FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 10 No. 21, November, 2026, pp 285 – 296
DOI: https://doi.org/10.33003/fjs-2026-1021-6359

Computational Screening of Phytochemicals from Nigerian Medicinal Plants as Potential Inhibitors of *Staphylococcus aureus* DNA Gyrase B

Jumai Ohunene Umazayi, Gideon Ampoma Gyebi and Oluchukwu Ogechukwu Anunobi

Department of Biochemistry, Faculty of Science and Technology, Bingham University, Karu, Nigeria.

*Corresponding authors' email: nenejumai@gmail.com Phone: +2348148892008

Received: 27 Aug. 2026
Accepted: 30 Oct. 2026
Published: 04 Nov. 2026

ABSTRACT

The increasing burden of antimicrobial resistance (AMR), particularly in Staphylococcus aureus, underscores the need to identify novel chemical scaffolds for targeting essential bacterial processes. DNA gyrase B (GyrB), the ATPase subunit of bacterial DNA gyrase, represents a promising antibacterial target.

Antimicrobial resistance in Staphylococcus aureus presents a continuing challenge to effective antibacterial treatment. This study computationally screened phytochemicals associated with Nigerian medicinal plants to identify potential inhibitors of S. aureus DNA gyrase B (GyrB). Candidate compounds were selected from published ethnobotanical and phytochemical literature, and their chemical structures were prepared for molecular docking against GyrB (PDB ID: 4URO) using AutoDock Vina through PyRx. Novobiocin was used as the reference inhibitor. Predicted protein–ligand interactions and absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties were subsequently examined. Tiliacorine exhibited the most favourable docking score (−9.5 kcal/mol), followed by ellagic acid (−9.2 kcal/mol), bidebiline (−9.0 kcal/mol), and diospyrin (−8.8 kcal/mol), compared with −8.6 kcal/mol for novobiocin. Interaction analysis indicated recurring predicted contacts involving Asp81 and Gly85, with additional interactions reported for tiliacorine involving Arg84 and Arg144. ADMET predictions suggested comparatively favourable drug-likeness characteristics for diospyrin and ellagic acid, although potential pharmacokinetic and toxicity limitations were identified. Tiliacorine and bidebiline also exhibited predicted safety concerns. These findings identify selected phytochemicals as candidates for further investigation but do not establish GyrB inhibition or antibacterial efficacy. Experimental enzyme-inhibition assays, antibacterial susceptibility testing, and safety evaluation are required to validate their therapeutic potential.

Keywords: Artificial Intelligence, Chatbot, Natural Language Processing, Academic Support

INTRODUCTION

Antimicrobial resistance (AMR) is a major challenge to infectious disease management, threatening the effectiveness of established therapies and increasing the complexity of treating bacterial infections. The global burden remains substantial: the Global Burden of Disease 2021 Antimicrobial Resistance Collaborators (2024) estimated that bacterial AMR was directly attributable to approximately 1.14 million deaths and associated with 4.71 million deaths worldwide in 2021, underscoring the need for sustained investment in antibacterial discovery. Among hospital associated bacterial pathogens, Staphylococcus aureus is particularly consequential because it causes infections ranging from skin and soft tissue infections to bacteraemia, endocarditis, and pneumonia. Methicillin-resistant *S. aureus* (MRSA) further complicates treatment by limiting the effectiveness of many β-lactam antibiotics, while resistance to other antimicrobial classes can narrow therapeutic options. These challenges make the discovery of antibacterial molecules with new chemical features and potentially useful mechanisms a continuing priority. However, the development of new agents requires more than identifying compounds with general antimicrobial activity; it also requires rational selection of molecular targets and credible approaches for prioritizing candidates for experimental validation.

DNA gyrase is an attractive target for antibacterial discovery because it performs an essential function in bacterial chromosome maintenance and has no direct functional equivalent in human cells. The enzyme is a type II topoisomerase composed of two GyrA and two GyrB subunits. GyrA primarily participates in DNA cleavage and religation, whereas GyrB contains the ATPase machinery required to drive the conformational changes that power the catalytic cycle. By introducing negative supercoils into DNA, DNA gyrase facilitates essential processes, including DNA replication and transcription, making disruption of its activity potentially lethal to bacterial cells (Collin et al., 2011). Unlike fluoroquinolones, which primarily stabilize the enzyme DNA cleavage complex, aminocoumarin antibiotics such as novobiocin inhibit gyrase by binding to the ATP-binding region of GyrB and interfering with ATP utilization. This mechanism establishes the GyrB ATPase domain as a distinct target for structure based antibacterial discovery (Bisacchi & Manchester, 2015; Collin et al., 2011). Targeting this enzyme region may therefore provide opportunities to investigate chemical scaffolds with binding characteristics different from those of established fluoroquinolones.

Natural products offer a compelling starting point for such investigations because plant secondary metabolites occupy diverse chemical spaces and possess varied structural features that can inform antibacterial lead discovery. Their relevance extends beyond traditional use: natural products and their derivatives have historically contributed to the development of medicines, while contemporary natural product research increasingly integrates chemical characterization, biological testing, and structure guided optimization (Newman & Cragg,

2020). For antibacterial discovery, the central opportunity is not to assume that phytocompounds are inherently safer or more effective than synthetic drugs, but to identify chemically promising molecules whose structures and biological properties justify further investigation. Natural product derived scaffolds may offer distinctive combinations of aromatic systems, hydrogen bond donors and acceptors, hydrophobic regions, and stereochemical features that can be explored for recognition of the GyrB ATP-binding pocket and subsequent medicinal chemistry optimization. Their potential value therefore depends on rigorous compound identification, reproducible evidence of activity, and the ability to distinguish plausible target directed interactions from nonspecific binding or computational artefacts.

Nigeria provides a particularly relevant context for this approach because its botanical resources are closely linked to extensive ethnomedicinal knowledge across diverse ecological and cultural settings. A systematic review of Nigerian ethnobotanical research identified 963 plant species across 144 families from 79 eligible studies, demonstrating the breadth of documented plant use while highlighting the value of preserving and systematically evaluating indigenous knowledge (Rafiu et al., 2025). A recent review of Nigerian medicinal plants further highlighted progress in documenting pharmacological activities alongside persistent barriers to moving from preliminary findings towards mechanistic studies, preclinical development, and therapeutic translation (Chukwudi et al., 2026). These findings support a research strategy that connects documented botanical knowledge with modern molecular investigation. However, ethnomedicinal use should be treated as a basis for prioritizing research hypotheses rather than as proof of efficacy against *S. aureus* or evidence that a plant constituent inhibits the GyrB ATPase domain.

A transparent account of plant provenance, accepted botanical nomenclature, reported plant parts, and the literature supporting the identification of their chemical constituents is therefore essential to the credibility and reproducibility of computational bioprospecting.

Despite extensive documentation of Nigerian medicinal plants and reported antibacterial activity, a notable challenge is translating broad antimicrobial observations into mechanistically informed candidate discovery. Previous research has screened Nigerian plant extracts against bacterial pathogens, while other studies have investigated plant derived compounds using molecular docking and related computational methods. These research streams are complementary but address different questions: extract-based assays can establish whether a complex mixture inhibits bacterial growth under specified experimental conditions, whereas computational docking estimates whether a selected molecule can adopt a plausible pose within a modelled binding site. Neither result alone demonstrates that a specific compound inhibits GyrB in bacterial cells. For example, Dorcheh et al. (2022) screened approximately 2,000 compounds reported from 87 medicinal plants against several *S. aureus* targets, including DNA gyrase, illustrating the existing application of plant compound libraries in target-based virtual screening. This precedent highlights why a geographically and ethnobotanically defined investigation must establish its contribution beyond simply performing docking. Botanical provenance, compound annotation, receptor selection, binding-site definition, interaction analysis, and validation strategy all influence the interpretability of predicted hits. A GyrB-focused investigation offers a distinct mechanistic emphasis by examining potential interactions with the ATPase region rather than treating DNA gyrase as a single, undifferentiated target.

