JPPIPA 12(1) (2026)

Jurnal Penelitian Pendidikan IPA

http://jppipa.unram.ac.id/index.php/jppipa/index

Investigation of Active Compounds in Vetiver Oil against Penicillin-Binding Protein 1 of *Acinetobacter baumannii*: A Bioinformatics Approach

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Received: September 03, 2025
Revised: December 01, 2025
Accepted: January 25, 2026
Published: January 31, 2026

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DOI: 10.29303/jppipa.v12i1.12734

Abstract: *Acinetobacter baumannii* is responsible for various infections in humans and is well known for its ability to develop antibiotic resistance. Therefore, exploring natural compounds, such as those found in vetiver oil, is crucial. Vetiver oil contains numerous compounds, including sesquiterpenes and sesquiterpenols; however, their activity against *A. baumannii* has not been previously reported. This research aims to investigate the potential of vetiver oil compounds in inhibiting penicillin-binding protein 1 (PBP1) in *Acinetobacter baumannii* using a bioinformatics approach. The methodology involved obtaining the 3D structure of PBP1 from the Protein Data Bank (PDB), while vetiver oil compounds were retrieved from the PubMed database. The first screening was conducted using ADMET Lab 3.0 to assess drug-likeness parameters, absorption, distribution, metabolism, excretion, and toxicity. The best-screened compounds were further evaluated through molecular docking using the Proteins Plus webserver to determine the binding residues. The results showed that vetiver oil compounds, including nootkatone, khusimol, and vetivenic acid, formed hydrogen bonds and hydrophobic interactions. Nootkatone, khusimol, and vetivenic acid have potential as inhibitors of PBP1; however, further in vitro studies are required to directly assess their biological activity and effectiveness.

Keywords: *Acinetobacter baumanii*; Antibiotic resistance; Bioinformatics; Penicillin-binding protein 1; Vetiver oil

Introduction

Acinetobacter baumannii is a Gram-negative, coccobacillus-shaped bacterium measuring approximately 0.9–1.5 µm × 0.6–0.9 µm (Morris et al., 2019). Unlike other Gram-negative bacteria, *A. baumanii* possesses lipooligosaccharides (LOS) (Bodea et al., 2022) in its outer membrane, which distinguishes it from other members of its class (Harding et al., 2018). This opportunistic pathogen is a major cause of infections in humans, including ventilator-associated pneumonia (Tsioutis et al., 2016), bloodstream infections (Boll et al., 2016), urinary tract infections, meningitis (Hamidian & Nigro, 2019), and skin infections (Morris et al., 2019). A significant challenge in treating *A. baumanii* infections is its ability to develop resistance to multiple antibiotics, leading to increased morbidity (Morris et al., 2019), mortality, and healthcare costs (Whiteway et al., 2022). Exploring natural compounds is crucial in combating the rise of antimicrobial resistance. One potential source of antibacterial agents is vetiver essential oil, which is derived from the roots of *Vetiveria zizanoides*, a species belonging to the Poaceae family (David et al., 2023).

Indonesia is a major producer of vetiver oil, along with Haiti and India, with an estimated annual production reaching 140 million tons per year (Nur

How to Cite:
Prasetya, Y. A., Setyawati, P., Wahjudi, M., & Kok, T. Investigation of Active Compounds in Vetiver Oil against Penicillin-Binding Protein 1 of Acinetobacter baumannii: A Bioinformatics Approach. *Jurnal Penelitian Pendidikan IPA*, *12*(1), 191-199. https://doi.org/10.29303/jppipa.v12i1.12734

Amalia et al., 2021). Vetiver oil primarily contains sesquiterpenes, sesquiterpenones, and sesquiterpenols (Chahal et al., 2015). It is widely used in the cosmetic and dermatological industries due to its fragrance and therapeutic properties (Han & Parker, 2017). Several studies have demonstrated its antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae,* and *Staphylococcus aureus* (Khater et al., 2018). However, its potential antibacterial activity against *A. baumannii* has not yet been investigated through an *in-silico* approach.

