

Research Article

In Silico Evaluation of Antibacterial Potential of *Ceiba Pentandra* (L.) Gaertn. Phytoconstituents Against Skin Infection-associated Pathogens

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Abstract

In particular, the emergence of multidrug-resistant (MDR) bacterial pathogens has complicated the management of skin and wound infections and has increased the need for alternative sources of antibacterial molecules. The plant *Ceiba pentandra* (L.) Gaertn., is one of the notable members of the family Malvaceae, and has been traditionally used for several of its ethnomedicinal properties, including management of skin infections. The present study aimed to explore the *in silico* antibacterial potential against *E. coli* and *S. aureus*. Physicochemical and drug-likeness assessments were performed on phytoconstituents obtained with *C. pentandra* from the IMPPAT database. Computational platforms were used to predict ADMET and toxicity profiles. The Lipinski RO5-compliant compounds were further investigated for molecular docking against *E. coli* DNA gyrase (PDB ID: 1KZN) and *S. aureus* DNA gyrase (PDB ID: 3G7B). Among the compounds, kaempferol showed the best binding with predicted binding energies of -8.0 kcal/mol and -7.8 kcal/mol with *E. coli* DNA gyrase and *S. aureus* DNA gyrase, respectively. The results indicated that *C. pentandra* contains phytoconstituents with potential for strong interactions with bacterial DNA gyrase, with kaempferol as the most notable constituent. The study provides a computational basis for future study of *C. pentandra*-derived compounds against bacterial pathogens associated with skin infections.

Keywords

DNA Gyrase, Phytocompounds, ADMET, *Ceiba Pentandra*, Skin Infection, Molecular Docking

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Received: 29 September 2026; **Accepted:** 9 October 2026; **Published:** 29 October 2026



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1. Introduction

Antimicrobial resistance (AMR) has emerged as a major global public health challenge, substantially compromising the effectiveness of antimicrobial therapy and increasing the difficulty of managing bacterial infections (Nazir et al., 2025) [9]. Inappropriate and excessive use of antimicrobial agents, along with inadequate infection prevention and control, has accelerated the selection and dissemination of resistant microorganisms. The increasing prevalence of multidrug-resistant (MDR) bacteria can lead to prolonged infections, limited therapeutic options, increased healthcare expenditure, and greater morbidity and mortality. Consequently, identifying alternative antimicrobial sources and new molecular scaffolds that act against resistant bacteria has become an important area of contemporary biomedical research [14].

Concomitantly, skin infections are among the most common bacterial infections, and antimicrobial resistance presents a significant therapeutic challenge. *Staphylococcus aureus* is a major Gram-positive pathogen associated with skin infections, wound infections, abscesses, and other soft-tissue infections, whereas *Escherichia coli*, a Gram-negative pathogen, also contributes to wound contamination and infection, particularly in compromised tissues [6].

In this context, plant-derived phytochemicals show potential as a reservoir of structurally diverse bioactive molecules that may provide alternative scaffolds for antibacterial drug discovery (Swain et al., 2025) [13]. Plant secondary metabolites interfere with bacterial survival through multiple mechanisms, including disruption of the bacterial cell membrane, alteration of membrane permeability, inhibition of essential metabolic enzymes, interference with nucleic-acid synthesis, impairment of energy metabolism, and modulation of bacterial virulence and biofilm-associated processes. In addition, computational approaches such as molecular docking, pharmacokinetic prediction, and molecular dynamics simulation may further facilitate systematic screening and prioritization of plant-derived compounds against selected bacterial targets (Parameswaran et al., 2026) [11].

Ceiba pentandra (L.) Gaertn., commonly known as the kapok or silk-cotton tree, belongs to the family Malvaceae and is widely distributed in tropical regions. The species has a history of ethnomedicinal use, with different plant parts traditionally employed for various ailments (Chan et al., 2022) [2]. Importantly, ethnomedicinal use of *C. pentandra* has shown efficacy in managing skin diseases, with the leaf used as an external paste (A. Elumalai et al., 2012) [1]. This traditional indication provides a rationale for investigating the phytoconstituents of *C. pentandra* in the context of bacterial skin infections. Although previously reported studies have shown the efficacy of different plant extracts against bacterial strains and identified diverse phytoconstituents, *in silico* predictions against target proteins remain limited. Furthermore, *E. coli* and *S. aureus* are important causative agents of skin and soft

tissue infections, and these pathogens also develop AMR, requiring alternative therapies (Monk et al., 2024) [8]. Concomitantly, the bacterial target DNA gyrase, which plays a pivotal role in DNA replication, requires the discovery of new natural compound-based druggable candidates to inhibit it and combat the growing AMR crisis (Dighe & Collet, 2020) [3]. The diverse phytochemical constituents reported for the species further support its consideration as a source of candidate molecules for computational antibacterial investigation.