Computational bioprospecting can help address this challenge by integrating literature based compound selection, chemical structure curation, and structure-based screening to prioritize molecules for experimental follow up. A rigorous workflow begins with verification of botanical names and compound provenance, followed by confirmation of chemical identity and standardization of ligand structures, including stereochemistry, ionization, and tautomeric state where relevant. The GyrB structure must likewise be selected and prepared with attention to sequence identity, structural completeness, the integrity of the ATPase domain, and the relevance of the proposed binding pocket. Molecular docking can then generate viable binding poses and rank candidates according to a scoring function, while interaction analysis can identify predicted hydrogen bonds, hydrophobic contacts, electrostatic interactions, and steric compatibility. For GyrB, particular attention should be paid to whether the docking region corresponds to the ATP-binding pocket and whether the predicted poses are structurally promising in relation to known GyrB ligands. These outputs are useful for comparing candidates within a consistent protocol, but docking scores are not direct measurements of binding affinity, ATPase inhibition, or antibacterial potency. Scores can be affected by receptor flexibility, protonation, solvent treatment, scoring function limitations, and ligand size or polarity. Robust interpretation therefore requires comparison with an appropriate reference ligand, scrutiny of Installation plausibility, consideration of target biology, and, where feasible, independent computational approaches and experimental confirmation. Molecular dynamics, free-energy calculations, pharmacokinetic predictions, and toxicity assessments may add value when performed, but their outcomes should not be inferred from docking alone.

Against this background, the specific opportunity is to connect Nigeria's documented medicinal-plant resources with a defined molecular target through a transparent and reproducible computational workflow. The contribution of such an investigation should not be framed as the discovery of a new antibiotic merely because a compound obtains a favorable docking score. Rather, its value lies in prioritizing underexplored plant associated chemical entities, examining their predicted interactions with S. aureus GyrB, and identifying candidate scaffolds that merit subsequent biochemical and microbiological evaluation. Since previous research has already explored herbal compounds against *S. aureus* proteins, and recent reviews have surveyed Nigerian ethnobotanical knowledge and the wider development of Nigerian medicinal plants for drug discovery (Chukwudi and al., 2026; Dorcheh and al., 2022; Rafiu and al., 2025), any claim of novelty should be tied to the current features of the present study.

Accordingly, this study aims to computationally investigate compounds associated with indigenous Nigerian antibacterial plants for their potential interactions with *S. aureus* DNA gyrase B, with the goal of prioritizing chemically diverse candidate scaffolds for further investigation. By combining botanical and ethnopharmacological context with structure-based molecular analysis, the study seeks to establish a transparent route from documented plant derived chemical diversity to testable molecular hypotheses. The resulting candidates should be regarded as computationally prioritized leads, not validated GyrB inhibitors or clinically effective antibacterial agents, until their activity, target engagement, selectivity, and safety have been established experimentally.

This study aims to computationally screen phytochemicals associated with indigenous Nigerian medicinal plants against Staphylococcus aureus DNA gyrase B and evaluate their predicted binding interactions, drug-likeness, and ADMET properties to identify candidates for further antibacterial investigation.

MATERIALS AND METHODS

Identification and Selection of Indigenous Nigerian Antibacterial Plants

Indigenous Nigerian medicinal plants were identified through a targeted review of published ethnobotanical, phytochemical, and pharmacological literature documenting their traditional uses and reported antibacterial properties. The search focused on plants native to Nigeria or documented as occurring within the country, particularly species associated with antibacterial activity against bacterial pathogens, including *Staphylococcus aureus*. Selection criteria included the relevance of reported antibacterial evidence, availability of phytochemical data, and the availability of structurally characterized compounds suitable for molecular docking. Recent reviews documenting Nigerian ethnobotanical diversity and plant-derived bioactive compounds informed the selection process (Achika et al., 2023; Rafiu et al., 2025). The botanical identity and Nigerian distribution of each selected species were checked against published botanical records and taxonomic resources, including Plants of the World Online (POWO), to verify accepted scientific names, synonyms, and geographical occurrence (Royal Botanic Gardens, Kew, 2026). Synonyms were considered during literature searches to improve retrieval of relevant phytochemical reports. Plant species were prioritized when their botanical provenance and relevant phytochemical evidence could be established from traceable sources.

As this study employed computational bioprospecting, plant-derived compounds were selected from published phytochemical studies rather than newly extracted or isolated. For each selected compound, the reported plant source, plant part, source publication, and available evidence of antibacterial relevance were documented. Compounds lacking adequate evidence of botanical provenance or reliable structural identification were excluded from the final screening library. This approach established a literature-based, traceable collection of plant-associated compounds for subsequent molecular docking analysis.

Retrieval and Preparation of Plant-Derived Chemical Structures

The chemical structures of reported phytochemicals from the selected Nigerian medicinal plants were retrieved from the PubChem database (Kim et al., 2023) using compound names, synonyms, and available identifiers. For each compound, the chemical identity was checked against the source publication, and the corresponding PubChem Compound Identifier (CID), where available, was recorded. Compounds with ambiguous identities, unresolved structural assignments, or insufficient information to distinguish between related chemical entities were excluded or flagged for further verification.

The retrieved structures were obtained in Structure Data File (SDF) and were prepared for molecular docking using the selected ligand preparation workflow. Where a compound was reported in the literature without a readily available database structure, its structure was obtained from a reliable primary source or reconstructed only when sufficient structural information was available. Chemical structures were checked for completeness, stereochemistry, bond orders, formal charges, and consistency with the reported compound. The prepared ligand library was then converted to the appropriate docking input format, with hydrogens, protonation states, and rotatable bonds assigned according to the requirements of the docking software.

Novobiocin an aminocoumarin was included as a reference ligand to facilitate comparison between the predicted docking performance of the plant derived compounds and clinically used fluoroquinolones. The phytochemical source, chemical identifier, structure-retrieval source, and any structure-preparation decisions were recorded to ensure reproducibility.

Retrieval and Preparation of *Staphylococcus aureus* DNA Gyrase B

The three-dimensional structure of *Staphylococcus aureus* DNA Gyrase B (GyrB) was obtained from the Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB). Where an experimentally determined structure suitable for the intended docking analysis was unavailable or incomplete, a GyrB model was generated using the relevant protein sequence and a suitable structural template. The selected structure was assessed for sequence correspondence, structural coverage, and suitability for investigating the intended ligand-binding region.

For homology modelling, the amino acid sequence of GyrB was aligned against candidate structural templates using sequence-similarity information and structural coverage. A suitable template was selected based on sequence correspondence, coverage of the region of interest, and the availability of a structurally relevant binding region. The target sequence was submitted to SWISS-MODEL for model construction where required (Waterhouse et al., 2018). The resulting model was evaluated using available model quality and stereochemical assessment tools. The assessment considered sequence coverage, model confidence, local geometry, and the conformation of residues surrounding the proposed ligand-binding region.

The selected protein structure was prepared for docking by checking residue identity and numbering, inspecting missing residues or atoms, and resolving structural inconsistencies relevant to the binding site. Unnecessary crystallographic molecules were removed where appropriate, while structurally important components were retained when required by the biological docking model. Hydrogen atoms and appropriate protonation states were assigned, and the prepared receptor was converted to the input format required by the docking software. The final receptor was visually inspected to confirm that the intended binding region was accessible and that the preparation procedure had not inadvertently altered key residues.

Molecular Docking of Phytocompounds Against DNA Gyrase B

Molecular docking was performed to investigate the predicted binding modes and relative docking scores of phytochemicals reported from indigenous Nigerian medicinal plants against *Staphylococcus aureus* DNA Gyrase B. Ciprofloxacin was included as the reference ligand. The prepared receptor and ligand structures were imported into the selected docking platform, and ligand structures were checked for appropriate protonation, hydrogen addition, and rotatable-bond assignment before docking.

Docking was conducted using AutoDock Vina through the PyRx virtual-screening interface, following the general approach described by Trott and Olson (2010) and Dallakyan and Olson (2015). The search region was defined around the selected GyrB binding site. Where a co-crystallized ligand or a well-supported binding-site annotation was available, its

position was used to guide grid placement. The grid centre and dimensions were recorded to enable reproducibility. All compounds were docked using the same receptor-preparation procedure and consistent search settings to support comparison of their predicted scores.