From a biophysical perspective, the membrane disruption theory explains that lipophilic essential oil components partition into the phospholipid bilayer of bacterial membranes, disturbing lipid packing, increasing membrane fluidity, and causing leakage of ions, ATP, and metabolites, ultimately leading to cell death (Grahl et al., 2021; Luo & Song, 2021). In Gram-negative bacteria, whose outer membrane normally provides a permeability barrier, sesquiterpenes such as nootkatone and vetivenic acid (Mercurio et al., 2019) can increase membrane permeability and weaken the lipopolysaccharide or lipooligosaccharide layer, thereby facilitating the entry of antibacterial compounds and sensitizing bacteria to additional stress (Munakata et al., 2022; Sauvage & Terrak, 2016).

In addition to membrane disruption, the multi-target inhibition theory supports the antibacterial role of vetiver oil. Sesquiterpenoids are known to interact with bacterial enzymes involved in energy metabolism, cell wall synthesis, and redox homeostasis (Singh et al., 2018). For example, ketone- and alcohol-containing sesquiterpenes can bind to protein active sites through hydrogen bonding and hydrophobic interactions, inhibiting key enzymes such as dehydrogenases, proteases, and cell wall biosynthetic enzymes (Qin et al., 2024). This multi-target mechanism reduces the likelihood of rapid resistance development compared with single-target antibiotics.

Furthermore, the quorum sensing and biofilm inhibition theory explains how essential oils, including vetiver oil, suppress bacterial communication systems that regulate virulence and biofilm formation (Shahavi et al., 2016). Biofilms protect bacteria from antibiotics and immune responses, and sesquiterpenes have been shown to interfere with quorum sensing signaling molecules, reduce extracellular polymeric substance (EPS) production, and destabilize established biofilms (Sauvage & Terrak, 2016). This property is particularly valuable against hospital pathogens such as *Acinetobacter baumannii*, which relies heavily on biofilm formation for persistence on medical devices and hospital surfaces (Kyriakidis et al., 2021).

This research aims to explore the bioactive compounds in vetiver essential oil that may inhibit *A. baumannii* using a bioinformatics-based approach. Penicillin-Binding Protein 1 (PBP1) is used in docking analysis because it is a key enzyme involved in bacterial cell wall synthesis and serves as a primary target for beta-lactam antibiotics such as imipenem (Mahmoud et al., 2021). By docking compounds to PBP1, researchers can evaluate the potential of these compounds as inhibitors of bacterial cell wall formation, which is essential in the development of novel antibacterial agents. Moreover, due to its well-characterized mechanism of action, PBP1 is frequently used as a reference target in studies of new compounds, including natural or synthetic substances, to assess their binding affinity and potential antimicrobial activity. The findings from this research are expected to identify promising vetiver-derived compounds, which can be further examined through *in vitro* studies to validate their antibacterial activity and potential therapeutic applications.

Method

Sample Retrieval

The workflow of the in-silico screening of vetiver oil compounds against PBP1 of *Acinetobacter baumannii* is shown Figure 1. This study was conducted using a laptop with the macOS operating system and several web servers, including Protein Data Bank (https://www.rcsb.org/) (Burley et al., 2017), PubChem (https://pubchem.ncbi.nlm.nih.gov/) (Kim et al., 2016), ADMETLab (https://admetlab3.scbdd.com/), and docking molecular and analysis profil interaction protein-ligand (https://cadd.labshare.cn/cb-dock2/index.php)(Liu et al., 2020). The target protein used in this study was penicillin-binding protein 1 (PBP1) with PDB ID: 3UE3, obtained from the Protein Data Bank. The ligands analyzed included nootkatone (CID 1268142), khusimol (CID 167519), and vetivenic acid (CID 85973), obtained from PubChem.

