Journal of Phytology 2026, 18: 25-33
https://doi.org/10.25081/jp.2026.v18.9910

Research Article

Essential oil of *Artemisia absinthium*: Chemical composition, antibacterial activity and molecular docking study targeting CTX-M-15 extended-spectrum beta-lactamase

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(Received: December 18, 2025; Revised: March 02, 2026; Accepted: March 03, 2026; Published: March 21, 2026)

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Abstract

Artemisia absinthium essential oil (*AabEO*) exhibits a range of biological properties. This investigation involved the extraction of the *AabEO* through hydro-distillation, followed by the identification of its chemical constituents using gas chromatography-mass spectrometry, and then the dominant compounds were screened as potential β-lactamase inhibitors *in silico*. ADMET analysis was conducted via the SwissADME web service to assess the drug-likeness of the phytochemicals. Antibacterial activity of *AabEO* was further evaluated. GC-MS analysis revealed camphor as the principal constituent of *AabEO*. Among the tested bacteria, *S. aureus* and *E. coli* were the most susceptible bacteria, with clear zones of bacterial growth inhibition of 12 mm each. The inhibition zone obtained for *K. pneumoniae* was 8 mm, while *P. aeruginosa* was resistant. The ADMET values of all evaluated constituents revealed favourable findings, validating the plants as potential candidates for the discovery of safe therapeutic agents. From the docking analysis, geranyl-α-terpinene, camphor, and terpinen-4-ol showed high inhibitory potentials against β-lactamase, binding within the active site with lower binding affinity energy. Geranyl-α-terpinene had an energy of -6.95 kcal/mol, compared to avibactam at -5.8 kcal/mol. Consequently, *AabEO* may be regarded as a prospective agent that could enhance the therapeutic arsenal for treating infections caused by β-lactamase-resistant bacteria.

Keywords: ADMET, Antibacterial, *Artemisia absinthium*, Essential oil, Molecular docking, β-lactamase inhibition

Introduction

Around the early 20th century, the appearance of antibiotics raised hopes that infectious diseases would be eradicated forever; however, prescribers were quickly disappointed by the emergence of resistant bacteria. Bacterial species develop defense mechanisms against antibiotics through several mechanisms. These include the production of resistance-associated enzymes that nullify antibiotic function, such as beta-lactamases, which cause β-lactam antibiotics to be ineffective (Blair *et al.,* 2015; Munita & Arias, 2016).

Consequently, resistance to such antibiotics has prompted several studies aimed at introducing alternative antibiotic compounds, specifically compounds of natural origin. Phytocompounds have garnered considerable academic attention lately due to their numerous benefits, comprising, great variety, availability, abundance, and low side effects compared to chemical medications (Yuan *et al.,* 2016).

The experimental investigation of numerous phytocompounds, to develop safe and novel antibiotics is a laborious and costly process. Thus, in contemporary research, bioinformatics-based studies are thought to be a supplementary method for the formulation of novel pharmaceuticals, particularly antibiotic agents (Anand *et al.,* 2019). Despite extensive research on the antibacterial properties of several plants, the active components in all of them remain unidentified. *A. absinthium* is one of the most extensively studied species for its antibacterial properties and it has been demonstrated that this plant is rich in active secondary metabolites that exhibit various activities such as anti-inflammatory, hypoglycemic, hepatoprotective, insecticidal, antiviral, wound healing, antioxidant, and anticancer activities (Batiha *et al.,* 2020).

This work seeks to investigate the antibacterial properties of *AabEO* and to screen its chemical constituents for potential inhibitory activities against β-lactamases.

Materials and methods

Collection of plant samples

Specimens of *Artemisia absinthium* were collected from Aflou, located in the north of Laghouat (Algeria) (Elevation: 1 443 m, 34°05’48” N 2°07’49” E). The sample was identified at the Fundamental Sciences Laboratory at Amar Telidji University, Laghouat, Algeria. The species of *A. absinthium* has been collected manually in November 2023. A voucher specimen was lodged at the same laboratory. The plant leaves were then air-dried in the shade at ambient temperature in the dark for approximately 15 days.