For each ligand, the predicted docking score and the corresponding binding pose were recorded. More negative docking scores were interpreted as more favorable predicted interactions within the scoring function, rather than as direct measurements of experimental binding affinity or antibacterial potency. The compounds were ranked according to their docking scores and then examined for pose plausibility, interactions with binding-site residues, and consistency with the structural context of GyrB.

The predicted ligand protein interactions were inspected using Discovery Studio Visualizer or the equivalent interaction-analysis software used in the study. The analysis considered hydrogen bonds, hydrophobic contacts, aromatic interactions, and other interactions supported by the resulting poses. Residue identities and numbering were checked against the actual receptor structure. Interactions were reported only when supported by the docked coordinates and appropriate geometric criteria. The interaction analysis was used to complement the docking scores rather than to infer binding mechanisms solely from the chemical structures of the ligands.

Where appropriate, the docking workflow was validated using redocking of a co-crystallized ligand or another suitable protocol-validation procedure. Validation outcomes, including the method used and the resulting pose comparison, were documented. The same docking and scoring settings were applied to the reference ligand and phytochemical library wherever possible. Compounds with favorable predicted scores and plausible binding poses were prioritized for subsequent investigation.

***In silico* Drug-Likeness and ADMET Analysis of Top Ranked Phytocompounds**

The top-ranked phytochemicals identified from the molecular docking analysis against *Staphylococcus aureus* DNA gyrase B were subjected to computational drug likeness and absorption, distribution, metabolism, excretion, and toxicity (ADMET) assessments to evaluate their preliminary suitability as potential antibacterial lead compounds. Drug likeness and physicochemical properties were assessed using the SwissADME web server (https://www.swissadme.ch/) following the approach described by (Daina et al., 2017) and (Lohohola et al., 2021) was used to conduct the drug-likeness analysis using the Lipinski filtering tools. The assessment included Lipinski's Rule of Five, which considers molecular weight, lipophilicity, hydrogen bond donors, and hydrogen bond acceptors, alongside other relevant physicochemical and pharmacokinetic descriptors. These parameters were used to evaluate the phytocompounds' predicted oral drug likeness and identify potential physicochemical limitations.

Furthermore, the SuperPred platform (http://lmmd.ecust.edu.cn/admetsar1/predict/) was used for computational prediction of selected pharmacokinetic and toxicity-related properties, where supported by the platform's available prediction modules. (Cheng et al., 2012) The resulting profiles were examined to complement the docking results and assist in prioritizing compounds with favourable predicted properties for further investigation. The combined analysis provided an initial screening framework for evaluating the drug-development potential of the selected plant-derived compounds. However, the predictions were interpreted as preliminary computational indicators rather than experimental evidence of pharmacokinetic behaviour, safety, or antibacterial efficacy.

RESULTS AND DISCUSSION

Molecular Docking of Phytocompounds Against *Staphylococcus aureus* DNA Gyrase B

Table 1: Docking Scores Top 20 Compounds Against *S. aureus* Gyrase B

S/No	Compounds	4URO
1	Ref compounds (Novobiocin)	-8.6
2	Tiliacorine	-9.5
3	Ellagic_acid	-9.2
4	Bidebiline	-9
5	Diospyrin	-8.8
6	Barbaloin	-8.6
7	Glabridin	-8.6
8	Withaferin	-8.6
9	Orientin	-8.5
10	Perforamone	-8.4
11	Cadabicine	-8.3
12	Alpha-mangostin	-8.3
13	Rhein	-8.3
14	Levofloxacin	-8.2
15	Alkaloids	-8.1
16	Greveichromenol	-8.1
17	Withafastuosin	-8.1
18	Butin	-8
19	Emodin	-8
20		

Molecular docking against *Staphylococcus aureus* DNA gyrase B revealed variation in the predicted docking scores of the screened plant-derived compounds. The scores ranged from -9.5 to -8.0 kcal/mol among the phytochemical entries, while the reference inhibitor novobiocin recorded a score of -8.6 kcal/mol. Tiliacorine exhibited the most favorable

predicted score (-9.5 kcal/mol), followed by Ellagic acid (-9.2 kcal/mol) and Bidebiline (-9.0 kcal/mol). These values were respectively 0.9, 0.6, and 0.4 kcal/mol more negative than the novobiocin docking score, identifying the three compounds as promising phytocompounds for further structural evaluation.

Diospyrin and Tiliacorinine each produced a score of -8.8 kcal/mol, while Barbaloin, Glabridin, and withaferin matched the novobiocin score of -8.6 kcal/mol. Orientin (-8.5 kcal/mol), Perforamone (-8.4 kcal/mol), Cadabicine, Alpha-mangostin, and Rhein (each -8.3 kcal/mol) also showed favorable predicted scores relative to the screening range. The remaining entries, including levofloxacin (-8.2 kcal/mol), Greveichromenol, Withafastuosin, and the reported alkaloid entry (each -8.1 kcal/mol), as well as Butin and Emodin (each -8.0 kcal/mol), occupied the lower end of the ranking.

The favorable score obtained for Tiliacorine suggests that its predicted pose was better accommodated by the docking scoring function than those of the other listed compounds. Ellagic acid and Bidebiline similarly warrant further investigation because their predicted scores were more negative than that of Novobiocin. Nevertheless, the relatively modest score differences should be interpreted as computational ranking results rather than evidence of superior inhibitory potency. Although docking scores do not directly measure binding affinity or enzyme inhibition, and their interpretation depends on the docking protocol, receptor preparation, ligand properties, and plausibility of the predicted binding poses.

The comparison with Novobiocin is particularly relevant because Novobiocin inhibits the ATPase function of GyrB by binding to its ATP-binding region (Bisacchi & Manchester, 2015; Collin et al., 2011). Levofloxacin, in contrast, primarily acts through stabilization of the DNA cleavage complex formed by bacterial topoisomerases and is therefore a less mechanistically matched reference for an investigation focused on the GyrB ATPase pocket. Its score of -8.2 kcal/mol should consequently be interpreted as a secondary computational comparison rather than direct evidence of relative antibacterial efficacy.

The docking results prioritize Tiliacorine, Ellagic acid, and Bidebiline for further investigation, with Diospyrin, Tiliacorinine, Barbaloin, Glabridin, and Withaferin representing additional candidates. The biological relevance of these predictions should be assessed by examining the docked poses and their interactions with residues in the intended binding pocket. Where the poses are structurally plausible, subsequent GyrB ATPase inhibition and antibacterial susceptibility assays would be required to determine whether the computationally prioritized compounds demonstrate measurable target inhibition and activity against *S. aureus*. Accordingly, the present findings identify candidate molecules for follow up rather than establishing validated GyrB inhibitors or new antibacterial agents.

Table 2: Amino Acid Interaction Analysis of GyrB–Ligand Complexes

Compound	Hydrogen Bonds	Hydrophobic Interactions	Van der Waals	Others
Novobiocin (Ref)	Asp81, Gly85, Thr173	Ile51, Val79, Pro87	Leu103, Ile175, Val130	
Tiliacorine	Asp81, Gly85, Arg144	Met112, Val130, Ile175	Val167, Pro87, Ile86	π-cation (Arg84)
Ellagic acid	Asp81, Arg84, Gly85	Ile51, Val79, Pro87	Ile86, Thr173, Val107	
Diospyrin	Asp81, Gly85	Val79, Ile86, Leu103	Met112, Val130, Phe173	
Glabridin	Asp81, Thr173	Ile51, Val79, Pro87	Ile102, Val107, Met112	
Barbaloin	Gly85, Thr173, Asp110	Ile51, Val79, Pro87	Leu103, Ile175, Val130	

Amino Acid Interaction Analysis of GyrB ligand Complexes

The predicted interactions between *Staphylococcus aureus* DNA gyrase B and the selected ligands were examined to characterize the potential molecular contacts contributing to the predicted stability of the protein ligand complexes. The analysis focused on hydrogen bonding, hydrophobic contacts, from the Van der Waals interactions, and other non-covalent interactions identified in the docked poses. Novobiocin, the reference inhibitor, was used as a comparator for evaluating the interaction profiles of the selected phytocompounds, particularly Tiliacorine, Ellagic acid, Diospyrin, Glabridin, and Barbaloin.

