Aframomum Danielli Phytocompounds as Promising Inhibitors of Salmonella Typhi Targets: An in Silico Approach

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ABSTRACT

The emergence of multidrug-resistant Salmonella enterica serovar Typhi, the causative agent of typhoid fever, has intensified the search for novel therapeutic agents, especially from natural sources. *Aframomum danielli*, a plant known for its medicinal properties, holds potential as a source of anti-typhoid compounds. This study aimed to identify and evaluate the anti-typhoid potential of phytochemical compounds from *Aframomum danielli* through molecular docking against key S. Typhi protein targets, followed by drug-likeness screening and ADMET profiling. Fourteen (14) bioactive compounds from *Aframomum danielli* were docked against four typhoid-related protein targets: DNA Gyrase B (1TM2), DNA Gyrase A (5ZTJ), L-lactate dehydrogenase (1LDJ), and OmpF porin (4KR4). Docking was performed using PyRx, and ligand-receptor interactions were visualized in Discovery Studio. The top-performing compounds were subjected to drug-likeness evaluation using Lipinski's Rule of Five and other filters. ADMET profiling was performed using SwissADME and ADMET Lab to assess pharmacokinetic properties and toxicity. Compounds such as Alloaromadendrene, Carotol, Caryophyllene oxide, Alpha-selinene, and Alpha-guaiol exhibited strong binding affinities with target proteins, particularly DNA Gyrase B, indicating possible inhibitory activity. These lead compounds passed key drug-likeness filters and showed favorable ADMET properties including high gastrointestinal absorption, low blood-brain barrier permeability, and minimal toxicity risks. This study highlights the potential of *Aframomum danielli* phytochemicals as promising leads in the development of novel anti-typhoid agents. Their multi-target interactions, favorable pharmacokinetics, and safety profiles underscore the importance of further in vitro and in vivo validation.

Keywords: *Aframomum danielli*, molecular docking, typhoid fever, DNA gyrase, phytochemicals

INTRODUCTION

Typhoid fever is a life-threatening systemic infection caused by *Salmonella enterica* serovar Typhi (*S. Typhi*), a Gram-negative bacterium transmitted primarily through ingestion of contaminated food or water (Hurley et al., 2014; Orish et al., 2014). The disease is prevalent in regions with poor sanitation and hygiene, where handwashing is infrequent, and asymptomatic carriers unknowingly contribute to its spread. Symptoms include prolonged high fever, diarrhea, vomiting, and in severe cases, intestinal perforation and death (Mulu et al., 2021).

The global burden of typhoid is significant, especially in low- and middle-income countries where diagnostic resources are limited. An estimated 21.5 million people contract typhoid annually, with about 75% of the few reported cases in developed nations like the United States acquired during international travel (Wibisono et al., 2020; Mulu et al., 2021). Due to diagnostic overlap with other febrile illnesses and insufficient laboratory infrastructure, typhoid is frequently underreported and misdiagnosed (Bhargava & Chandra, 2016).

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One of the key therapeutic targets for typhoid treatment is the *Salmonella Typhi* DNA gyrase B subunit, a vital component of the bacterial replication machinery. DNA gyrase, a type II topoisomerase, facilitates negative supercoiling of DNA, which is essential for bacterial DNA replication. Inhibition of this enzyme disrupts chromosomal replication, making it an effective target for antibacterial drug design (Kourlaba et al., 2016).

Molecular docking, a computational tool in drug discovery, enables virtual screening of bioactive compounds to predict their binding affinity and interaction with target proteins (Ibrahim et al., 2020a). Additionally, assessing drug-likeness through Lipinski's Rule of Five and ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) profiling helps predict a compound's pharmacokinetic and safety profile (Lei et al., 2019; Chandrasekaran et al., 2018).

Phytochemicals, which are naturally occurring bioactive compounds in plants, have gained attention as promising alternatives in antimicrobial therapy. *Aframomum danielli*, commonly known as alligator pepper, is an indigenous West African plant rich in essential oils and secondary metabolites with demonstrated antibacterial, antioxidant, and anti-inflammatory properties (Inegbenebor et al., 2009). Previous studies have highlighted the antimicrobial potential of its seed extracts, supporting its candidacy for further investigation in infectious disease drug discovery.