Therefore, the present study investigates the potential of *C. pentandra* phytoconstituents against bacterial pathogens associated with skin infections using an integrated *in silico* approach. Phytoconstituents associated with *C. pentandra* were retrieved from the Indian Medicinal Plants, Phytochemistry and Therapeutics (IMPPAT) database and subjected to physicochemical and drug-likeness assessment. Selected compounds were subsequently evaluated through molecular docking against relevant protein targets of *E. coli* and *S. aureus* to identify favorable ligand-protein interactions. The prioritized compounds can further be assessed through ADMET profiling and molecular dynamics simulations to evaluate the stability and pharmacokinetic suitability of the predicted interactions.

2. Materials and Methods

2.1. Ligand Library Preparation

Phytoconstituents associated with *C. pentandra* were retrieved from the Indian Medicinal Plants, Phytochemistry and Therapeutics (IMPPAT) database (<https://cb.imsc.res.in/imp-pat/>) After removal of duplicate entries, 15 phytoconstituents with their corresponding IMPPAT identifiers were selected for further *in silico* evaluation. The chemical structures of the selected compounds were obtained from the PubChem database (<https://pubchem.ncbi.nlm.nih.gov/>) in Structure Data File (.sdf) format (Mejari et al., 2026) [7]. The retrieved ligand structures were subsequently prepared and their three-dimensional geometries were optimized using Avogadro software prior to molecular docking (Pakeeraiah et al., 2024) [10]. The 15 compounds were initially screened for drug-likeness properties based on Lipinski RO5. Compounds satisfying the predefined screening criteria were prioritized for subsequent molecular docking studies.

2.2. Test Protein Retrieval

The crystal configurations of bacterial DNA gyrase from *E. coli* (PDB ID: 1KZN) and *S. aureus* (PDB ID: 3G7B) were obtained from the Protein Data Bank (<https://www.rcsb.org/>) in PDB format. The frameworks were examined and arranged utilizing PyMOL (<https://www.pymol.org/>) These two pathogens are clinically important bacterial species primarily associated with skin, wound and soft-tissue infections and may complicate

the infection management due to rapid AMR. Furthermore, DNA gyrase plays a role in DNA replication; thus, inhibiting it may interfere with bacterial growth and survival, making it a notable target for antibacterial drug discovery (Dighe & Collet, 2020) [3]. Water molecules were removed, hydrogen atoms were added, and co-crystallized/non-protein ligand molecules were extracted from the bacterial targets before molecular docking. The generated protein structures were then used as receptor entities for molecular docking with the selected *C. pentandra* phytochemicals (Sahoo et al., 2022) [12].

2.3. Physicochemical and Pharmacokinetics Studies

The Lipinski rule of 5 (RO5) is the standard method for assessing a molecule's potential as a medicine. To qualify as drug-like, a molecule must satisfy these five criteria (Ivanović et al., 2020) [5].

- 1) Molar mass: Below 500 Daltons,
- 2) Hydrogen bond acceptor: 10 or less than 10,
- 3) Hydrogen bond donor: 5 or less,
- 4) logP (lipophilicity): 5 or fewer,

The Lipinski prediction was evaluated utilizing sources including Molsoft (<https://www.molsoft.com/>), focusing on molecular weight, hydrogen bond acceptors, hydrogen bond donors, and MolLogP. ADMET encompasses the parameters of

Adsorption, Distribution, Metabolism, Excretion, and Toxicity. The ADMET characteristics of the bioactive compounds derived from *C. pentandra* were acquired by ProTox-3.0 (<https://tox.charite.de/protox3/>) and ADMELab 2.0 (<https://admetmesh.scbdd.com/>). Compounds that met all four criteria were retained for docking analysis, and compounds that violated Lipinski's rule of five were excluded from further *in silico* analysis.

2.4. Molecular Docking and Binding Affinity Studies

The three-dimensional structures of the target proteins were retrieved from the RCSB Protein Data Bank (PDB), following which heteroatoms and water molecules were removed utilizing PyMOL. Protein and ligand preparation was performed with AutoDockTools v1.5.6; Kollman charges and solvation parameters were assigned to protein atoms, while Gasteiger charges were applied to ligand atoms. The docking grid box was defined based on the co-crystallized ligand, and molecular docking was performed using the Lamarckian Genetic Algorithm (Table 1). The derived docking conformations were further evaluated for protein-ligand interactions using BIOVIA Discovery Studio Visualizer (Sahoo et al., 2022) [12].

Table 1. Molecular docking grid parameters used for bacterial target proteins.

Target Proteins	Grid centre X	Grid centre Y	Grid centre Z	Grid centre Dimension (X x Y x Z)
1KZN	20.154	23.677	35.508	21 x 21 x 21
3G7B	7.462	-6.293	-3.521	21 x 21 x 21

3. Results and Discussion

3.1. Ligands from *C. Pentandra*

All 15 ligands from the IMPPAT database were drawn in ChemBiodraw Ultra 14 and used to determine ligand-specific properties, including chemical formula and exact mass (Table 2, Figure 1).

Table 2. Selected ligands from *C. pentandra* with IMPPAT Identifiers and Chemical profiling.