The interaction profile of Novobiocin included hydrogen bonds involving Asp81, Gly85, and Thr173, hydrophobic contacts with With51, Val79, and Pro87, and from the Walloon contacts involving Leu103, With175, and Val130. Water mediated interactions were also reported. This interaction pattern provides a reference for examining how the phytocompounds may be accommodated within the selected GyrB binding region. However, the listed residue contacts alone do not establish that all compounds occupy identical binding poses or reproduce the complete binding mechanism of novobiocin.

Among the selected plant-derived compounds, Tiliacorine demonstrated a diverse interaction profile involving hydrogen bonds, hydrophobic contacts, Van der Waals interactions, and a reported π-cation interaction. Its hydrogen bonding residues included Asp81, Gly85, and Arg144, while Met112, Val130, and Ile175 were identified as hydrophobic contact residues. Additional Van der Waals contacts involved Val167, Pro87, and Ile86. A π-cation interaction with Arg84 was also reported.

The combination of these interactions suggests that Tiliacorine may be accommodated by several regions of the binding pocket through complementary polar and non-polar contacts. Hydrogen bonding with Asp81 and Gly85 is particularly noteworthy because these residues also appeared in the reported interaction profile of novobiocin. Their recurrence suggests that they may contribute to ligand recognition within the selected binding region. The additional reported hydrogen bond with Arg144 and π-cation interaction with Arg84 further establish Tiliacorine's interaction profile from that of the reference compound.

These observations are consistent with the favorable docking score obtained for Tiliacorine (-9.5 kcal/mol), the most negative score among the compounds in the supplied ranking. The agreement between its docking score and the breadth of its reported interactions makes Tiliacorine a preferred candidate for further structural and experimental investigation. Nevertheless, the number of interactions alone does not establish greater binding stability, and the reported contacts must be interpreted in relation to their distances, geometry, chemical plausibility, and the accuracy of the

docked pose. Experimental testing would be needed to determine whether Tiliacorine inhibits GyrB ATPase activity.
Ellagic acid formed reported hydrogen bonds with Asp81, Arg84, and Gly85. Its hydrophobic interactions involved Ile51, Val79, and Pro87, while Ile86, Thr173, and Val107 were listed among the residues contributing Van der Waals contacts.
The participation of Asp81 and Gly85 in the reported hydrogen bonding network is consistent with the interaction pattern described for Novobiocin and Tiliacorine. This overlap suggests that Ellagic acid may engage a similar region of the selected binding pocket, although confirmation would require comparison of the current docked coordinates. The involvement of Arg84 also distinguishes its reported polar interaction profile from that of novobiocin, for which Arg84 was not listed as a hydrogen bonding residue.
The combination of polar contacts and non-polar interactions may support a favourable orientation of Ellagic acid within the pocket. Its docking score of -9.2 kcal/mol, the second most negative among the screened compounds, is consistent with favorable predicted accommodation by the docking scoring function. However, the interaction map does not establish whether these contacts are sufficient or appropriately positioned to interfere with ATP binding or hydrolysis. Ellagic acid should therefore be regarded as a high priority candidate for further investigation rather than a validated GyrB inhibitor.
Diospyrin was reported to form hydrogen bonds with Asp81 and Gly85, alongside hydrophobic contacts involving Val79, Ile86, and Leu103. Its Van der Waals interactions included Met112, Val130, and Phe173, and an additional π interaction was recorded.
The involvement of Asp81 and Gly85 mirrors part of the hydrogen-bonding pattern reported for Novobiocin, Tiliacorine, and Ellagic acid. This recurring pattern may indicate that these residues contribute to the recognition of multiple ligands within the selected GyrB binding region. The hydrophobic contacts with Val79 and With86, together with the reported from the Walloon contacts, suggest additional non-polar accommodation of the compound.
Diospyrin achieved a docking score of -8.8 kcal/mol, which was 0.2 kcal/mol more negative than the Novobiocin score. Its interaction profile is therefore compatible with its favorable computational ranking. Although fewer hydrogen bonding residues were listed for Diospyrin than for Tiliacorine or Ellagic acid, this does not necessarily indicate weaker binding. Docking outcomes depend on the comprehensive geometry and energetic contribution of the Installation rather than simply on the number of interactions. The precise nature and location of the reported pi interaction should also be specified from the interaction analysis output before it is interpreted mechanistically.
Glabridin was reported to form hydrogen bonds with Asp81 and Thr173. Its hydrophobic-contact residues were Ile51, Val79, and Pro87, while Ile102, Val107, and With112 were identified as contributing from the Walloon interactions.
The interaction profile indicates that Glabridin may be accommodated through a combination of polar anchoring and non-polar contacts. Its hydrophobic contact residues overlap with those listed for Novobiocin, particularly Ile51, Val79, and Pro87. This overlap suggests that the two ligands may interact with some of the same pocket residues, although it does not mean that they adopt the same orientation or occupy an identical binding site.
Glabridin's docking score of -8.6 kcal/mol matched that of Novobiocin. The agreement between the numerical scores and the presence of overlapping contact residues makes Glabridin worthy of further examination. Nevertheless, equivalent scores do not imply equivalent inhibitory activity. A detailed comparison of the docked poses, including hydrogen bond distances and the position of the ligand relative to the ATP-binding region, would be required to assess whether Glabridin could apparently interfere with GyrB function.
Barbaloin was reported to form hydrogen bonds with Gly85, Thr173, and Asp110. Its hydrophobic interactions involved Ile51, Val79, and Pro87, while Leu103, Ile175, and Val130 were listed among the residues contributing van the Walloon contacts.
The hydrophobic-contact profile overlapped with that of novobiocin, while the van der Waals-contact residues also included Leu103, Ile175, and Val130, which were reported for the reference compound. These shared contacts suggest that barbaloin and novobiocin may interact with some of the same regions of the selected binding pocket. However, the hydrogen-bonding profiles were not identical: barbaloin's reported contacts included Asp110 rather than Asp81, and its hydrogen bonds involved Gly85 and Thr173.
Barbaloin's docking score of −8.6 kcal/mol was identical to that of novobiocin. Its reported interaction network therefore supports further examination of its binding pose, especially the positioning of its hydrogen-bonding groups relative to the pocket residues. These observations of the not, however, establish that barbaloin reproduces novobiocin's inhibitory mechanism or has comparable effects on GyrB ATPase activity.

Comparative Interpretation of the Interaction Profiles

Comparison between the five phytocompounds reveals both shared and compound specific residue contacts. Asp81 and Gly85 appeared repeatedly among the reported hydrogen bonding residues, occurring in the interaction profiles of Novobiocin, Tiliacorine, Ellagic acid, and Diospyrin. Asp81 was also reported for Glabridin, while Gly85 was reported for Barbaloin. This recurrence identifies Asp81 and Gly85 as residues of interest for comparative analysis of the selected ligand poses.
The hydrophobic residues Ile51, Val79, and Pro87 were reported for Novobiocin, Ellagic acid, Glabridin, and Barbaloin. Their repeated reoccurance suggests that these residues may contribute to non-polar ligand accommodation within the selected binding region. Tiliacorine displayed a different listed hydrophobic contact profile, involving Met112, Val130, and Ile175, while Diospyrin involved Val79, Ile86, and Leu103. Such differences may reflect variation in ligand orientation, molecular shape, or the distribution of chemical groups across the binding pocket.
The Van der Waals contacts also showed partial overlap among the compounds. Leu103, Ile175, and Val130 were reported for both Novobiocin and Barbaloin, whereas Val130 and With175 appeared in Tiliacorine's hydrophobic contact list. These contacts may contribute to the close packing of ligands within the protein structure. However, from the Van der Waal interactions contacts are common in protein ligand complexes, and their presence alone does not establish specificity or inhibition.
Tiliacorine and Ellagic acid combined the most favorable docking scores with reported hydrogen bonding interactions involving Asp81 and Gly85, alongside additional contacts that distinguish their interaction profiles. Diospyrin, Glabridin, and Barbaloin also displayed overlapping contacts with residues listed for novobiocin, despite differences in their hydrogen-bonding networks and docking scores. These results provide a structural basis for prioritizing the compounds for further investigation, but they of the not

independently establish that the compounds inhibit GyrB or possess antibacterial activity against *S. aureus.*