This study aims to employ molecular docking to identify promising phytochemical compounds from *Aframomum danielli* as potential inhibitors of *S. Typhi* DNA gyrase B, and to evaluate their drug-likeness and ADMET properties, which could inform future drug development efforts.

Statement of the Problem

Typhoid fever remains a persistent public health challenge in developing nations, including Nigeria, where inadequate sanitation, limited diagnostic tools, and growing antibiotic resistance exacerbate the disease burden. In light of these challenges, the exploration of plant-derived compounds, particularly phytochemicals with antimicrobial properties, presents a valuable and underutilized avenue for novel drug discovery against typhoid.

Aim of the Study

This study aims to identify bioactive lead compounds from *Aframomum danielli* with high binding affinity to *Salmonella Typhi* DNA gyrase B using molecular docking. By evaluating their drug-likeness and ADMET properties, the study seeks to propose viable candidates for future development of anti-typhoid agents.

MATERIAL AND METHODS

Preparation of In-House Library of Compounds from *Aframomum danielli*

An in-house library of 14 compounds from *Aframomum danielli* was prepared by compiling phytochemicals previously reported from this plant through an extensive literature search performed on public databases including PubMed, Google Scholar, and Google. Keywords such as "*Aframomum danielli*", "phytochemicals", and "bioactive compounds" were used (Akinmoladun et al., 2020; Nwachukwu et al., 2019).

Preparation of Ligands

Fourteen bioactive phytochemicals in Structured Data Format (SDF) were derived from *Aframomum danielli*. They were retrieved from databases including PubChem (https://pubchem.ncbi.nlm.nih.gov/) and PubMed (https://pubmed.ncbi.nlm.nih.gov/) (Kim et al., 2021). The ligand molecules were subsequently converted to dockable PDBQT format using AutoDock Tools (Morris et al., 2009).

Table 1 List of bioactive phytochemicals derived through a in house research from *Aframomum danielli*

S/N	COMPOUNDS
1	Spathulenol

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

2	Alloaroma dendrene
3	Beta-bourbonene
4	Beta-caryophyllene
5	Beta-cubebene
6	Beta –guaiene
7	Ledol
8	Longipinocarvone
9	Beta-selinene
. 10	Carotol
. 11	Caryophyllene
. 12	Caryophyllene oxide
. 13	Cyperene
. 14	Alpha-seliene

Preparation of protein

The crystal protein structures as presented in Table 2 were retrieved from the Protein Data Bank (https://www.rcsb.org). From the retrieved structures, the native ligands were extracted, and water molecules removed using Autodock Vina version 4.2 programs.

Table 2. Target receptors of typhoid fever

S/N	PROTEINS	PDB NUMBER
1	DNA gyrase B	1TM2
2	Gyrase –A	5ZTJ
3	lactate Dehydrogenase	1LDG
4	Salmonella Typhi OMPF	4KR4

Drug-Likeness Screening

The bioactive ligands that showed the highest binding affinity were subjected to various drug-likeness filtering analyses. These analyses—including Lipinski, Veber, Ghose, Egan, and Muegge rules—were performed using the SwissADME web server (Daina et al., 2017). Drug-likeness properties were evaluated based on Lipinski's rule of five, which considers molecular mass (MM) below 500 Da, no more than five hydrogen bond donors (HBD), no more than ten hydrogen bond acceptors (HBA), and a partition coefficient (logP) threshold.

ADMET Analysis

The ADMET profiles of the selected ligands were predicted using the ADMET lab 2.0 online server (Xiong et al., 2021), accessible at https://admetmesh.scbdd.com/. This server estimates absorption, distribution,

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

metabolism, excretion, and toxicity (ADMET) characteristics based on statistical models derived from natural compound datasets. This in silico technique is widely applied to screen compounds for favorable pharmacokinetic and toxicity profiles in early-stage drug discovery programs.