Sl. No.	Phytoconstituent	IMPPAT Identifier	Present in Plant part	PubChem ID	Properties
1	L- (+)-Arabinose	IMPHY004187	Bark	439195	Chemical Formula: C ₅ H ₁₀ O ₅ Exact Mass: 150.05
2	L-Rhamnose	IMPHY015056	Bark	25310	Chemical Formula: C ₆ H ₁₂ O ₅ Exact Mass: 164.07

Sl. No.	Phytoconstituent	IMPPAT Identifier	Present in Plant part	PubChem ID	Properties
3	7-Hydroxycadalene	IMPHY006334	Root	608115	Chemical Formula: C ₁₅ H ₁₈ O Exact Mass: 214.14
4	2,7-Dimethoxy-5-isopropyl-3-methyl-8,1-naphthalene carbo-lactone	IMPHY014151	Root	9994145	Chemical Formula: C ₁₇ H ₁₈ O ₄ Exact Mass: 286.12
5	Gossypol	IMPHY003281	Seed	3503	Chemical Formula: C ₃₀ H ₃₀ O ₈ Exact Mass: 518.19
6	2,7-Dihydroxy-3-methyl-5-isopropyl-8-formyl-1,4-naphtho-quinone	IMPHY014204	Wood	11108542	Chemical Formula: C ₁₅ H ₁₄ O ₅ Exact Mass: 274.08
7	Tetracosanoic acid	IMPHY000165	-	11197	Chemical Formula: C ₂₄ H ₄₈ O ₂ Exact Mass: 368.37
8	Kaempferol	IMPHY004388	-	5280863	Chemical Formula: C ₁₅ H ₁₀ O ₆ Exact Mass: 286.05
9	Linarin	IMPHY004984	-	5317025	Chemical Formula: C ₂₈ H ₃₂ O ₁₄ Exact Mass: 592.18
10	1-Hentriacontanol	IMPHY007132	-	68345	Chemical Formula: C ₃₁ H ₆₄ O Exact Mass: 452.50
11	Hentriacontane	IMPHY008910	-	12410	Chemical Formula: C ₃₁ H ₆₄ Exact Mass: 436.50
12	Arachidic acid	IMPHY011394	-	10467	Chemical Formula: C ₂₀ H ₄₀ O ₂ Exact Mass: 312.30
13	Caffeic acid	IMPHY011933	-	689063	Chemical Formula: C ₉ H ₈ O ₄ Exact Mass: 180.04
14	beta-Sitosterol	IMPHY014836	-	222284	Chemical Formula: C ₂₉ H ₅₀ O Exact Mass: 414.39
15	beta-Sitosterol-beta-D-glucoside	IMPHY015072	-	12309055	Chemical Formula: C ₃₅ H ₆₀ O ₆ Exact Mass: 576.44