The favorable docking scores obtained for Tiliacorine (-9.5 kcal/mol) and Ellagic acid (- 9.2 kcal/mol), together with their predicted hydrogen bonding interactions involving Asp81 and Gly85, are consistent with previous computational investigations identifying these residues as important components of the *Staphylococcus aureus Gyr*B binding pocket. Durdagi et al. (2018), for example, identified mangostenone E, candenatenin A, and 2,4,4′-trihydroxydihydrochalcone as promising phytochemical candidates through virtual screening and molecular dynamics simulations, highlighting the importance of interactions involving Asp81. Similarly, a more recent study by Pereira-Filho et al. (2026) predicted that silibinin interacts with Asp81 and Gly85, among other GyrB residues, with a docking score of -8.703 kcal/mol, comparable to novobiocin at -8.465 kcal/mol. These observations support the relevance of the recurring contacts in the present study, although shared residue interactions alone do not establish equivalent binding modes or inhibitory activity.

The docking result for ellagic acid also has a relevant precedent in El-Shibani et al. (2023), who reported a docking score of -9.3 kcal/mol for Ellagic acid against an *S. aureus* Gyrase DNA complex. Their study additionally reported antimicrobial activity of the *Cistus parviflorus* extract against *S. aureus*. However, this comparison requires caution because their receptor was a gyrase DNA complex, whereas the present study targets GyrB using PDB 4URO. Differences in receptor composition, binding-site location, and docking protocols mean that the numerical scores cannot be treated as directly equivalent. Moreover, antimicrobial activity of a plant extract does not establish that ellagic acid alone was responsible for the observed effect or that GyrB inhibition was its mechanism.

Recent experimental research further illustrates why computational ranking should be treated as a prioritization step rather than proof of activity. Ismael et al. (2025) combined molecular docking with antibacterial testing and a DNA gyrase activity assay for *Allium sativum* derived compounds and extract, reporting inhibition of bacterial growth and reduced gyrase activity under their experimental conditions. Similarly, Pudipeddi et al. (2023) progressed beyond docking by synthesizing a designed GyrB inhibitor and demonstrating *in vitro* activity against a novobiocin resistant clinical *S. aureus* isolate, including evidence of on target *Gyr* B inhibition. These studies demonstrate the value of pairing structural predictions with direct biological assays. In the present study, the scaffolding predicted contacts of Diospyrin, Glabridin, and Barbaloin with residues also listed for novobiocin therefore support their selection for further testing, but do not establish that these compounds inhibit *Gyr* B. The next steps should include confirming the docking protocol through redocking of the co-crystallized ligand, testing purified GyrB inhibition, determining the minimum inhibitory concentration against S. aureus, and assessing cytotoxicity and selectivity.

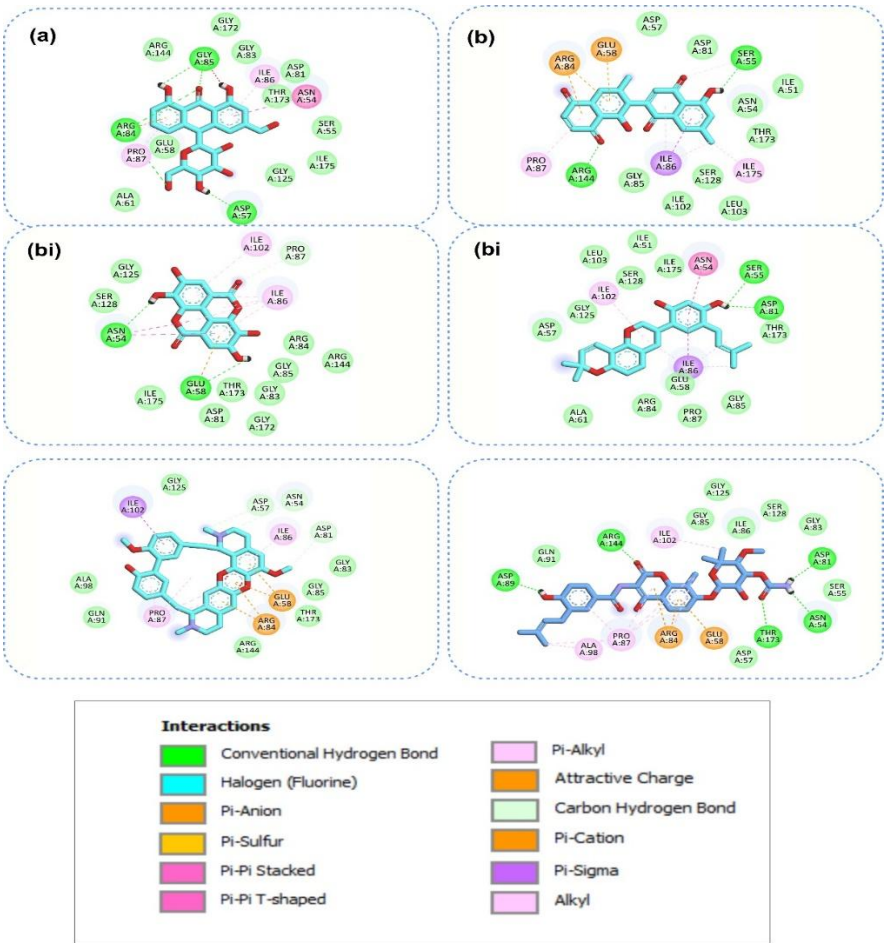


Figure 1: Amino Acid Interactive Plots of Top-Six-Secondary Metabolites from *G. latifolium* Fruits, Identified from the Docking Analysis Against Staph Gyrase B: (a) Barbaloin; (b) Diospyrin (c) Ellagic Acid (d) Glabridin (e) Tiliacorine (f) Reference Inhibitor

Figure 1 illustrates the predicted molecular interactions of five secondary metabolites reported from *Gongronema latifolium* fruits with Staphylococcus aureus DNA gyrase B (GyrB), using novobiocin as the reference inhibitor. The interaction profiles revealed recurring contacts involving Asp81 and Gly85 in the reported hydrogen bonding patterns and With51, Val79 and Pro87 in the hydrophobic interaction profiles, suggesting that these residues may contribute to the accommodation of multiple ligands within the modelled binding pocket. Among the evaluated metabolites, Tiliacorine exhibited the most favourable docking score (-9.5 kcal/mol), followed by ellagic acid (-9.2 kcal/mol) and diospyrin (-8.8 kcal/mol), compared with -8.6 kcal/mol for novobiocin. Tiliacorine's predicted interaction profile included hydrogen bonds with Asp81, Gly85 and Arg144, alongside a reported π-cation interaction involving Arg84, while Ellagic acid was predicted to form hydrogen bonds with Asp81, Arg84 and Gly85. Barbaloin and Glabridin each produced a docking score of -8.6 kcal/mol, matching that of the reference at the reported precision, although their interaction profiles differed. These findings identify Tiliacorine and Ellagic acid as promising candidates for further investigation based on the docking protocol employed. Nonetheless, the predicted contacts and scores should be interpreted as computational evidence of potential binding rather than confirmation of GyrB inhibition. Verification of the docking poses, residue identities and binding-site location, followed by appropriate biochemical and antibacterial assays, is required to determine the biological significance of these interactions.

This study demonstrates the potential of computational bioprospecting as a strategic approach for identifying promising antibacterial chemical scaffolds from indigenous Nigerian medicinal plants targeting DNA gyrase B of *Staphylococcus aureus*. The investigation integrates ethnobotanical knowledge, phytochemical evidence, and structure based molecular docking to prioritize phytocompounds from indigenous plants for further antibacterial drug discovery research. This approach is particularly relevant given the chemical diversity of natural products and their continuing contribution to the discovery and development of pharmacologically active compounds (Asiamah et al., 2023; Wang and al., 2024).