Essential oil isolation procedure

The isolation of *AabEO* was carried out using a Clavenger-type apparatus hydrodistiller. This technique consists of introducing about 100 grams of the sample, which was subjected to hydrodistillation for 3 hours with 1L of distilled water. The oil obtained was separated from the distillate, dried, and kept in a glass vial in a refrigerator at -4 °C for subsequent analysis. The presented formula served to determine the essential oil content:

Yield (%) = (essential oil weight in grams/dried plant weight in grams) x 100

Essential oil analysis

The analysis was conducted at the Technical Platform of Physico-Chemical Analysis (PTAPC-CRAPC) in Laghouat, Algeria. A Shimadzu GC-MS-QP2020 device was used, with a capillary column of the type fused Rxi®-5ms (Phase Crossbond®, 5% diphenyl, 95% dimethyl polysiloxane) with dimensions of 30 m × 0.25 mm and film thickness of 0.25 µm. A volume of 0.5 µL of the sample was diluted in solvent (n-hexane) and then injected in split mode (1:80). Temperatures of the detector and the injector were fixed at 310 °C and 250 °C, respectively. The column temperature was initially established at 50 °C for 2 minutes, then raised to 310°C at a rate of 3 °C per minute, and fixed at 310 °C for 2 min. Helium (99.995% purity) with a flow rate of 1 mL/min was utilized as a carrier gas. The conditions of the mass spectrometer were that the ionization voltage was 70 eV, the ion source temperature was 200 °C, and electron ionization mass spectra were obtained over the mass range of 45-600 m/z. Retention indices (LRI) were calculated in relation to homologous n-alkanes serial (n-C7-C33) injected and analyzed under the same conditions as *AabEO*.

Bacterial strains

Antibacterial activity was evaluated using Gram-negative bacteria, *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922, and *Klebsiella pneumoniae* (clinical isolate), as well as Gram-positive bacteria, *Staphylococcus aureus* ATCC 25923.

In-vitro antimicrobial screening assays

Qualitative method

The antibacterial susceptibility test of the *AabEO* was evaluated with the disc diffusion method. Briefly, the bacterial suspension was standardized to the turbidity of a 0.5 McFarland reference, then aseptically spread onto Muller-Hinton agar petri dishes. Paper discs impregnated with 10 µL of *AabEO*, as well as a positive control disc (gentamicin 10 µg/disc), were aseptically placed on the swabbed agar plates and then incubated for 24 hours at 37° C. Areas of bacterial growth suppression were measured in mm (Mathers *et al.,* 2025).

Quantitative method

A broth micro-dilution procedure was applied to determine the minimum inhibitory concentration (MIC) as defined by the National Committee for Clinical Laboratory Standards (Mathers *et al.,* 2025). The test was performed in MHB. Bacterial suspension was dispensed into the wells of a microtitre plate, and then twofold serial dilutions of the essential oil were added, succeeded by incubation at 37 °C for 24 hours. Finally, 40 µL of p-iodonitrotetrazolium violet (INT) dissolved in water (0.2 mg/mL) was introduced to the microplate wells and then incubated at 37 °C for 10-30 min. The MIC was determined as the lowest possible concentration of essential oil that prevented the color transition of INT to pink (Eloff, 1998).

The minimal bactericidal concentration (MBC) was obtained by swabbing the suspensions from wells that exhibited no growth during the MIC assays. These cultures were re-incubated at 37 °C for 24 hr. The MBC was defined as the smallest concentration of essential oil that completely suppressed the growth of microorganisms (Faujdar *et al.,* 2020).

ADMET properties

The drug-likeness, physicochemical characteristics, and ADMET profiles of the major compounds identified in *A. absinthium* were systematically assessed using SwissADME (Daina *et al.,* 2017) and pkCSM computational platforms (Pires *et al.,* 2015). Canonical SMILES retrieved from the PubChem repository (Kim *et al.,* 2025), were used as input for SwissADME to predict key molecular descriptors including molecular weight (MW), hydrogen bond donors (HBD) and acceptors (HBA), lipophilicity (logP), total polar surface area (TPSA), molar refractivity (MR), aqueous solubility, Lipinski's rule compliance, and bioavailability. Complementary ADMET and toxicity predictions were performed using the pkCSM online platform (https://biosig.lab.uq.edu.au/pkcsm/).