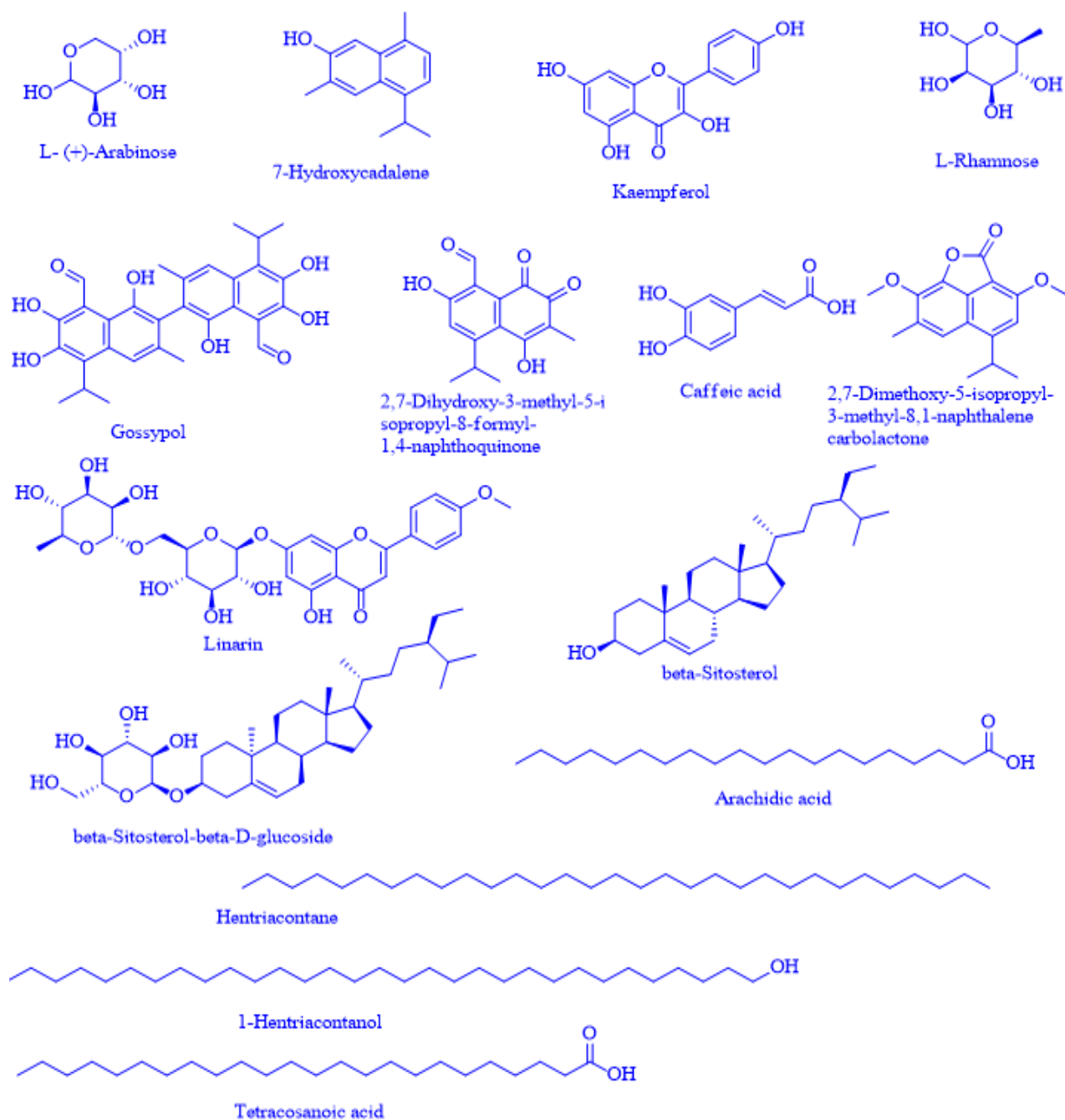


Figure 1. Chemical structures of phytoconstituents from *C. pentandra*.

3.2. Physicochemical and Pharmacokinetics Studies

The 15 IMPPAT-derived phytoconstituents were initially evaluated for their physicochemical and drug-likeness characteristics. Based on the criteria applied in the present study, seven compounds namely, L-(+)-arabinose, L-rhamnose, 7-hydroxycadalene, 2,7-dimethoxy-5-isopropyl-3-methyl-8,1-naphthalene carbolactone, 2,7-dihydroxy-3-methyl-5-isopropyl-8-formyl-1,4-naphthoquinone, kaempferol and caffeic acid were prioritized for subsequent molecular docking as

they satisfied the Lipinski RO5 (Tables 3, 4 and Figure 2).

Furthermore, computational toxicity prediction further indicated that the seven prioritized compounds were distributed across toxicity classes 4-6, with predicted LD₅₀ values ranging from 1,030 to 23,000 mg/kg. L-(+)-arabinose and L-rhamnose were assigned to toxicity class 6 with predicted LD₅₀ values of 23,000 mg/kg, whereas 7-hydroxycadalene and the naphthoquinone derivative were assigned to class 4, with predicted LD₅₀ values of 1,030 mg/kg. Kaempferol and caffeic acid were assigned to toxicity class 5, with predicted LD₅₀ values of 3,919 and 2,980 mg/kg, respectively. These predictions pro-

vide preliminary computational information regarding the toxicity profiles of the prioritized compounds.

Overall, physicochemical and ADMET screening identified compounds with comparatively favorable computational pro-

files for subsequent molecular docking. Kaempferol was particularly notable because it combined acceptable drug-like physicochemical characteristics with a favorable predicted toxicity profile and subsequently exhibited the most favorable docking scores against both bacterial DNA gyrase targets.

Table 3. Lipinski Rule of five of the compounds.

Sl. No.	Compound	MW	HBA	HBD	clogP
1	L- (+)-Arabinose	150.05	5	4	-2.93
2	L-Rhamnose	164.07	5	4	-2.30
3	7-Hydroxycadalene	214.14	1	1	4.87
4	2,7-Dimethoxy-5-isopropyl-3-methyl-8,1-naphthalene carbolactone	286.12	4	0	3.78
5	Gossypol	518.19	8	6	7.63
6	2,7-Dihydroxy-3-methyl-5-isopropyl-8-formyl-1,4-naphthoquinone	274.08	5	2	1.91
7	Tetracosanoic acid	368.37	2	1	10.68
8	Kaempferol	286.05	6	4	1.61
9	Linarin	592.18	14	7	0.42
10	1-Hentriacontanol	452.50	1	1	14.73
11	Hentriacontane	436.50	0	0	16.46
12	Arachidic acid	312.30	2	1	8.66
13	Caffeic acid	180.04	4	3	1.27
14	beta-Sitosterol	414.39	1	1	8.45
15	beta-Sitosterol-beta-D-glucoside	576.44	6	4	6.31

Table 4. Toxicity analysis of top-seven compounds.