Among the investigated compounds, Tiliacorine exhibited the most favourable predicted binding score (-9.5 kcal/mol), followed by Ellagic acid (-9.2 kcal/mol) and Bidebiline (-9.0 kcal/mol). Diospyrin and Tiliacorinine also demonstrated promising predicted binding scores of --8.8 kcal/mol. These compounds achieved more favourable docking scores than the reference inhibitor novobiocin (-8.6 kcal/mol) and levofloxacin (-8.2 kcal/mol) under the computational conditions utilized. The predicted interactions involving key binding site residues, particularly Asp81 and Gly85, provide a structural basis for ranking these molecules for further investigation. The additional interactions involving Arg84 and Arg144 in the Tiliacorine complex further support its selection as a candidate for future studies. However, these findings indicate predicted binding compatibility rather than experimentally established binding affinity, target inhibition, or antibacterial potency. Docking scores alone cannot establish that a compound is more effective than a reference drug (Asiamah and al., 2023; Wang and al., 2024).

The findings also substantiate the scientific value of investigating Nigeria's medicinal plant resources for potentially promising antibacterial chemical scaffolds. Previous research has documented substantial phytochemical diversity among Nigerian indigenous medicinal plants, including numerous isolated flavonoids with reported biological activities (Achika and al., 2023). Similarly, recent reviews have highlighted the potential of medicinal plants as sources of antibacterial compounds while emphasizing the importance of phytochemical characterization and experimental evaluation in establishing biological efficacy (Zouine and al., 2024). The present study extends this research direction by applying a target focused computational approach to prioritize plant derived metabolites against *S. aureus* DNA gyrase B, thereby providing a rational basis for subsequent compound selection and experimental investigation.

Notwithstanding these promising computational findings, further validation is necessary before the identified compounds can be considered credible antibacterial leads. Future investigations should include docking-protocol validation, molecular dynamics simulations to evaluate the persistence of predicted protein ligand interactions and binding free energy estimation where appropriate. Biochemical assays measuring GyrB ATPase inhibition, followed by in-vitro antibacterial susceptibility testing against relevant *S. aureus* strains, would help establish whether the predicted interactions translate into measurable biological activity. Subsequent structure activity relationship studies, selectivity assessment, and preliminary cytotoxicity evaluation would further clarify the suitability of the prioritized compounds for antibacterial development. Such complementary computational and experimental approaches are essential for translating natural product screening results into Reproducible drug-discovery evidence (Wang et al., 2024; Zouine and al., 2024).

Pharmacokinetic and ADMET Properties of the Compounds

The predicted physicochemical, drug-likeness, pharmacokinetic and toxicity properties of tiliacorine, ellagic acid, bidebiline, diospyrin and barbaloin, with novobiocin as the reference compound is shown in table 1 above. The predictions were generated using ADMETlab 3.0. The molecular weights varied from 302.01 g/mol for ellagic acid to 612.23 g/mol for novobiocin. Tiliacorine (576.26 g/mol) and bidebiline (584.19 g/mol) had values above 500 g/mol, while diospyrin (374.08 g/mol) and barbaloin (418.13 g/mol) were below 500 g/mol. The table records Lipinski compliance for tiliacorine, ellagic acid, diospyrin and barbaloin, but not for novobiocin or bidebiline. Ellagic acid and diospyrin passed the Pfizer, GSK and Golden Triangle filters; novobiocin and barbaloin passed the Pfizer filter, while barbaloin also passed the Golden Triangle filter. Tiliacorine passed none of these three filters, and bidebiline passed only the Pfizer filter. Diospyrin had the highest QED score (0.794), while novobiocin had the lowest (0.184). Two alerts for PAINS, ellagic acid and diospyrin were recorded. Bidebiline had the lowest predicted aqueous solubility (LogS = -9.86), whereas barbaloin had the highest natural product-likeness score (2.071).

For absorption, the Caco-2 predictions were positive for tiliacorine, bidebiline and diospyrin, and negative for novobiocin, ellagic acid and barbaloin. None of the six compounds was predicted to inhibit P-glycoprotein. Tiliacorine and bidebiline were predicted to be P-glycoprotein substrates; the other four compounds were negative for this endpoint. Human intestinal absorption (HIA) was classified as good for novobiocin, tiliacorine, bidebiline and diospyrin, moderate for ellagic acid, and poor for barbaloin. The F20% and F30% predictions were favourable for bidebiline and diospyrin, poor for novobiocin, tiliacorine and ellagic acid, and mixed for barbaloin (moderate for F20% and poor for

F30%). For distribution, tiliacorine was the only compound predicted to cross the blood-brain barrier. Plasma protein binding ranged from 68.54% for ellagic acid to 96.62% for diospyrin. The predicted unbound fraction ranged from 2.91% for diospyrin to 24.25% for ellagic acid, while the volume of distribution ranged from 0.444 L/kg for ellagic acid to 2.599 L/kg for bidebiline.

The predicted CYP450 profiles differed among the compounds. Novobiocin was identified as a CYP2C19 inhibitor and was considered a substrate of CYP2C9 and CYP2C19. Tiliacorine was not predicted to inhibit any of the five CYP450 isoforms, but it was classified as a substrate of CYP1A2, CYP2C9, CYP2C19, CYP2D6 and CYP3A4. Ellagic acid was predicted to inhibit CYP1A2 and to be a CYP2C9 substrate. Bidebiline and diospyrin were predicted to inhibit all five isoforms; bidebiline was also predicted to be a substrate of CYP1A2, CYP2C9, CYP2C19 and CYP2D6, whereas diospyrin was negative for substrate predictions across the five isoforms. Barbaloin was negative for inhibition and substrate predictions across the five isoforms. The predicted half-lives ranged from 0.500 h for bidebiline to 2.372 h for tiliacorine. Clearance ranged from 0.868 mL/min/kg for diospyrin to 14.743 mL/min/kg for ellagic acid.

For the toxicity endpoints, all six compounds were predicted to be AMES-positive, hepatotoxic (H-HT-positive) and skin sensitisers. Tiliacorine and bidebiline were positive for hERG-blocker predictions, whereas novobiocin, ellagic acid, diospyrin and barbaloin were negative. Carcinogenicity predictions were positive for tiliacorine, ellagic acid, bidebiline and diospyrin, and negative for novobiocin and barbaloin. The DILI prediction was negative only for tiliacorine; the other five compounds, including novobiocin, were positive. Synthetic accessibility scores ranged from 2.98 for ellagic acid to 5.79 for tiliacorine. These are computational predictions, and the classifications and probabilities for each compound are reported in Table 1.

The predicted pharmacokinetic and toxicity profiles provided more criteria for prioritizing the selected compounds beyond their molecular docking scores. Diospyrin and ellagic acid demonstrated comparatively favorable drug-likeness characteristics, although their predicted absorption limitations and potential toxicity liabilities require further investigation. Tiliacorine, despite exhibiting the most favorable docking score against *Staphylococcus aureus* DNA gyrase B (-9.5 kcal/mol), presented potential safety concerns, including predicted hERG blockade, carcinogenicity, mutagenicity, and hepatotoxicity. Bidebiline also showed substantial predicted liabilities, particularly very low aqueous solubility and inhibition of multiple CYP450 isoforms, while barbaloin's favorable natural product-likeness score was offset by its predicted poor intestinal absorption and potential toxicity. These findings align with recent literature emphasizing the value of computational ADMET tools for early-stage drug prioritization while recognizing that their predictions require experimental validation (Ancuceanu et al., 2025; Fu et al., 2024; Shinde et al., 2025). Overall, diospyrin and ellagic acid warrant further assessment based on their drug-likeness profiles, while tiliacorine remains a promising docking hit whose predicted safety liabilities must be carefully investigated. However, none of the compounds can yet be considered a validated antibacterial lead based on computational results alone. Experimental studies should therefore assess GyrB inhibitory activity, antibacterial efficacy, solubility, permeability, cytotoxicity, genotoxicity, cardiac safety, and metabolic stability to establish their suitability for further antibacterial drug development.

