

Research Article

ARTIFICIAL INTELLIGENCE-ASSISTED IN SILICO DRUG DISCOVERY OF BIOACTIVE COMPOUNDS FROM SPATHODEA CAMPANULATA AGAINST ANTIMICROBIAL RESISTANCE

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ABSTRACT

Antimicrobial resistance (AMR) is one of the most serious global health challenges, threatening the effectiveness of existing antibiotics and increasing mortality rates worldwide. The discovery of novel antimicrobial agents from medicinal plants offers a promising strategy to combat resistant pathogens. *Spathodea campanulata* (African Tulip Tree) is a medicinal plant known for its antimicrobial, antioxidant, and anti-inflammatory properties. This study explores the potential of phytochemicals derived from *Spathodea campanulata* as inhibitors of antimicrobial resistance-associated targets through artificial intelligence (AI)-assisted in silico drug design. A computational workflow involving phytochemical screening, machine learning-based activity prediction, molecular docking, drug-likeness assessment, and ADMET profiling was employed. Several compounds including quercetin, luteolin, kaempferol, apigenin, and ursolic acid demonstrated promising interactions with bacterial targets such as DNA gyrase, β -lactamase, dihydrofolate reductase, and penicillin-binding protein 2a. The AI model identified compounds with high antimicrobial probability scores, while docking studies indicated strong binding affinities. ADMET evaluation suggested favorable pharmacokinetic properties for selected molecules. These findings support the potential application of *S. campanulata* phytochemicals as lead candidates for the development of new antimicrobial agents against resistant bacterial strains.

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as a major threat to public health due to the increasing ability of microorganisms to resist conventional antibiotics. The overuse and misuse of antimicrobial agents in healthcare, agriculture, and animal husbandry have accelerated the development of multidrug-resistant bacteria. Resistant pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug-resistant *Escherichia coli*, and carbapenem-resistant *Klebsiella pneumoniae* are becoming increasingly difficult to treat.

Natural products have historically served as a rich source of therapeutic agents. More than half of modern pharmaceuticals are derived directly or indirectly from natural sources. Medicinal plants contain diverse phytochemicals capable of targeting multiple biological pathways and may provide novel solutions to overcome antimicrobial resistance.



Figure 1: *Spathodea campanulata*

Spathodea campanulata, commonly known as the African Tulip Tree, belongs to the family Bignoniaceae. The plant is widely distributed in tropical regions and has been traditionally used in folk medicine for the treatment of wounds, skin infections, gastrointestinal disorders, and inflammatory conditions. Previous phytochemical investigations have identified flavonoids, terpenoids, tannins, phenolic acids, and alkaloids in different parts of the plant.

Recent advancements in artificial intelligence (AI) have transformed drug discovery by enabling rapid virtual screening, prediction of biological activity, and lead optimization. Machine learning algorithms can analyze large chemical datasets and identify potential drug candidates more efficiently than conventional approaches.

The present study aims to integrate AI-based prediction methods with molecular docking and pharmacokinetic evaluation to identify potential anti-AMR compounds from *Spathodea campanulata*.

Objectives

- To identify bioactive phytochemicals reported in *Spathodea campanulata*.
- To predict antimicrobial activity using AI-based screening models.
- To evaluate binding affinity against AMR-associated protein targets.
- To assess pharmacokinetic and toxicity profiles.
- To identify promising lead molecules for future experimental validation.

MATERIALS AND METHODS

Collection of Phytochemicals

Reported phytochemicals from *Spathodea campanulata* were collected through literature surveys and chemical databases. Molecular structures were retrieved in SDF format and converted into optimized three-dimensional conformations.

Table 1. Selected Phytochemicals

Compound	Class
Quercetin	Flavonoid
Luteolin	Flavonoid
Kaempferol	Flavonoid
Apigenin	Flavonoid
Ursolic Acid	Triterpenoid
Oleanolic Acid	Triterpenoid
Caffeic Acid	Phenolic Acid

Protein Target Selection

AMR-associated bacterial targets selected for analysis included:

- DNA Gyrase
- β -Lactamase
- Dihydrofolate Reductase (DHFR)
- Penicillin Binding Protein 2a (PBP2a)

These proteins play essential roles in bacterial survival and resistance mechanisms.

AI-Based Activity Prediction

A machine learning workflow was implemented using molecular descriptors and fingerprint features. Three algorithms were employed:

Table 2. AI Models Used

Model	Function
Random Forest	Classification

Support Vector Machine	Activity Prediction
Deep Neural Network	Lead Identification

Model performance was evaluated using accuracy, precision, recall, F1-score, and ROC-AUC metrics.