Sl. No.	Compounds	Toxicity analysis				
		Class	LD ₅₀ (mg/kg)	BBB	HIA	Caco-2 permeability
1.	L- (+)-Arabinose	6	23000	+++	-	-5.223
2.	L-Rhamnose	6	23000	--	++	-5.267
3.	7-Hydroxycadalene	4	1030	---	++	-4.743
4.	2,7-Dimethoxy-5-isopropyl-3-methyl-8,1-naphthalene carbolactone	5	2900	---	--	-4.896
5.	2,7-Dihydroxy-3-methyl-5-isopropyl-8-formyl-1,4-naphthoquinone	4	1030	---	---	-4.860
6.	Kaempferol	5	3919	---	---	-4.974
7.	Caffeic acid	5	2980	---	---	-4.959

For the categorization endpoints, the predicted probability values are converted into four symbols: 0-0.1 (---), 0.1-0.3 (--), 0.7-0.9 (++), and 0.9-1.0 (+++).

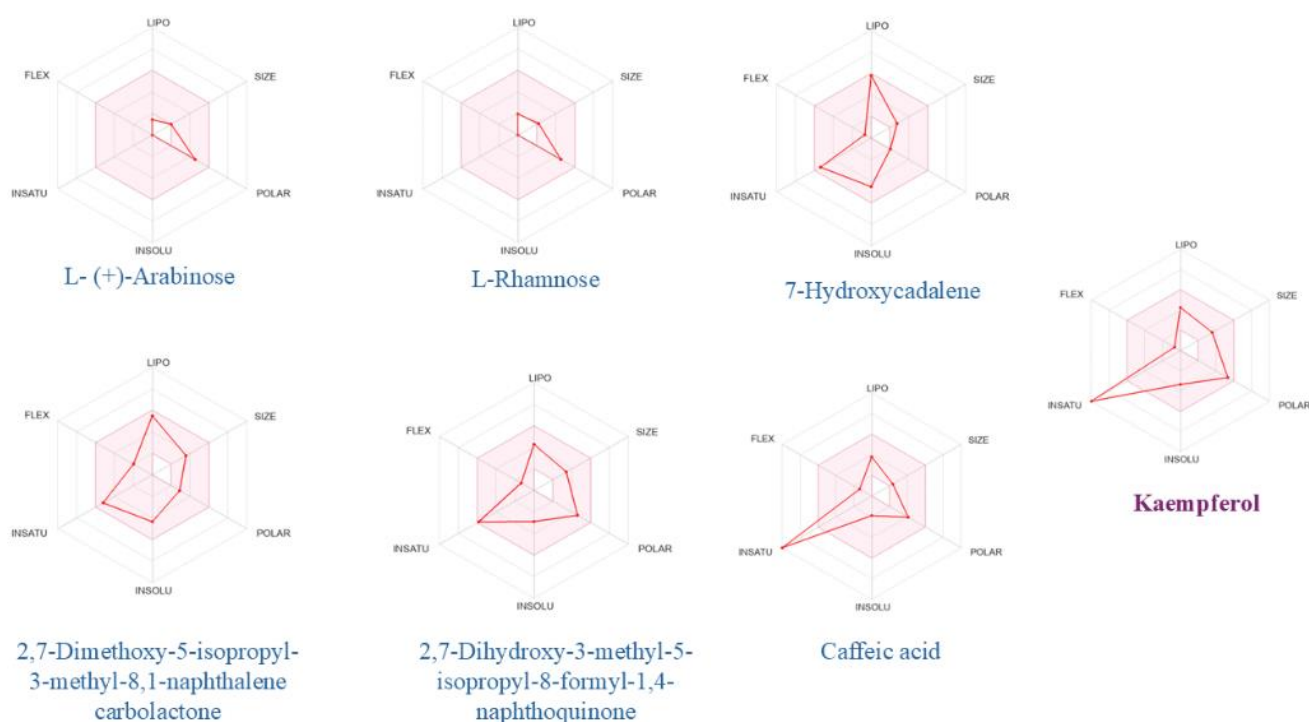


Figure 2. Radar plots for Phytocompounds from *C. pentandra*.

3.3. Molecular Docking Analysis

Molecular docking was conducted to assess the anticipated interaction of the seven selected *C. pentandra* phytoconstituents with bacterial DNA gyrase targets from *E. coli* and *S. aureus*. All seven compounds exhibited negative estimated binding energies for both targets, suggesting notable anticipated ligand-protein interactions. Binding energies for *E. coli* DNA gyrase ranged from -5.1 to -8.0 kcal/mol, while those for *S. aureus* DNA gyrase ranged from -4.4 to -7.8 kcal/mol. Among the evaluated substances, kaempferol showed the most favorable estimated binding energy for both targets, with -8.0 kcal/mol for *E. coli* DNA gyrase and -7.8 kcal/mol for *S. aureus* DNA gyrase. Kaempferol is a natural flavonoid commonly found in plants, tea, broccoli, and other vegetables. It displays various biological effects, including antioxidant, anti-inflammatory, antimicrobial, and anticancer activities. Additionally, kaempferol is frequently utilized as a ligand in molecular docking to evaluate its binding affinity and interactions