Molecular docking

Molecular docking simulations were performed on the major bioactive constituents of *AabEO* using AutoDock Vina 1.2.0 (Trott & Olson, 2010; Eberhardt *et al.,* 2021). The three-dimensional crystal structure of the target CTX-M-15 extended-spectrum β-lactamase in complex with avibactam (PDB ID 4HBU) was retrieved from the Protein Data Bank (Berman *et al.,* 2000; Lahiri *et al.,* 2013) in PDB file format. Before docking, the target was prepared by removing water molecules and small molecules, and then adding polar hydrogen atoms and charges to the structure. Additionally, the ligand structures were retrieved from the PubChem database as a single file in a 3D spatial data file (SDF) format (Kim *et al.,* 2025). The ligand SDF files were converted to PDB files using the openbabel tool (O'Boyle *et al.,* 2011). Ligand preparation was performed by adding polar hydrogen and Gasteiger charges, and defining the rotatable bonds. Subsequently, the prepared protein and ligands were saved in PDBQT file format. The grid box was adjusted to

cover the active site residues that include CYS69, SER70, LYS73, ASN104, TYR105, SER130, ASN132, ASN170, THR216, LYS234, THR235, GLY236, SER237, and GLY238 to ensure the accurate docking of the ligands within the inhibitor binding sites (Lahiri *et al.,* 2013). A grid box with a size of 60 Å × 60 Å × 60 Å³ was created around the protein. The values -6.643882, -2.634176, and 11.573353 were used for the x, y, and z position coordinates. The molecular docking was then performed by setting the exhaustiveness to 8 for more precise and accurate docking scores. Further, the docking score for all the compounds and the reference drug Avibactam was noted. The protein-ligand conformations were analyzed using the PyMOL Molecular Graphics System, Version 3.0, Schrödinger, LLC. Additionally, the ligand interactions were generated using BIOVIA Discovery Studio Visualizer (v21.1.0.20298; Dassault Systèmes, 2020).

Results and discussion

GC-MS characterization of AabEO

Hydrodistillation of the plant material of *A. absinthium* gave dark blue oil with an intense and penetrating odour, with a yield of 0.54% (w/w). This extraction yield is comparable to the yields reported as (0.67%) by Benmimoune *et al*. (2023) and (0.53%) by Aouir *et al*. (2025) in Algeria. In Iran Zanousi *et al*. (2016) obtained a yield ranging from 0.35% to 0.75%. While in Tunisia, the extraction yield was more critical, ranging from 1.24% to 2.22% (Riahi *et al.,* 2015).

The *AabEO* was analyzed by GC-MS (Table 1). Ten compounds were identified, corresponding to the totality of the constituents detected in the essential oil.

The primary constituents of this essential oil comprise camphor, which accounts for 46.45%, chamazulene with 29.71 %, geranyl-α-terpinene with 6.07%, and Terpinen-4-ol with 5.72%. Other components are also found in low amounts, such as camphene (2.92%), cis-Sabinene hydrate (2.34%), myrcene (2.02%), α-thujene (1.94%) and germacrene D (1.89%).

The strong predominance of camphor indicates that it represents the essential oil chemotype of *A. absinthium*. Camphor, as a major compound, has also been reported by Aouir *et al.* (2025) to have a value of 39.01% in Algeria and by Riahi *et al*. (2015) from Tunisia (33.29%).

For more comparison, trans-thujone represents the principal constituent with a high level (54.7%) in a sample collected in Cherchell (Tipaza, Algeria), followed by chamazulene (10.05%) (Benmimoune *et al.,* 2023). Eucalyptol has been identified as the major component (25.59%) of *AabEO* in Shawan County (China), followed by linalool (11.99%) (Jiang *et al.,* 2021). However, a study conducted on *A. absinthium* reported that the main chemical profile was characterized by the predominance of borneol (18.7% and 16.7%) (Joshi, 2013).

Consequently, these discrepancies in the essential oil yields and compositions of a given species can be attributed to several parameters, including growth stages, regional pedoclimatic factors, and extraction methods (Riahi *et al.,* 2015; Zanousi *et al.,* 2016; Hayani *et al.,* 2022; Haddou *et al.,* 2023).

Table 1: Chemical composition of *AabEO*

S. No.	Retention time	Retention index (LRI)	Area (%)	Compounds
1	8.33	924	1.94	α-thujene
2	8.87	938	2.92	Camphene
3	10.64	983	2.02	Myrcene
4	13.56	1058	0.95	γ-Terpinene
5	13.87	1066	2.34	Cis-Sabinene hydrate
6	17.31	1153	46.45	Camphor
7	18.91	1194	5.72	Terpinen-4-ol
8	32.21	1472	1.89	Germacrene D
9	41.62	1685	29.71	Chamazulene
10	51.06	1998	6.07	Geranyl-α-terpinene
		Total	100.0	

Antimicrobial activity

The antibacterial efficacy of *AabEO* against pathogenic bacteria was evaluated qualitatively and quantitatively (Table 2).