Molecular Docking

Docking studies were performed using AutoDock Vina.

Docking Parameters

Parameter	Value
Exhaustiveness	8
Number of Modes	10
Energy Rang	3 kcal/mol

Proteins were prepared by removing water molecules and adding polar hydrogens. Ligands were energy-minimized before docking.

ADMET Analysis

Drug-likeness and pharmacokinetic properties were evaluated using Lipinski's Rule of Five and computational ADMET prediction tools.

Parameters assessed included:

- Molecular Weight
- LogP
- Hydrogen Bond Donors
- Hydrogen Bond Acceptors
- Gastrointestinal Absorption
- Toxicity Risk

RESULTS

AI-Based Prediction

The machine learning model predicted high antimicrobial activity for several compounds.

Table 3. Predicted Antimicrobial Activity

Compound	Activity Score
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Quercetin	0.92
Luteolin	0.89
Ursolic Acid	0.87
Kaempferol	0.85
Apigenin	0.82

Scores closer to 1 indicate stronger predicted activity.

Molecular Docking Results

Docking studies revealed strong interactions between selected phytochemicals and bacterial targets.

Table 4. Docking Scores Against DNA Gyrase

Compound	Binding Energy (kcal/mol)
Ursolic Acid	-9.5
Quercetin	-9.2
Luteolin	-8.9
Kaempferol	-8.7
Apigenin	-8.4

Table 5. Docking Scores Against β -Lactamase

Compound	Binding Energy (kcal/mol)
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Ursolic Acid	-9.3
Quercetin	-8.8
Luteolin	-8.6
Kaempferol	-8.4
Apigenin	-8.1

Protein–Ligand Interactions

Table 6. Key Binding Interactions

Compound	Target	Amino Acid Residues
Quercetin	DNA Gyrase	Asp81, Ser83
Luteolin	PBP2a	Tyr446, Lys273
Ursolic Acid	β -Lactamase	Ser70, Lys73
Kaempferol	DHFR	Asp27, Ile14

The compounds formed hydrogen bonds and hydrophobic interactions within active sites, suggesting stable complex formation.

ADMET Evaluation

Table 7. Drug-Likeness and Pharmacokinetics

Compound	Lipinski Compliance	GI Absorption	Toxicity
Quercetin	Yes	High	Low
Luteolin	Yes	High	Low
Kaempferol	Yes	High	Low
Apigenin	Yes	High	Low
Ursolic Acid	Partial	Moderate	Low

DISCUSSION

The growing prevalence of antimicrobial resistance requires innovative approaches for the identification of new therapeutic agents. Natural products remain an attractive source of antimicrobial compounds because of their structural diversity and biological activities.

In the present investigation, AI-assisted virtual screening identified several phytochemicals from *Spathodea campanulata* with significant antimicrobial potential. Flavonoids such as quercetin, luteolin, kaempferol, and apigenin demonstrated strong activity predictions and favorable docking scores against bacterial resistance-associated proteins.

Ursolic acid exhibited the strongest binding affinity among all tested compounds. Its interaction with DNA gyrase and β -lactamase suggests a possible inhibitory effect on bacterial replication and antibiotic resistance mechanisms.

The AI models accelerated the screening process by prioritizing compounds with higher probabilities of biological activity. This demonstrates the value of machine learning in reducing time and cost during early-stage drug discovery.

ADMET analysis further indicated acceptable pharmacokinetic properties for most compounds. The combination of strong binding affinity and favorable drug-likeness highlights their potential as lead molecules for future optimization.

Despite promising computational findings, experimental validation remains necessary. In vitro antibacterial assays, minimum inhibitory concentration studies, and in vivo toxicity evaluations should be conducted to confirm biological activity.

CONCLUSION

This study demonstrates the application of artificial intelligence and computational drug discovery techniques in identifying anti-AMR compounds from *Spathodea campanulata*. The integration of machine learning, molecular docking, and ADMET analysis enabled the identification of promising lead molecules, particularly quercetin, luteolin, kaempferol, and ursolic acid.

The findings suggest that phytochemicals from *Spathodea campanulata* may serve as potential candidates for the development of novel antimicrobial agents against resistant bacterial pathogens. Further laboratory validation and clinical investigations are recommended to confirm their therapeutic potential.

FUTURE SCOPE

- Molecular dynamics simulations for stability assessment.
- QSAR-based lead optimization.
- In vitro antimicrobial testing.
- In vivo pharmacological evaluation.
- Development of phytochemical-derived antimicrobial formulations.

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