with targeted proteins. The hydroxyl groups and planar structure of flavonoids facilitate hydrogen bonding, hydrophobic interactions, and other non-covalent interactions in protein-binding pockets. Docking analysis helps predict binding energy, identify interacting amino acid residues, and explore its potential as a lead compound for developing therapeutic agents. These findings highlight kaempferol as the top-ranked ligand in the docking assessment (Tables 5, 6 and Figures 3 and 4). These findings are consistent with previously reported antibacterial activity of kaempferol against *E. coli* and its inhibition of purified DNA Gyrase (Wu et al., 2013) [15]. Concomitantly, another report identified favorable interactions between kaempferol and key residues of *E. coli* gyrase through molecular docking, including ASN 46, ASP 37, and GLY 77, further supporting the plausibility of the predicted binding mode (Fang et al., 2016) [4]. However, the current results are from *in silico* studies and require *in-depth* experimental validation to determine biological efficacy.

Table 5. Binding energy evaluation for *C. pentandra* phytoconstituents.

Sl. No.	Phytoconstituent	IMPPAT Identifier	Binding energy (kcal/mol)	
			<i>E. coli</i>	<i>S. aureus</i>
1	L- (+)-Arabinose	IMPHY004187	-5.1	-4.4
2	L-Rhamnose	IMPHY015056	-5.1	-4.9

Sl. No.	Phytoconstituent	IMPPAT Identifier	Binding energy (kcal/mol)	
			<i>E. coli</i>	<i>S. aureus</i>
3	7-Hydroxycadalene	IMPHY006334	-6.3	-7.4
4	2,7-Dimethoxy-5-isopropyl-3-methyl-8,1-naphthalene carbolactone	IMPHY014151	-7.1	-7.6
5	2,7-Dihydroxy-3-methyl-5-isopropyl-8-formyl-1,4-naphthoquinone	IMPHY014204	-7.0	-7.7
6	Kaempferol	IMPHY004388	-8.0	-7.8
7	Caffeic acid	IMPHY011933	-6.2	-6.2

Table 6. Binding interaction evaluation for *C. pentandra* phytoconstituents.

Sl. No.	Phytoconstituent	IMPPAT Identifier	Binding interaction	
			<i>E. coli</i>	<i>S. aureus</i>
1	Kaempferol	IMPHY004388	H-bond: ARG 136 and ASN 46 Pi-Anion: GLU 50, ASP 73 Pi-alkyl: ILE 78, ALA 47, PRO 79 Van der Waals: VAL 43, VAL 120, GLY 77, ARG 76, ASP 49, THR 165, VAL 167	H-bond: SER 55, GLU 58 Pi-Anions: ASP 81 Pi-Alkyl: ILE 51, ILE 175 Pi-sigma: ILE 86 Van der Waals: VAL 79, THR 173, GLY 85, PRO 87, ILE 102 Unfavourable donor-donor: ARG 84

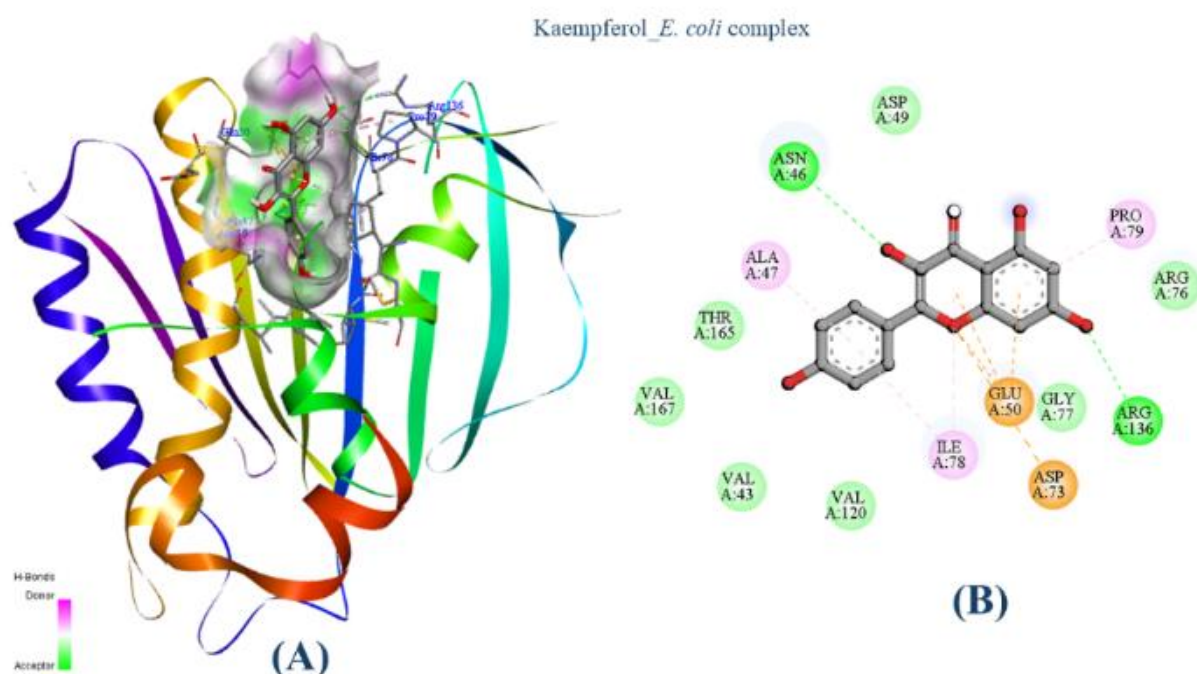


Figure 3. Molecular docking analysis of Kaempferol with the target protein of *E. coli*: (A) 3D illustration, (B) 2D illustration.