The DIZs obtained indicated that the oil does not affect *P. aeruginosa* and *K. pneumoniae*, with DIZs of 6 mm and 8 mm, respectively. In comparison, *E. coli* and *S. aureus* are sensitive, with a DIZ of 12 mm.

MICs varied according to the bacteria tested, with values of 11.15 mg/mL for *E. coli* and *S. aureus*, 22.3 mg/mL for *P. aeruginosa* and *K. pneumoniae*. The MBCs reflect the lowest concentration at which the essential oil completely eradicates bacteria. The MBC for *E. coli* was 22.3 mg/mL, while for the other strains it is indicated as being greater than 44.6 mg/mL.

Bezzezi *et al*. (2025) showed the antimicrobial activity of the *AabEO* against *S. aureus* and *E. coli*, with MICs of 5 mg/mL and 10 mg/mL, respectively. Also, Riahi *et al.* (2015) evaluated the effectiveness of *AabEO* against *E. coli*, *S. aureus*, and *P. aeruginosa*, and reported the following MICs: (12.5 to 25% V/V), (12.5 to 25% V/V), (6.25 to 12.5% V/V), respectively. On the other hand, Joshi (2013) found that *AabEO* was completely inactive against those bacterial strains.

Table 2: Antibacterial activity of *AabEO*: inhibition zone diameters (DIZ, mm), minimum inhibitory concentrations (MIC, mg/mL), and minimum bactericidal concentrations (MBC, mg/mL) against tested bacterial strains

Strains	DIZs		MIC	MBC
	AabEO	Gentamicin		
E. coli ATCC 25922	12	19	11.15	22.3
S. aureus ATCC 25923	12	20	11.15	>44.6
P. aeruginosa ATCC 27853	6	21	22.3	>44.6
K. pneumoniae	8	6	22.3	>44.6

Essential oils' capacity to eradicate bacteria depends on several factors. It is established that their components, especially the main ones, have hydrophilic functionalities within a lipophilic skeleton. The chemical structure of oil's components, their relative amounts, and how they interact with each other should all affect its intrinsic activity. Also, Wan *et al.* (1998) found that most investigated essential oils performed better against Gram-positive bacteria. Gram-negative bacteria are resistant to essential oils because their outer membrane is hydrophilic, which keeps hydrophobic substances from getting into the target cell membrane (Wan *et al.,* 1998; Burt, 2004; Khan *et al.,* 2022).

ADMET analysis

The physicochemical properties, solubility, lipophilicity, and violations of the Lipinski rule of five, as well as human oral bioavailability, were evaluated using the SwissADME tool. All seven compounds were predicted to have a MW between 150-500 g/mol, HBA values of ≤10, HBD values of ≤5, and MR values within the range of 40-130 Å^2. Furthermore, the compounds fell within the acceptable range for bioavailability, with a value of 0.55, and they had no more than one violation of the Lipinski rule of five. The chemical structures of compounds identified in *A. absinthium* through the GC-MS study are shown in Figure 1. Additionally, their corresponding bioavailability radar plots are given in Figure 2.

ADMET evaluates the pharmacokinetics of a drug by focusing on predicting how a drug behaves in the body. It assesses how effectively the drug is absorbed, distributed, metabolised, and excreted when orally administered. Furthermore, poor ADME can potentially lead to toxicity (Guan *et al.,* 2019). To evaluate the ADMET profile of all the compounds, we have used the pkCSM pharmacokinetics web tool.

The absorption properties include Caco-2 permeability, Intestinal absorption (%), Skin Permeability, and P-glycoprotein I inhibitor. All the compounds were predicted to have acceptable Caco-2 and skin permeability and exhibited high intestinal absorption of more than 95%. The volume of distribution (VD) parameter was evaluated to predict how extensively a drug distributes throughout the body and the total dose required to achieve tissue concentrations similar to those in plasma. Compounds with a log VDss value less than -0.15 L/kg are considered to have a low distribution, whereas those with a VDss value greater than 0.45 L/kg are categorized as having a high distribution. The VDss predictions for all compounds from *A. absinthium* range from 0.2 to 0.7(log mL/min/kg). Camphor, Terpinen-4-ol, and Myrcene showed lower distribution levels, with VDss scores below 0.4 L/kg, suggesting that all other compounds have a higher distribution rate within the body.

Metabolism predictions provide valuable insights into a compound's interaction with cytochrome P450 (CYP) enzymes, which are crucial for drug metabolism in the body. The results revealed that geranyl-α-terpinene was predicted to inhibit the CYP1A2 enzyme, while the remaining compounds do not show any inhibition against the drug metabolizing enzyme.