Drug Likeness Analysis

The prediction of these three ligands was performed using the ADMET Lab 3.0 web server (Xiong et al., 2021), evaluating multiple parameters, including compound identity, which consists of molecular weight (MW), LogP, and topological polar surface area (TPSA). Drug-likeness properties were assessed through Lipinski's rule of five, quantitative estimate of drug-likeness (QED), and fraction of sp^3 hybridized carbons (Fsp^3). Absorption parameters included Caco-2 permeability, MDCK permeability, P-glycoprotein (Pgp) inhibition, and human intestinal absorption (HIA). Distribution properties were evaluated by plasma protein binding (PPB), blood-brain barrier (BBB) permeability, and volume of distribution (VDss).

Excretion factors included plasma clearance (CLplasma) and half-life ($T_{1/2}$). Toxicity predictions covered hERG inhibition, hepatotoxicity, Ames test (mutagenicity), carcinogenicity, neurotoxicity, and hematotoxicity.

Antibacterial Probability Prediction

Probability prediction of biological activity as an antibacterial agent on the bioactive compounds of nootkatone, khusimol, and vetivenic acid was performed using the PASS web server (http://way2drug.com/PassOnline/) (Lagunin et al., 2000). The threshold prediction with probability activation (Pa) score > 0.3 was considered as potential antibacterial. The probability of inactivity (Pi) was calculated to indicate the likelihood that the compound would not exhibit the predicted activity.

Virtual Screening, Chemical Interaction, and 3D Molecular Visualization

The preparation of the target protein (PBP1) and ligands was performed using ChimeraX software (Pettersen et al., 2021). The vetiver oil compounds retrieved from PubChem were saved in SDF format, while the target protein was saved in PDB format. The preparation process involved removing water molecules, ligands, and irrelevant metal ions from the protein structure, followed by optimizing the structure for docking simulations. Molecular docking was conducted using the CADD Labshare platform, and the interactions were visualized in three-dimensional (3D) representations to analyze the binding interactions between the ligands and PBP1.

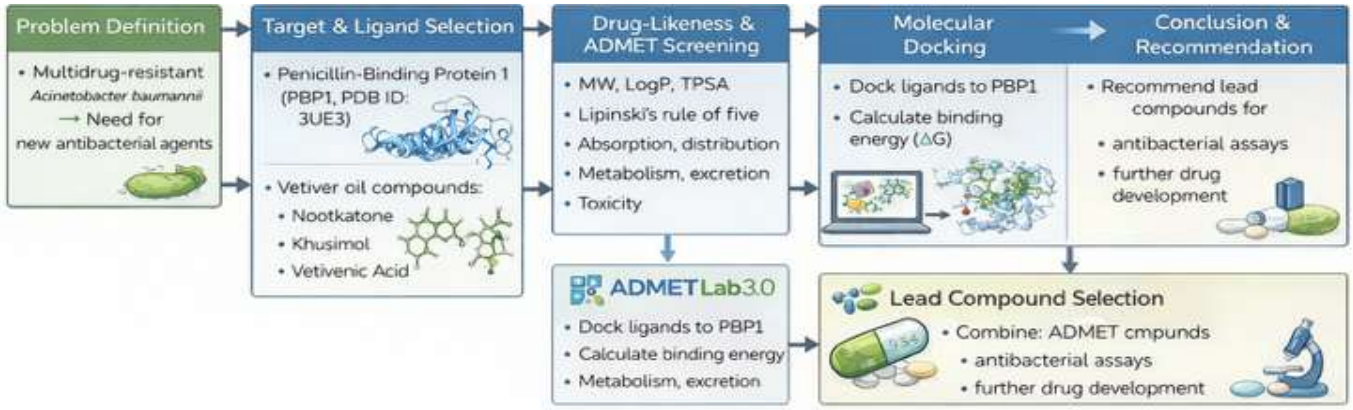


Figure 1. Flow chart of the *in-silico* screening of vetiver oil compounds against PBP1 of *Acinetobacter baumannii*