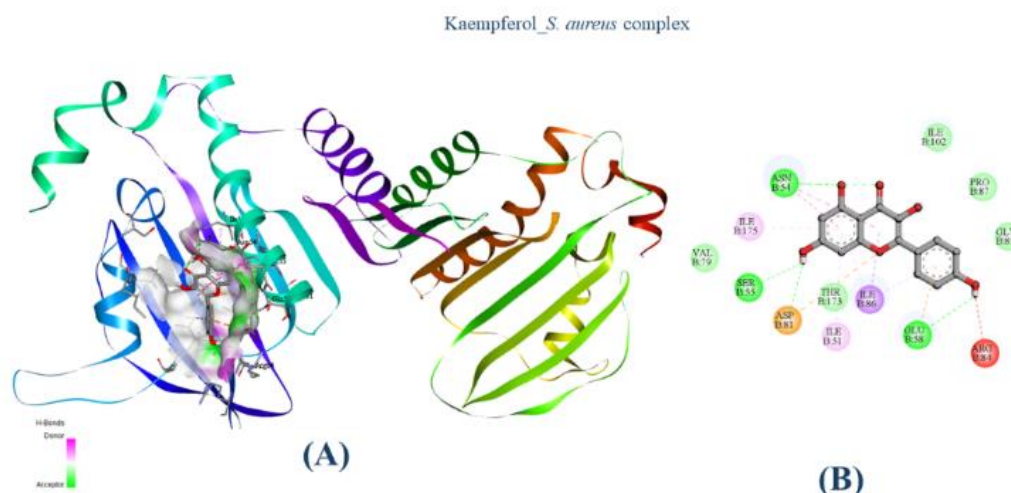


Figure 4. Molecular docking analysis of Kaempferol with the target protein of *S. aureus* (A) 3D illustration (B) 2D illustration.

4. Conclusion

This *in silico* investigation provides a computational assessment of *C. pentandra* phytoconstituents against DNA gyrase targets of *E. coli* and *S. aureus*, supporting the plant's ethnomedicinal use for skin diseases in Koraput district, Odisha. Fifteen phytoconstituents retrieved from the IMPPAT database were evaluated for their physicochemical and drug-like properties, followed by ADMET and toxicity prediction and molecular docking of the prioritized compounds. Among the seven compounds subjected to docking, kaempferol demonstrated the most favorable predicted binding energies against both *E. coli* and *S. aureus* DNA gyrase, suggesting its potential as a candidate for further investigation. The computational findings support the ethnomedicinal relevance of *C. pentandra* as a source of structurally diverse compounds with potential antibacterial activity. Nevertheless, these docking predictions served as a basis for hypothesis generation about the possible interaction of the prioritized phytoconstituents with bacterial DNA gyrase, not as evidence of confirmed antibacterial activity. The generated hypotheses would then be validated experimentally, including *in vitro* antibacterial assays, target-based studies, and appropriate toxicity assessments to assess their biological efficacy and therapeutic potential.

Abbreviations

ADMET	Absorption, Distribution, Metabolism, Excretion and Toxicity
AMR	Antimicrobial Resistance
BBB	Blood-Brain Barrier
Caco-2	Human Intestinal Epithelial Cell Permeability Model

DNA	Deoxyribonucleic Acid
E. coli	Escherichia Coli
HBA	Hydrogen Bond Acceptor
HBD	Hydrogen Bond Donor
HIA	Human Intestinal Absorption
IMPPAT	Indian Medicinal Plants Phytochemistry and Therapeutics
LD ₅₀	Median Lethal Dose
MDR	Multi Drug Resistance
MW	Molecular Weight
PDB	Protein Data Bank
RO5	Rule of Five (Lipinski's Rule of Five)
RCSB	Research Collaboratory for Structural Bioinformatics
SDF	Structure Data File

Author Contributions

Manoja Das: Formal Analysis, Methodology, Supervision, Investigation. **Manish Kumar:** Writing – review & editing, Writing– original draft, Validation. **Pallabi Mohapatra:** Investigation, Writing– original draft Conceptualization

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Elumalai, Nikhitha Mathangi, Adarsh Didala, Raju Kasarla, & Yetcharla Venkatesh. (2012). A Review on Ceiba pentandra and its medicinal features. Asian Journal of Pharm. Tech., 83-86.