Total clearance and Renal OCT2 substrate status provide insights into how compounds are excreted from the body. This excretion rate was evaluated using the total clearance values (log ml/min/kg) for all seven compounds and showed a rate from 0.07 to 1.4, which indicates variability in their elimination rates. Additionally, alpha-Thujene showed the lowest total clearance rate of 0.07 log mL/min/kg, and geranyl-α-terpinene with 1.48log mL/min/kg.

The toxicity profiles of the bioactive compounds from both plants were predicted to ensure a safe profile for their potential therapeutic use. These predictions provide significant informationon possible adverse effects, AMES toxicity, Oral Rat Acute Toxicity (LD50), Hepatotoxicity, Max. Tolerated dose (human) (log mg/kg/day), Skin Sensitisation, and hERG II inhibition. The results indicated that none of the compounds studied showed AMES toxicity, and were non-inhibitors of the hERG I and II channels, suggesting their non-mutagenic potential and lower risk of

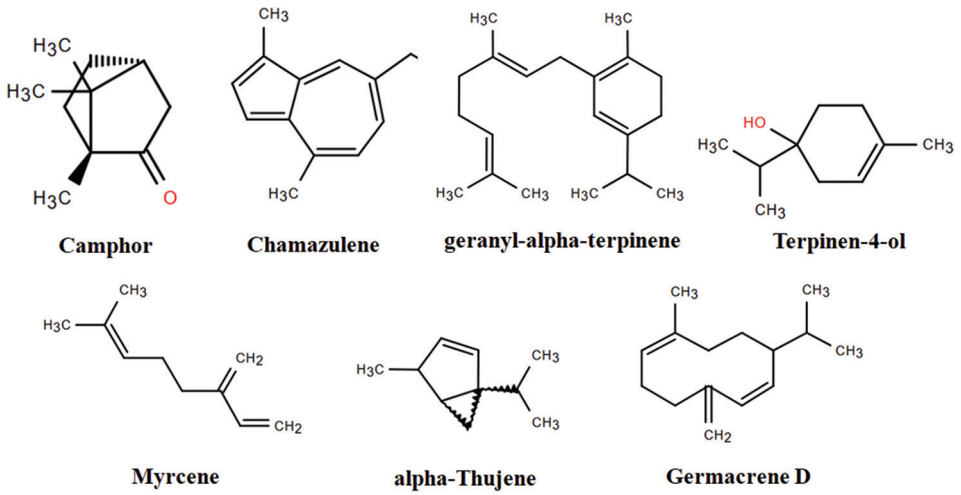

Figure 1: Two-dimensional chemical structures of the phytochemicals identified from the *AabEO*

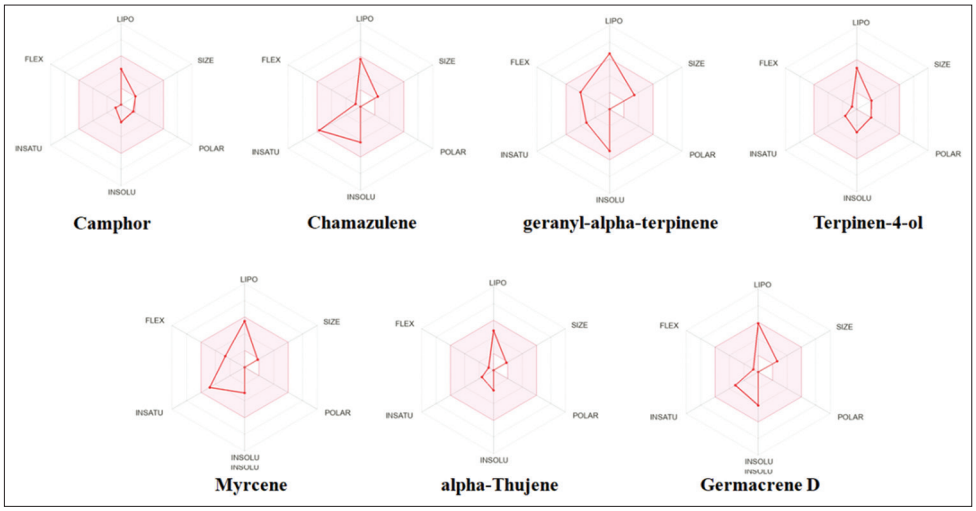

Figure 2: Bioavailability radar plot for the phytochemicals identified from the *AabEO*. The colored zone is the acceptable range for each parameter. LIPO denotes (Liphophilicity), XLOGP3 between -0.7 and +5.0, SIZE (MW) 150 and 500 g/mol, POLAR (Polarity) TPSA between 20 and 130 Å^2, INSOLU (Insolubility) log *S* not higher than 6, INSATU (Insaturation) sp3 hybridization not less than 0.25, and FLEX (Flexibility) no more than 9 rotatable bonds