Results and Discussion

Chemical Characteristics of Ligands

Nootkatone is a sesquiterpenoid ketone with a characteristic bicyclic structure and a conjugated ketone functional group (Figure 1a). It is commonly found in grapefruit and vetiver oil and is known for its distinctive citrus aroma (Leonhardt & Berger, 2014). Nootkatone has been widely studied for its biological activities, including insecticidal, antimicrobial, and anti-inflammatory properties (Li et al., 2021). Its structure consists of a fused ring system with a ketone (-C=O) group, which contributes to its reactivity and biological interactions. Khusimol is a sesquiterpenoid alcohol that differs from nootkatone by the presence of a hydroxyl (-OH) group instead of a ketone (Figure 2b). This structural difference influences its solubility and interaction with biological targets. Khusimol is one of the major constituents of vetiver essential oil and is known for its woody and earthy aroma (Nur Amalia et al., 2021). It has been reported to possess antioxidant and antimicrobial activities, making it a valuable component in perfumes, cosmetics, and pharmaceuticals (Oliveira et al., 2022). Vetivenic acid is a sesquiterpenoid carboxylic acid, characterized by the presence of both a carboxyl (-COOH) and a ketone (-C=O) group in its structure (Figure 1c) (Papari et al., 2020). This structural feature makes it more polar compared to nootkatone and khusimol, potentially influencing its bioavailability and interaction with biological membranes. Vetivenic acid is one of the unique acidic components of vetiver oil and may contribute to its therapeutic effects (Khater et al., 2018).

a) Nootkatone b) Khusimol c) Vetivenic acid

Figure 2. The 3D ligands used in this research from vetiver oil

The structural differences among these three compounds significantly impact their chemical reactivity, biological interactions, and potential pharmaceutical applications. Nootkatone and khusimol,

as ketone and alcohol derivatives, respectively, are more hydrophobic and likely to interact with lipid membranes, whereas vetivenic acid, due to its carboxyl functional group, exhibits higher polarity and may have different pharmacokinetic properties. These three sesquiterpenoids have been investigated for their potential roles in drug development, particularly in antimicrobial research, including their potential to inhibit bacterial enzymes such as penicillin-binding proteins.

In addition to functional group differences, these three compounds also vary in key physicochemical parameters such as molecular size, polar surface area, and conformational flexibility, which directly influence their ability to enter enzyme active sites and form stable ligand–protein complexes (Jang et al., 2024). In the case of penicillin-binding proteins, which possess catalytic pockets composed of both hydrophobic and polar residues, compounds that achieve an optimal balance between lipophilicity and hydrogen-bonding capacity are more likely to act as effective inhibitors (Solanki et al., 2023). Therefore, comparing nootkatone, khusimol, and vetivenic acid provides a comprehensive assessment of how subtle structural variations among vetiver sesquiterpenoids can lead to significant differences in binding affinity and antibacterial potential (Veeraraghavan et al., 2025). This approach is consistent with the principles of structure–activity relationship (SAR) in drug discovery, in which the correlation between chemical structure and biological activity is used to identify the most promising lead compounds for further development.

Drug-likeness and ADMET

The physicochemical, pharmacokinetic, and toxicological properties of the three ligands—nootkatone, khusimol, and vetivenic acid—are presented in Table 1. The compound identity section includes molecular weight (MW), where nootkatone has a weight of 218.17 g/mol, khusimol has a weight of 220.18 g/mol, and vetivenic acid has a weight of 234.16 g/mol. The LogP values indicate the lipophilicity of the compounds, with vetivenic acid having the highest value at 3.326, followed by nootkatone at 2.812 and khusimol at 2.01. The topological polar surface area (TPSA) values are 17.07 Å² for nootkatone, 20.23 Å² for khusimol, and 37.3 Å² for vetivenic acid, which can influence their ability to permeate biological membranes (Lagunin et al., 2014).