Table 3: Predicted Physicochemical, Pharmacokinetic and ADMET Properties of Novobiocin and the Five Compounds

Property	Novobiocin (reference)	Tiliacorine	Ellagic Acid	Bidebiline	Diospyrin	Barbaloin
Physicochemical Properties						
Molecular weight (g/mol)	612.23	576.26	302.01	584.19	374.08	418.13
Num. rings	4	8	4	10	4	4
Num. rotatable bonds	10	2	0	3	1	3
Num. H-bond acceptors	13	7	8	8	6	9
Num. H-bond Donors	6	1	4	2	2	7
LogP	1.79	3.78	0.95	6.54	3.10	0.50
LogD (pH 7.4)	1.90	3.10	0.75	4.67	2.88	1.02
LogS (log mol/L)	-4.47	-4.99	-3.37	-9.86	-5.31	-2.68
TPSA (Å²)	200.01	63.63	141.34	79.44	108.74	167.91
Fsp3	0.387	0.333	0.000	0.222	0.091	0.381
Drug-likeness						
Lipinski	No	Yes	Yes	No	Yes	Yes
Pfizer	Yes	No	Yes	Yes	Yes	Yes
GSK	No	No	Yes	No	Yes	No
Golden Triangle	No	No	Yes	No	Yes	Yes
QED	0.184	0.247	0.216	0.209	0.794	0.334
PAINS alert	No	No	Yes	No	Yes	No
Natural product-likeness	1.394	1.454	1.071	0.709	1.604	2.071
Absorption (Probability)						
Caco-2 permeability (log cm/s)	Caco2- (-5.837)	Caco2+ (-4.844)	Caco2- (-5.167)	Caco2+ (-5.085)	Caco2+ (-4.812)	Caco2- (-6.297)
P-glycoprotein inhibitor	Neg. (<0.001)	Neg. (0.110)	Neg. (<0.001)	Neg. (0.372)	Neg. (<0.001)	Neg. (<0.001)

Property	Novobiocin (reference)	Tiliacorine	Ellagic Acid	Bidebiline	Diospyrin	Barbaloin
P-glycoprotein substrate	Neg. (0.131)	Pos. (0.768)	Neg. (0.041)	Pos. (0.708)	Neg. (<0.001)	Neg. (0.149)
HIA (probability of low absorption)	Good (0.122)	Good (<0.001)	Moderate (0.500)	Good (0.029)	Good (0.027)	Poor (0.738)
F20% (probability of F < 20%)	Poor (0.997)	Poor (0.862)	Poor (0.953)	Good (0.018)	Good (<0.001)	Moderate (0.426)
F30% (probability of F < 30%)	Poor (0.998)	Poor (0.960)	Poor (0.967)	Good (0.016)	Good (0.004)	Poor (>0.999)
Distribution (Probability)						
Blood-brain barrier	BBB- (<0.001)	BBB+ (0.723)	BBB- (0.001)	BBB- (0.126)	BBB- (<0.001)	BBB- (0.004)
PPB %	93.76	75.20	68.54	95.16	96.62	79.05
VDss (L/kg)	1.252	1.691	0.444	2.599	0.799	0.880
Fu %	4.91	23.54	24.25	4.27	2.91	19.18
Metabolism (Probability)						
CYP450 1A2 inhibitor	Neg. (<0.001)	Neg. (0.137)	Pos. (0.904)	Pos. (>0.999)	Pos. (>0.999)	Neg. (<0.001)
CYP450 1A2 substrate	Neg. (<0.001)	Pos. (0.999)	Neg. (0.009)	Pos. (>0.999)	Neg. (0.029)	Neg. (0.005)
CYP450 2C9 inhibitor	Neg. (0.007)	Neg. (<0.001)	Neg. (0.028)	Pos. (0.994)	Pos. (>0.999)	Neg. (<0.001)
CYP450 2C9 substrate	Pos. (0.758)	Pos. (0.989)	Pos. (0.564)	Pos. (>0.999)	Neg. (<0.001)	Neg. (<0.001)
CYP450 2C19 inhibitor	Pos. (0.711)	Neg. (0.001)	Neg. (<0.001)	Pos. (>0.999)	Pos. (>0.999)	Neg. (<0.001)
CYP450 2C19 substrate	Pos. (>0.999)	Pos. (0.999)	Neg. (<0.001)	Pos. (>0.999)	Neg. (<0.001)	Neg. (<0.001)
CYP450 2D6 inhibitor	Neg. (<0.001)	Neg. (0.005)	Neg. (<0.001)	Pos. (>0.999)	Pos. (>0.999)	Neg. (0.022)
CYP450 2D6 substrate	Neg. (0.001)	Pos. (>0.999)	Neg. (0.035)	Pos. (>0.999)	Neg. (<0.001)	Neg. (<0.001)
CYP450 3A4 inhibitor	Neg. (<0.001)	Neg. (0.014)	Neg. (0.004)	Pos. (>0.999)	Pos. (>0.999)	Neg. (<0.001)
CYP450 3A4 substrate	Neg. (0.002)	Pos. (0.997)	Neg. (<0.001)	Neg. (<0.001)	Neg. (<0.001)	Neg. (0.310)
Elimination						
T 1/2 (half-life)	1.679 h	2.372 h	1.648 h	0.500 h	1.343 h	2.264 h
CL (clearance) mL/min/kg	4.304	12.173	14.743	3.353	0.868	2.947
Toxicity (Probability)						
hERG blockers	Neg. (0.141)	Pos. (0.778)	Neg. (0.028)	Pos. (0.957)	Neg. (0.048)	Neg. (0.010)
AMES	Pos. (0.749)	Pos. (0.838)	Pos. (0.670)	Pos. (0.994)	Pos. (0.895)	Pos. (0.969)
H-HT (human hepatotoxicity)	Pos. (0.889)	Pos. (0.737)	Pos. (0.616)	Pos. (0.960)	Pos. (0.906)	Pos. (0.709)
Carcinogenicity	Neg. (0.347)	Pos. (0.853)	Pos. (0.666)	Pos. (0.948)	Pos. (0.891)	Neg. (0.309)
SkinSen	Pos. (0.911)	Pos. (0.730)	Pos. (0.895)	Pos. (0.714)	Pos. (0.996)	Pos. (0.992)
DILI (drug-induced liver injury)	Pos. (0.998)	Neg. (0.029)	Pos. (0.984)	Pos. (>0.999)	Pos. (0.936)	Pos. (0.882)
Synthetic accessibility	4.00	5.79	2.98	3.53	3.02	4.00

Predictions are from ADMETlab 3.0. Pos./Neg. = Probability Above/Below 0.5. For HIA, F20% and F30% the Value is the Probability of the Unfavourable Class (0 to 0.3 Good, 0.3 to 0.7 Moderate, 0.7 to 1.0 poor). Novobiocin is the Reference Compound.

CONCLUSION

This study identified several phytochemicals associated with Nigerian medicinal plants that exhibited favourable predicted binding interactions with *Staphylococcus aureus* DNA gyrase B. Tiliacorine, ellagic acid, and bidebiline produced the most favourable docking scores, while the ADMET analysis indicated comparatively promising drug-likeness characteristics for diospyrin and ellagic acid. Nevertheless, the predicted pharmacokinetic limitations and toxicity alerts associated with several compounds highlight the importance of evaluating both binding compatibility and safety during candidate prioritisation. The findings provide a computational basis for selecting compounds for further investigation but do not establish antibacterial efficacy or direct GyrB inhibition. Experimental enzyme-inhibition assays, antimicrobial susceptibility testing, molecular dynamics studies, and appropriate toxicological evaluations are recommended to validate the identified candidates and assess their suitability for subsequent antibacterial drug development.