Table 3: Binding affinities (docking scores) of *Artemisia absinthium* compounds and the reference inhibitor avibactam against β-lactamase (PDB ID: 4HBU)

S. No.	Compound name	Docking score	Hydrogen bond/Salt bridge	Hydrophobic interaction (Alkyl, Pi-Alkyl)	Van der Waals interaction
1	Camphor	-4.66	SER70 (2.6Å, 2.15Å), SER237 (2.08Å)	TYR105	LYS73, ASN132, GLU166, ASN170, GLY238, CYS69, AS104, THR235, GLY236, SER130
2	Chamazulene	-5.2		ARG274	THR216, TYR105, ASN170, SER237, SER220, ASN244, THR235, GLY236, SER130, TYR129, SER70, SER237, LEU277, THR243
3	Geranyl-α-terpinene	-6.95		TYR105, ARG274	THR216, TYR105, LYS73, SER272, GLY238, GLY239 ASN170, SER237, SER220, ASN244, THR235, GLY236, SER130, TYR129, SER70, SER237, LEU277, THR243
4	Terpinen-4-ol	-4.945	SER70 (2.2 Å), SER130 (1.9Å)	TYR105	SER237, ASN104, GLU166, ASN170, ASN132, LYS73, TYR129, THR216, THR235, GLY236, LYS234
5	Myrcene	-4.8		TYR105, ARG274	SER70, LYS73, SER130, GLY236, TYR129, GLY236, SER237. THR235, ASN244, THR216, THR243, SER220
6	alpha-Thujene	-4.7		ARG274	SER237, TYR105, LEU277, ASN244, SER220, SER130, ASN132, LYS73, TYR129, THR216, THR235, GLY236, LYS234
7	Germacrene D	-4.8			SER237, LEU277, SER220, SER130, ASN132, LYS73, THR216, THR235, GLY236, LYS234
8	Avibactum (NXL104) (Reference drug)	-5.8	SER130, THR235, SER70, ASN132, ASN132, ASN104	TYR105	GLY236, SER237, ASN104, ASN170, ASN132, LYS73, THR216, THR235, SER70

cardiotoxicity. Additionally, they were predicted to be non-hepatotoxic, revealing their safer profile for liver function. The ADMET properties for all compounds in *A. absinthium* are given in Supplementary Table S1.

Molecular docking

The present study selected β-lactamase as the target for molecular docking analysis due to its crucial role in bacterial resistance to β-lactam antibiotics. β-lactamases are enzymes that can hydrolyze the β-lactam ring, a significant structural feature of β-lactam antibiotics. This hydrolysis neutralizes the antibacterial activity of these antibiotics and contributes significantly to the growing issue of antibiotic resistance (Tooke *et al.,* 2019). Therefore, inhibiting this enzyme is a key strategy for overcoming resistance and restoring the effectiveness of antibiotics. In addition, we have used avibactam (crystallised ligand), a non-β-lactam β-lactamase inhibitor, as a reference compound in this study because of its clinically proven ability to inhibit a wide range of β-lactamases and enhance the activity of β-lactam antibiotics against resistant strains (Huang & Zhou, 2025). Based on the antibacterial effect of the *A. absinthium* plant extract, we investigated whether the phytochemicals in the plant could interact and inhibit their action, similar to avibactam. To identify these compounds, molecular docking analysis was conducted by targeting β-lactamase.