Nootkatone, khusimol, and vetivenic acid (Table 1) comply with Lipinski's Rule of Five, indicating good oral bioavailability. Vetivenic acid shows higher lipophilicity (LogP 3.326) and greater plasma protein binding (96.5%), while khusimol has the lowest value (73.2%). In metabolism, nootkatone is a CYP3A4 substrate, while the others are not. Vetivenic acid has the longest half-life (0.922 hours), suggesting better stability. Toxicity analysis indicates that vetivenic acid has the lowest risk of mutagenicity, carcinogenicity, and hematotoxicity, while nootkatone shows higher neurotoxicity and carcinogenic risk. Overall, vetivenic acid has favorable drug-like properties and lower toxicity risks, making it a promising candidate for further development.

Taken together, the physicochemical and ADMET profiles indicate that vetivenic acid represents the most pharmacologically balanced candidate among the three ligands (Ferrari et al., 2021). Its moderate molecular weight, optimal lipophilicity, and higher polar surface area suggest a favorable compromise between membrane permeability and target specificity, which is essential for enzyme-directed antibacterial agents. Importantly, the absence of predicted CYP3A4 metabolism reduces the risk of rapid hepatic clearance and drug–drug interactions, a limitation commonly observed in terpenoid-based compounds (Dong et al., 2018). Moreover, the high plasma protein binding and longer half-life of vetivenic acid indicate improved systemic stability, which is beneficial for maintaining therapeutic concentrations in vivo.

These in-silico predictions are consistent with previous pharmacological studies reporting that carboxylated sesquiterpenoids exhibit enhanced metabolic stability and reduced cytotoxicity compared with their ketone or alcohol counterparts (Bugnon et al., 2024). In particular, acidic terpenoids have been shown to form stronger and more selective interactions with bacterial enzyme targets due to their ability to establish ionic and hydrogen-bond interactions within active sites, thereby improving inhibitory potency while minimizing off-target toxicity (Gupta et al., 2013). Furthermore, lower mutagenic and carcinogenic risks, as predicted for vetivenic acid, are critical criteria in early-stage antibacterial drug discovery, where safety profiles often limit the translational potential of natural compounds (Gogoi et al., 2023).

Therefore, integrating its favorable ADMET properties with its predicted molecular interactions against PBP1, vetivenic acid emerges as a promising lead compound for further in vitro and vivo validation. These results support the hypothesis that selective structural features of vetiver-derived sesquiterpenoids can be exploited to design safer and more effective antibacterial agents targeting multidrug-resistant *Acinetobacter baumannii*.

Molecular Interaction with PBP1

Three-dimensional molecular interaction diagrams of the three compounds—(a) Nootkatone, (b) Khusimol, (c) Vetivenic acid, are constructed with the active site of Penicillin-Binding Protein 1 (PBP1) from *Acinetobacter*

baumannii along with (d) Imipenem (as a reference). The protein is visualized in blue, while ligands are shown in orange. Key interactions are depicted: hydrophobic contacts are represented by dotted grey lines and hydrogen bonds are indicated by solid blue lines. The charge center (yellow) symbols mark specific chemical environments contributing to ligand binding. Several conserved residues such as TYR450A, TYR539A, and THR528A are involved across multiple ligand complexes, highlighting their importance in substrate recognition. The 3D model illustrates how the molecules interact with the protein surface, forming key molecular interactions.