REFERENCES

Achika, J. I., Yusuf, A. J., Ayo, R. G., & Liman, D. U. (2023). Flavonoids from Nigerian indigenous medicinal plants and their bioactivities: A review. Phytomedicine Plus, 3(2), Article 100405. https://doi.org/10.1016/j.phyplu.2023.100405

Adebayo, J. O., Ceravolo, I. P., Gyebi, G. A., Olorundare, O. E., Babatunde, A. S., Penna-Coutinho, J. P., Koketsu, M., & Krettli, A. U. (2022). Iloneoside, an antimalarial pregnane glycoside isolated from *Gongronema latifolium* leaf, potentiates the activity of chloroquine against multidrug resistant *Plasmodium falciparum*. *Molecular and Biochemical Parasitology, 249*, Article 111474. https://doi.org/10.1016/j.molbiopara.2022.111474

Ancuceanu, R., Lascu, B. E., Drăgănescu, D., & Dinu, M. (2025). In silico ADME methods used in the evaluation of natural products. Pharmaceutics, 17(8), Article 1002. https://doi.org/10.3390/pharmaceutics17081002

Asiamah, I., Obiri, S. A., Tamekloe, W., Armah, F. A., & Borquaye, L. S. (2023). Applications of molecular docking in natural products-based drug discovery. Scientific African, 20, Article e01593. https://doi.org/10.1016/j.sciaf.2023.e01593

Bisacchi, G. S., & Manchester, J. I. (2015). A new-class antibacterial - Almost. Lessons in drug discovery and development: A critical analysis of more than 50 years of effort toward ATPase inhibitors of DNA gyrase and topoisomerase IV. ACS Infectious Diseases, 1(1), 4–41. https://doi.org/10.1021/id500013t

Cheng, F., Li, W., Zhou, Y., Shen, J., Wu, Z., Liu, G., Lee, P. W., & Tang, Y. (2012). admetSAR: A comprehensive source and free tool for assessment of chemical ADMET properties. Journal of Chemical Information and Modeling, 52(11), 3099–3105. https://doi.org/10.1021/ci300367a

Chukwudi, C. U., Enwonwu, A., Oyeyemi, O. T., Malami, I., Oyeyemi, I. T., Ibrahim, M. A., Adebayo, E. A., Kazeem, M. I., & Atilola, O. (2026). Nigerian medicinal plants on the road to drug discovery: Prospects and challenges. Clinical Phytoscience, 12, Article 16. https://doi.org/10.1186/s40816-026-00429-1

Collin, F., Karkare, S., & Maxwell, A. (2011). Exploiting bacterial DNA gyrase as a drug target: Current state and perspectives. Applied Microbiology and Biotechnology, 92, 479–497. https://doi.org/10.1007/s00253-011-3557-z

Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Scientific Reports, 7, Article 42717. https://doi.org/10.1038/srep42717

Dorcheh, F. A., Balmeh, N., & Sanjari, S. (2022). In-silico investigation of antibacterial herbal compounds in order to find new antibiotic against Staphylococcus aureus and its resistant subtypes. Informatics in Medicine Unlocked, 28, Article 100843. https://doi.org/10.1016/j.imu.2021.100843

Dallakyan, S., & Olson, A. J. (2015). Small-molecule library screening by docking with PyRx. In J. E. Hempel, C. H. Williams, & C. C. Hong (Eds.), *Chemical biology: Methods and protocols* (pp. 243–250). Humana Press. https://doi.org/10.1007/978-1-4939-2269-7_19

Durdagi, S., Ul Qamar, M. T., Salmas, R. E., Tariq, Q., Anwar, F., & Ashfaq, U. A. (2018). Investigating the molecular mechanism of staphylococcal DNA gyrase inhibitors: A combined ligand-based and structure-based resources pipeline. Journal of Molecular Graphics and Modelling, 85, 122–129. https://doi.org/10.1016/j.jmgm.2018.07.010

El-Shibani, F. A. A., Sulaiman, G. M., Abouzied, A. S., Al Ali, A., Abdulkarim, A. K., Alamami, A. D., Asiri, M., & Mohammed, H. A. (2023). Polyphenol fingerprint, biological activities, and *in silico* studies of the medicinal plant Cistus parviflorus L. extract. ACS Omega, 8(50), 48269–48279. https://doi.org/10.1021/acsomega.3c07545

Fu, L., Shi, S., Yi, J., Wang, N., He, Y., Wu, Z., Peng, J., Deng, Y., Wang, W., Wu, C., Lyu, A., Zeng, X., Zhao, W., Hou, T., & Cao, D.(2024). ADMETlab 3.0: An updated comprehensive online ADMET prediction platform enhanced with broader coverage, improved performance, API functionality and decision support. Nucleic Acids Research, 52(W1), W422–W431. https://doi.org/10.1093/nar/gkae236

GBD 2021 Antimicrobial Resistance Collaborators. (2024). Global burden of bacterial antimicrobial resistance 1990–2021: A systematic analysis with forecasts to 2050. The Lancet, 404(10459), 1199–1226. https://doi.org/10.1016/S0140-6736(24)01867-1

Ismael, M. H., Al-Musawi, B. H., Alyasery, R. A., Taha, A. H., Merza, N. A. R., & Farhood, A. N. (2025). An in-silico study of garlic extract compounds targeting DNA gyrase in *Staphylococcus aureus*. Plant Science Today, 12(4). https://doi.org/10.14719/pst.9621

Newman, D. J., & Cragg, G. M. (2020). Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. Journal of Natural Products, 83(3), 770–803. https://doi.org/10.1021/acs.jnatprod.9b01285

Pereira-Filho, J. L., Mendes, A. G. G., Campos, C. D. L., Almeida, V. S. S., Pereira, A. P. A., Moreira, I. V., Monteiro, C. R. A. V., Gomes, L. N., Rhoden, C. R., Cantanhede-Filho, A. J., Silva, L. A., Lopes, A. J. O., Carvalho, R. C., & Monteiro-Neto, V. (2026). Silibinin potentiates antimicrobial action and reduces staphyloxanthin in Staphylococcus aureus. Pharmaceuticals, 19(4), Article 643. https://doi.org/10.3390/ph19040643

Pudipeddi, A., Vasudevan, S., Shanmugam, K., Mohan, S., Vairaprakash, P., Neelakantan, P., Balraj, A. S., & Solomon, A. P. (2023). Design, dynamic docking, synthesis, and in vitro validation of a novel DNA gyrase B inhibitor. Journal of Biomolecular Structure and Dynamics, 41(13), 6345–6358. https://doi.org/10.1080/07391102.2022.2107073

Rafiu, B. O., Omotayo, A. O., Lawal, I. O., & Aremu, A. O. (2025). Ethnobotanical uses of plants in Nigeria: An analysis of current research trends and patterns. Journal of Ethnobiology and Ethnomedicine, 21, Article 57. https://doi.org/10.1186/s13002-025-00788-y

Royal Botanic Gardens, Kew. (2026). Plants of the World Online. Retrieved October 21, 2026, from https://powo.science.kew.org/

Shinde, S. S., Giram, P. S., Wakte, P. S., & Bhusari, S. S. (2025). ADMET tools in the digital era: Applications and limitations. Advances in Pharmacology, 103, 65–80. https://doi.org/10.1016/bs.apha.2025.01.004

Trott, O., & Olson, A. J. (2010). AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. *Journal of Computational Chemistry*, *31*(2), 455–461. https://doi.org/10.1002/jcc.21334

Wang, Y., Wang, F., Liu, W., Geng, Y., Shi, Y., Tian, Y., Zhang, B., Luo, Y., & Sun, X. (2024). New drug discovery and development from natural products: Advances and strategies. Pharmacology & Therapeutics, 264, Article 108752. https://doi.org/10.1016/j.pharmthera.2024.108752

Waterhouse, A., Bertoni, M., Bienert, S., Studer, G., Tauriello, G., Gumienny, R., Heer, F. T., de Beer, T. A. P., Rempfer, C., Bordoli, L., Lepore, R., & Schwede, T. (2018). SWISS-MODEL: Homology modelling of protein structures and complexes. *Nucleic Acids Research*, *46*(W1), W296–W303. https://doi.org/10.1093/nar/gky427

Zouine, N., El Ghachtouli, N., El Abed, S., & Ibnsouda Koraichi, S. (2024). A comprehensive review on medicinal plant extracts as antibacterial agents: Factors, mechanism insights and future prospects. Scientific African, 26, Article e02395. https://doi.org/10.1016/j.sciaf.2024.e02395

©2026 This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International license viewed via https://creativecommons.org/licenses/by/4.0/ which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is cited appropriately.