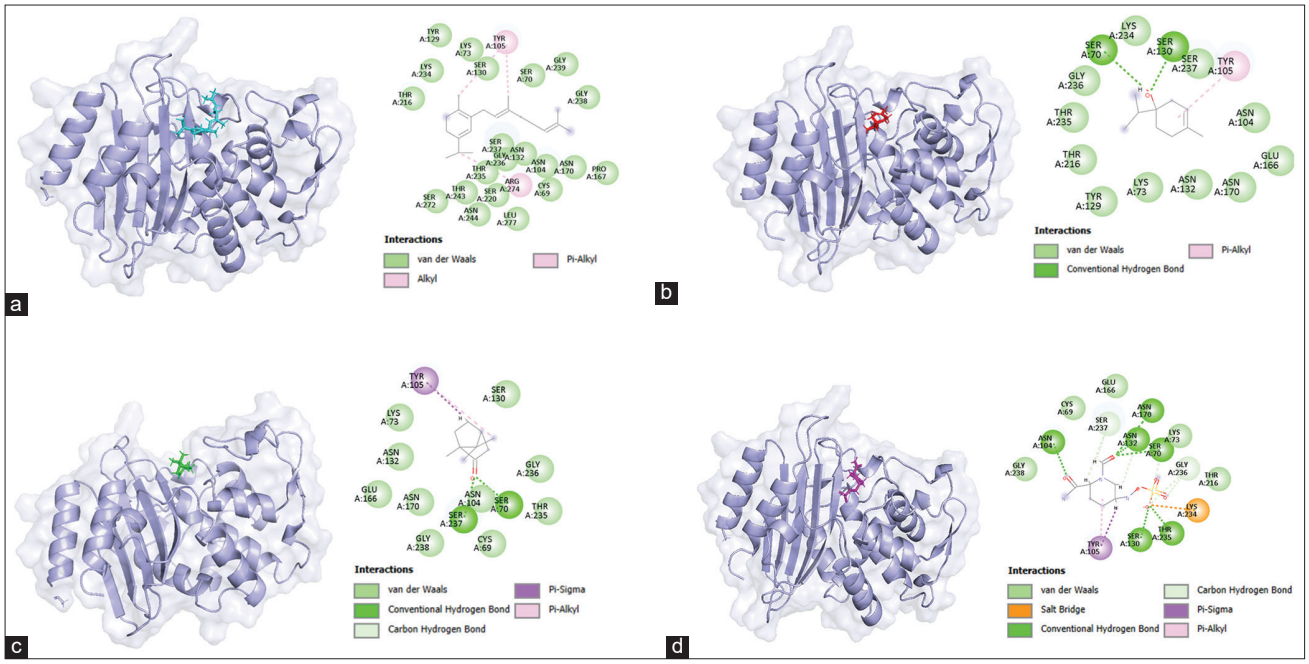

Figure 3: The diagram shows the surface view of β-lactamase bound to the ligand a) geranyl-α-terpinene (cyan), b) terpinen-4-ol (red), c) Camphor (green), and d) avibactam (control) (violet) shown as sticks. Protein-ligand interaction diagrams show the hydrogen bonds, π-alkyl, alkyl, salt bridge, and van der Waals interactions

The molecular docking of the *A. absinthium* against the target β-lactamase showed that among all seven compounds, geranyl-α-terpinene, diterpenoids displayed the highest docking score of -6.95 kcal/mol, indicating strong binding affinity towards β-lactamase enzyme. The compound exhibited hydrophobic and van der Waals interactions with critical residues such as TYR105, ARG274, SER70, and GLY236, indicating stable binding within the active site (Figure 3a). Notably, Camphor and terpinen-4-ol exhibited hydrogen bonding interactions with the critical catalytic residues involved in avibactam binding. Camphor formed hydrogen bonds with SER70 and SER237, terpinen-4-ol with SER70and SER130, along with van der Waals contacts with GLU166 (Figure 3b & c). These residues are significant residues of the β-lactamase active site and play critical roles in its enzymatic activity. Avibactam displayed a docking score of -5.8 kcal/mol with hydrogen bonds at SER70, SER130, ASN132, ASN170, THR235, and ASN104 (Figure 3d). The docking scores, protein-ligand interactions for all seven compounds as well as the reference drug avibactam, are given in Table 3. A previous study on the mechanism of avibactam on class A CTX-M-15 extended-spectrum β-lactamase reported that avibactam forms multiple hydrogen bonds, blocking the hydrolysis of β-lactam antibiotics. It forms hydrogen bonds with LYS73, SER130, GLU166, ASN132, and ASN170, polar and van der Waals contacts with residues,and with TYR105, contributing to its strong inhibitory property (Lahiri *et al.,* 2013).

Overall, the docking analysis indicates that geranyl-α-terpinene, Camphor, and terpinen-4-ol compounds from *A. absinthium* interact effectively with critical residues in the β-lactamase active site, resembling the interactions similar to those of avibactam. This highlights their promise as natural scaffolds for developing new inhibitors to address β-lactamase-mediated antibiotic resistance.