Nootkatone, a bicyclic sesquiterpene ketone, exhibited favorable binding within the catalytic groove of PBP1 by engaging two adjacent tyrosine residues: TYR450A (3.70 Å) and TYR448A (3.68 Å). These hydrophobic interactions suggest π–π stacking or alkyl–π contributions (Figure 3a), which have been characterized as stabilizing forces in PBP-ligand complexes (Singh & Katoch, 2021). TYR448A is particularly significant, as it also forms consistent contacts in the vetivenic acid and imipenem models, strengthening its relevance as a conserved binding anchor. The ability of nootkatone to dock into similar binding pockets as standard β-lactams suggests its potential for disrupting peptidoglycan synthesis in multidrug-resistant *A. baumannii*, a notion supported by prior docking-based screening studies on terpenoid scaffolds (Panda & Tiwari, 2023; Tang & Wang, 2022).

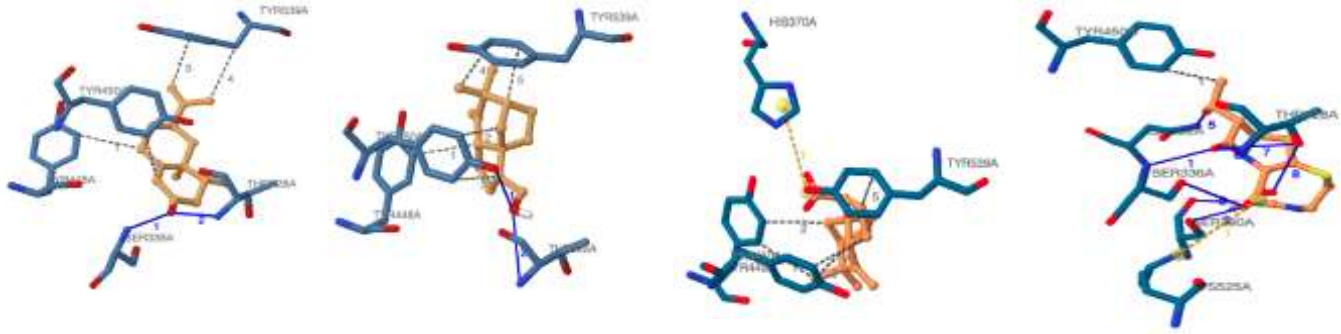
Table 1. Physicochemical and Pharmacokinetic and Toxicity of Vetiver Oil Ligands

Category		Nookatkone	Khusimol	Vetivenic acid
Compund Identity	MW (g/mol)	218.17	220.18	234.16
	LogP	2.812	2.010	3.326
	TPSA (Å²)	17.07	20.23	37.30
Drug-likeness	Lipinski's Rule	Accepted	Accepted	Accepted
	QED	0.610	0.672	0.705
	SAscore	Easy	Easy	0.8
	Fsp^3	0.667	-0.867	0.800
Absorption	Caco-2 Permeabilty (cm/s)	-4.548	-4.926	-4.909
	MDCK Permeability (cm/s)	0.0	0.0	0.0
	Pgp-inhitor	+	+++	-
	HIA	- - -	- - -	- - -
Distribution	PPB	93.1%	73.2%	96.5%
	BBB Permeability	++	- - -	
	VDss (L/kg)	1.294	1.516	0.384
Metabolism	CYP2C19 inhibitor	-	- - -	-
	CYP3A4 subtrate	+++	- -	- -
	CYP2C9 inhibitor	- - -	- - -	- - -
	HLM stablitiy	++	+++	- -
Excretion	CL_{plasma} (mL/min/kg)	10.718	10.188	7.402
	Half-life ($T_{1/2}$) (hours)	0.578	0.906	0.922
Toxicity	hERG Blockers (10 μM)	0.316	0.082	0.180
	Probability of hepatotoxicity	0.625	0.662	0.499
	Probability of Ames toxicity	0.509	0.558	0.103
	Probability of carcinogenicity	0.793	0.714	0.327
	Probability of neurotoxicity	0.750	0.479	0.443
	Probability of hematotoxicity	0.480	0.459	0.259

Notes: +++ (strong activity); ++ (moderate activity); + (weak activity); - - - (inactive); - - (very low activity); - (low activity)