- [2] Chan, E. W. C., Yeong, S. W., Wong, C. W., Soo, O. Y. M., Phua, A. C. Y., & Ng, Y. K. (2022). *Ceiba pentandra* (L.) Gaertn.: An overview of its botany, uses, reproductive biology, pharmacological properties, and industrial potentials. *Journal of Applied Biology & Biotechnology*.
<https://doi.org/10.7324/JABB.2023.110101>
- [3] Dighe, S. N., & Collet, T. A. (2020). Recent advances in DNA gyrase-targeted antimicrobial agents. *European Journal of Medicinal Chemistry*, 199, 112326.
<https://doi.org/10.1016/j.ejmech.2020.112326>
- [4] [Fang, Y., Lu, Y., Zang, X., Wu, T., Qi, X., Pan, S., & Xu, X. (2016). 3D-QSAR and docking studies of flavonoids as potent *Escherichia coli* inhibitors. *Scientific Reports*, 6(1), 23634.
<https://doi.org/10.1038/srep23634>
- [5] Ivanović, V., Rančić, M., Arsić, B., & Pavlović, A. (2020). Lipinski's rule of five, famous extensions and famous exceptions. *Popular Scientific Article*, 3(1), 171-177.
- [6] Kumar, S., Mahato, R. P., Ch, S., & Kumbham, S. (2025). Current strategies against multidrug-resistant *Staphylococcus aureus* and advances toward future therapy. *The Microbe*, 6, 100281. <https://doi.org/10.1016/j.microb.2025.100281>
- [7] Mejari, M., Suresh, N., Vishe, B., Raza, A., Jangam, S., & Choure, R. (2026). In-silico identification of *Kalanchoe pinnata* phytochemicals as potential natural inhibitors of *Escherichia coli* dihydrofolate reductase. In *Silico Research in Biomedicine*, 2, 100473. |
<https://doi.org/10.1016/j.ins.2026.100473>
- [8] Monk, E. J. M., Jones, T. P. W., Bongomin, F., Kibone, W., Nsubuga, Y., Ssewante, N., Muleya, I., Nsenga, L., Rao, V. B., & van Zandvoort, K. (2024). Antimicrobial resistance in bacterial wound, skin, soft tissue and surgical site infections in Central, Eastern, Southern and Western Africa: A systematic review and meta-analysis. *PLOS Global Public Health*, 4(4), e0003077. <https://doi.org/10.1371/journal.pgph.0003077>
- [9] Nazir, A., Nazir, A., Zuhair, V., Aman, S., Sadiq, S. U. R., Hasan, A. H., Tariq, M., Rehman, L. U., Mustapha, M. J., & Bulimbe, D. B. (2025). The Global Challenge of Antimicrobial Resistance: Mechanisms, Case Studies, and Mitigation Approaches. *Health Science Reports*, 8(7).
<https://doi.org/10.1002/hsr2.71077>
- [10] Pakeeraiah, K., Swain, P. P., Sahoo, A., Panda, P. K., Mahapatra, M., Mal, S., Sahoo, R. K., Sahu, P. K., & Paidesetty, S. K. (2024). Multimodal antibacterial potency of newly designed and synthesized Schiff's/Mannich based coumarin derivatives: potential inhibitors of bacterial DNA gyrase and biofilm production. *RSC Advances*, 14(43), 31633-31647.
<https://doi.org/10.1039/D4RA05756B>
- [11] Parameswaran, S., Natarajan, S. B., Shanmugam, N., & Kalusalingam, A. (2026). Plant Secondary Metabolites as Next-Generation Antibiofilm and Antimicrobial Agents: Mechanisms, Synergistic Effects, and Clinical Translation. *Drugs and Drug Candidates*, 5(3), 38.
<https://doi.org/10.3390/ddc5030038>
- [12] Sahoo, C. R., Paidesetty, S. K., Sarathbabu, S., Dehury, B., Senthil Kumar, N., & Padhy, R. N. (2022). Molecular dynamics simulation, synthesis and topoisomerase inhibitory actions of vanillin derivatives: a systematic computational structural integument. *Journal of Biomolecular Structure and Dynamics*, 40(22), 11653-11663.
<https://doi.org/10.1080/07391102.2021.1961867>
- [13] [Swain, P., Kumari, R., Biswas, S., Misra, N., Kushwaha, G. S., & Suar, M. (2025). Plant natural products for antibacterial drug development against ESKAPE pathogens. *The Microbe*, 9, 100610. <https://doi.org/10.1016/j.microb.2025.100610>
- [14] Temesgen, A. B., & Shiferaw, S. A. (2025). Antimicrobial Multidrug Resistance and Mechanisms of Action: An Overview. *BioMed Research International*, 2025(1).
<https://doi.org/10.1155/bmri/8847267>
- [15] Wu, T., Zang, X., He, M., Pan, S., & Xu, X. (2013). Structure-Activity Relationship of Flavonoids on Their Anti-*Escherichia coli* Activity and Inhibition of DNA Gyrase. *Journal of Agricultural and Food Chemistry*, 61(34), 8185-8190.
<https://doi.org/10.1021/jf402222v>