather than strong evidence of antibacterial activity.[23]

CONCLUSION

This in silico study demonstrates that γ-cadinene, kessane, and α-gurjunene from agarwood (*Aquilaria malaccensis*) bind to Acinetobacter baumannii PBP1a (3UE3) and PBP3 (3UDF) with comparable affinities and conserved interaction regions within catalytic pockets. ADMET analysis indicates acceptable physicochemical properties but highlights limitations related to lipophilicity, absorption, and protein binding. These findings support the role of sesquiterpene hydrocarbons as comparative ligands in structure-based screening of *A. baumannii* PBPs. Further studies involving molecular dynamics simulations, structure optimization, and experimental antibacterial assays are required to validate the predicted interactions and clarify their potential biological relevance.

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