Table 2. Ligand Interaction with PBP 1 Active Site

Compund	Protein	Binding affinity (kcal/mol)	Antibacteria Probability	Interacting with amino acid residues
Khusimol	PBP 1	-6,5	Pa 0.451	Hydrogen bond: THR528, SER336A
			Pi 0.033	Hydrofobic interaction: TYR450A, TYR448A, TYR 539A
Nootkatkone	PBP 1	-6,9	Pa 0.644	Hydrogen bond: THR528, TYR448
			Pi 0.0065	Hydrofobic interaction: TYR450A, TYR448A, TYR 539A
Vetivenic acid	PBP 1	-6,8	Pa 0.503	Hydrogen bond: THR528
			Pi 0.021	Hydrofobic interaction: TYR450A, TYR 448A, TYR 539A
Imipenem	PBP 1	-6,8	Pa 0.789	Hydrogen bond: THR528A, TYR450A,
			Pi 0.002	Hydrofobic interaction: TYR450A, TYR 448A, TYR 539A



(a) (b) (c) (d)

Figure 3. 3D molecular interactions between three compounds—nootkatone (a), khusimol (b), vetivenic acid (c), and imipenem (d)— with Penicillin-Binding Protein 1 (PBP1). Color legend: protein (blue), ligand (orange), charge center (yellow), hydrophobic interactions (dotted lines), hydrogen bonds (solid blue lines)

Compared to nootkatone, khusimol exhibits a slightly different binding orientation within the active site of PBP1. Khusimol, a sesquiterpene alcohol commonly found in vetiver oil, interacted with PBP1 through two key hydrophobic contacts involving TYR450A (3.62 Å) and TYR539A (3.46 Å) (Figure 3b). These residues have been previously identified as conserved anchor points for substrate recognition in β-lactam–PBP complexes (Sauvage & Kerff, 2014; Gajdács, 2019).

Vetivenic acid, a sesquiterpenoid compound derived from *Vetiveria zizanioides*, displayed promising binding features against PBP1. It formed hydrophobic interactions with TYR448A (3.55 Å), TYR450A (3.70 Å), and TYR539A (3.58 Å), as well as hydrogen bonds with THR528A (3.56 Å) and SER336A (2.04 Å) (Figure 3c). The overlap of binding residues with those of imipenem highlights the potential of vetivenic acid to act via a similar mechanism of inhibition. Studies have shown that aromatic residues like TYR and polar residues such as THR and SER contribute significantly to ligand anchoring within β-lactam targets (Panda & Tiwari, 2023; Ahmad & Faizan, 2023). Moreover, computational work targeting natural compounds also emphasized the inhibitory relevance of the THR528–TYR450 motif in multiple PBP isoforms (Elmi & Zeid, 2021; Olivares & Blázquez, 2020). This suggests that vetivenic acid may serve as a viable natural scaffold for future β-lactam antibiotic development.

Imipenem exhibited strong molecular interactions with several active-site residues of Penicillin-Binding Protein 1 (PBP1) of *Acinetobacter baumannii*, particularly TYR450A, THR528A, HIS370A, PHE358A, and ASN365A. Hydrophobic interactions were observed between imipenem and TYR450A (3.62 Å), PHE358A (3.71 Å), and ASN365A (3.61 Å) (Figure 3d), indicating stabilization within the binding cleft. The hydrogen bond with THR528A (3.08 Å) and a salt bridge with HIS370A (4.65 Å) contribute to enhanced ligand binding.

Notably, the reference drug imipenem exhibits both hydrogen bonding and electrostatic interactions, which are partially mirrored by vetiver oil constituents, suggesting their potential as alternative PBP1 inhibitors. These observations corroborate previous structural analyses of β-lactam–PBP complexes, which identify these residues as crucial for catalysis and inhibitor binding (Sauvage & Kerff, 2014; Gajdács, 2019). The conserved interactions found here reinforce the essential role of PBP1 in the resistance mechanism of *A. baumannii* and confirm the relevance of imipenem as a positive control (Tang & Wang, 2022; Singh & Katoch, 2021).