Conclusion

This study examined the chemical profile and antibacterial activity of *A. absinthium* essential oil. Analysis showed camphor and chamazulene dominated the essential oil. The oil was shown to be active against both *S. aureus* and *E. coli.* Additionally, molecular docking simulations evaluated the inhibitory effect of major oil constituents on the β-lactamase enzyme, a crucial bacterial resistance factor. Docking data suggest that substances such as geranyl-α-terpinene, camphor, and terpinen-4-ol may have inhibitory effects comparable or superior to traditional β-lactamase inhibitors. These compounds show promise for generating new treatment medicines for β-lactamase-resistant bacteria.

Acknowledgements

We would like to express our gratitude to the entire personnel of the Akid Lotfi central laboratory at the Laghouat hospital for their invaluable assistance in collecting reagents and operating various types of equipment.

Author contributions

Turkiya Touhami: Conceptualization, investigation, visualization, writing-original draft preparation. Khadidja Houda Benabed: Supervision, investigation. Fatima Zohra Guellouma: Methodology, supervision. Hadjer Boussoussa: Conception and supervision of the study, project administration. Haritha Kalath: Writing-original draft, software, formal analysis. Ihcen Khacheba: Critical revision of the manuscript. Mohamed Yousfi: Supervision, resources. Muhammad Suleman and Abdullah A. Shaito: Data curation, formal analysis.

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Supplementary material

Supplementary Table S1: Physicochemical, Drug-Likeness, Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) prediction for *Artemisia absinthium* phytochemical compounds

Compound Name	Camphor	Chamazulene	geranyl-alpha-terpinene	Terpinen-4-ol	Myrcene	alpha-Thujene	Germacrene D
Physicochemical properties							
MW (g/mol)	152.23	184.28	272.47	154.25	136.23	136.23	204.35
Hydrogen bond acceptors (HBA)	1	0	0	1	0	0	0
Hydrogen bond donor (HBD)	0	0	0	1	0	0	0
Molar refractivity (MR)	45.64	62.77	94.24	48.8	48.76	45.22	70.68
TPSA (Å2)	17.07	0	0	20.23	0	0	0
Consensus Log P	2.37	4.24	5.87	2.6	3.43	3.15	4.3
ESOL Class	Soluble	Moderately soluble	Moderately soluble	Soluble	Soluble	Soluble	Moderately soluble
Lipinski rule	0	1	1	0	0	1	1
Bioavailability Score	0.55	0.55	0.55	0.55	0.55	0.55	0.55
Absorption							
Caco2 permeability	1.499	1.402	1.442	1.502	1.4	1.386	1.436
Intestinal absorption (% Absorbed)	95.965	94.503	93.917	94.014	94.696	95.256	95.59
Skin Permeability	-2.002	-1.41	-1.939	-2.182	-1.043	-1.371	-1.429
P-glycoprotein substrate	No	No	No	No	No	No	No
P-glycoprotein I inhibitor	No	No	No	No	No	No	No
P-glycoprotein II inhibitor	No	No	No	No	No	No	No
Distribution							
VDss (human) (L/kg)	0.331	0.639	0.721	0.21	0.363	0.575	0.544
BBB permeability	0.612	0.792	0.85	0.563	0.781	0.81	0.723
CNS permeability	-2.158	-1.829	-1.515	-2.473	-1.902	-1.793	-2.138
Metabolism							
CYP2D6 substrate	No	No	No	No	No	No	No
CYP3A4 substrate	No	No	Yes	No	No	No	No
CYP1A2 inhibitor	No	No	Yes	No	No	No	No
CYP2C19 inhibitor	No	No	No	No	No	No	No
CYP2C9 inhibitor	No	No	No	No	No	No	No
CYP2D6 inhibitor	No	No	No	No	No	No	No
CYP3A4 inhibitor	No	No	No	No	No	No	No
Excretion							
Total Clearance (log ml/min/kg)	0.109	0.257	1.489	1.269	0.438	0.077	1.42
Renal OCT2 substrate	No	No	No	No	No	No	No
Toxicity							
AMES toxicity	No	No	No	No	No	No	No
Max tolerated dose (log mg/kg/day)	0.473	0.051	0.016	0.857	0.617	0.353	0.497
hERG I inhibitor	No	No	No	No	No	No	No
hERG II inhibitor	No	No	Yes	No	No	No	No
Oral Rat Acute Toxicity (LD50)	1.653	1.454	1.485	1.811	1.643	1.589	1.634
Hepatotoxicity	No	No	No	No	No	No	No
Skin Sensitisation	Yes	Yes	Yes	Yes	No	No	Yes