The interaction pattern observed mirrors that of vetivenic acid and imipenem, suggesting a convergent binding mechanism. Notably, the involvement of TYR539A, a residue also targeted by both imipenem and vetiver-derived compounds, underscores its potential as a pharmacophoric hotspot (Ahmad & Faizan, 2023). These findings are further supported by computational evidence that highlights the hydrophobic patch surrounding TYR450A as a recurrent docking site for lipophilic ligands in PBP1 structures (Elmi & Zeid, 2021).

The interaction patterns observed in this study are highly consistent with previous structural and computational investigations of β-lactam–PBP complexes. Earlier crystallographic and docking studies have demonstrated that aromatic residues such as TYR450 and TYR539, together with polar residues including THR528 and SER336, form a conserved recognition motif within the catalytic cleft of PBP1 and related PBP isoforms (Sauvage & Terrak, 2016). Similar binding hotspots have also been reported in recent virtual screening campaigns targeting natural product libraries, where sesquiterpenoid and polyphenolic compounds preferentially occupied the hydrophobic pocket surrounding TYR450 and established stabilizing hydrogen bonds with THR528, leading to inhibition of peptidoglycan synthesis (Yang et al., 2022). In particular, the ability of vetivenic acid to engage both hydrophobic and polar residues mirrors the binding mode of

imipenem, which relies on a combination of hydrogen bonding and electrostatic interactions to achieve high-affinity inhibition of PBP1 (Veeraraghavan et al., 2025). These similarities strongly support the hypothesis that vetiver-derived sesquiterpenoids do not merely bind nonspecifically but interact with PBP1 in a mechanistically relevant manner comparable to clinically used β-lactam antibiotics. Therefore, the present findings extend previous computational and structural studies by identifying vetivenic acid as a natural scaffold capable of exploiting conserved PBP1 pharmacophoric hotspots, highlighting its potential for further optimization and experimental validation against multidrug-resistant *Acinetobacter baumannii*.

Conclusion

This research showed that vetiver oil constituents—nootkatone, khusimol, and vetivenic acid—can bind to penicillin-binding protein 1 (PBP1) of *Acinetobacter baumannii* through hydrogen-bond and hydrophobic interactions with key residues TYR450A, TYR448A, TYR539A, and THR528A. Molecular docking revealed binding energies of −6.9 kcal/mol (nootkatone), −6.5 kcal/mol (khusimol), and −6.8 kcal/mol (vetivenic acid), which were comparable to imipenem (−6.8 kcal/mol). PASS analysis predicted antibacterial potential with Pa values of 0.644, 0.451, and 0.503, respectively. ADMET and toxicity profiling indicated that vetivenic acid exhibited the most favorable pharmacokinetic stability and lowest predicted toxicity, including reduced mutagenic and carcinogenic risks. Overall, these results identify vetivenic acid as the most promising vetiver-derived lead compound for further *in vitro* and *in vivo* evaluation against multidrug-resistant *A. baumannii*.

Acknowledgments
Thanks to Center of Excellence for Food Products and Health Supplements for Degenerative Conditions, University of Surabaya who supported the implementation of this research.

Author Contributions
Conceptualization, Y.A.P.; methodology, T.K.; software, Y.A.P., P.S.; validation, M.W.; formal analysis, T.K.; investigation, M.W.; resources, Y.A.P. P.S.; data curation, T.K.; writing—original draft preparation, Y.A.P.; writing—review and editing, T.K.; visualization, Y.A.P. All authors have read and agreed to the published version of the manuscript.

Funding
The APC is funded by Directorate of Research and Community Service, General Directorate of Research and Development, Ministry of Higher Education, Science, and Technology (DPPM, Ditjen Risbang, Kemdiktisaintek).

Conflicts of Interest
The authors declare no conflict of interest.

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