RESULTS AND DISCUSSION

Results

Table 3. Molecular docking results

The results of molecular docking against the selected targets in Typhoid fever are shown in table 3 as interpreted by the docking scores. The docking scores of the compounds range from -7.4 to -8.6 for 1TM2, -5.9 to -6.5 for 5ZTY, -5.6 to -6.1 for 4KRK and -5.4 to -7.0 for 1LDG.

S/N	COMPOUNDS	1LDG	1TM2	4KR4	5ZTJ
15. 1	Spathulenol	-5.7	-7.9	-6.1	-6.1
16. 2	Alloaroma dendrene	-5.8	-7.8	-6.1	-6.0
17. 3	Beta-bourbonene	-5.8	-7.4	-5.8	-5.9
18. 4	Beta-caryophyllene	-5.7	-8.0	-5.6	-5.9
19. 5	Beta-cubebene	-7.0	-7..8	-5.7	-6.4
20. 6	Beta –guaiene	-6.1	-8.0	-5.7	-6.5
21. 7	Ledol	-5.8	-8.6	-6.1	-6.4
22. 8	Longipinocarvone	-5.7	-8.0	-6.0	-6.2
23. 9	Beta-selinene	-6.2	-7.8	-6.1	-6.1
24. 10	Carotol	-5.4	-7.5	-5.7	-6.4
25. 11	Caryophyllene	-6.7	-8.0	-5.6	-5.9
26. 12	Caryophyllene oxide	-6.3	-7.8	-5.8	-6.1
27. 13	Cyperene	-5.9	-7.6	-5.7	-6.4
28. 14	Alpha-seliene	-6.0	-7.7	-5.8	-6.1
	SELECTED DRUGS USED IN TREATING THYPOID .F				
29. 1	Ciprofloxacin	-7.4	-7.4	-7.1	-7.3
30. 2	Ceftriaxone	-6.5	-7.9	-8.0	-8.7
31. 3	Ofloxacin	-7.3	-7.7	-6.9	-8.1
32. 4	Cefixime	-6.6	-7.6	-7.4	-7.6

Table 4.1 Docking score of phytochemicals from *Aframmomum danielli* with target proteins.

NB: 5ZTJ-gryaseA**, 4KRK –** salmonella typhi ompf **1TM2-DNA gryase B**, **LDG** -1-lactate dehydrogenase

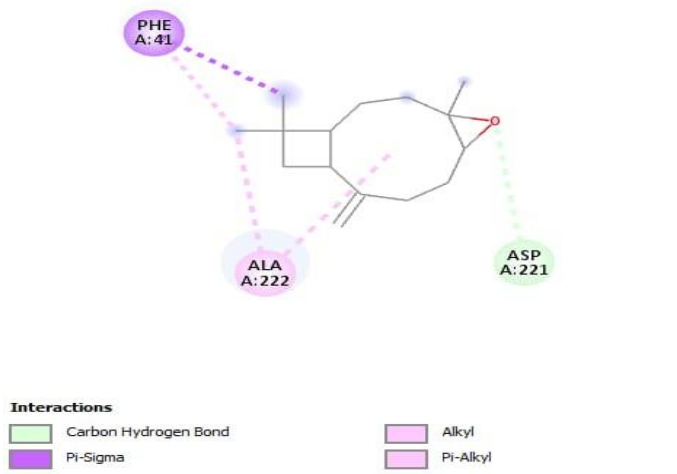
Table 4. Showing Grid Box Measurement of the Protein's Active Site

DIMENSION	1LDG	1TM2	4KRK	5ZTJ
Center_X	24.67	10.57	-25.38	22.61
Center_Y	17.07	-6.79	16.25	23.44
Center_Z	35.30	149.15	-17.91	25.03
Size_X	15.88	23.44	18.85	30.76
Size_Y	25.17	19.93	42.75	22.54
Size_Z	31.03	23.36	39.47	21.50

Druglikeness screening

Table 5. Drug-likeness screening of selected ligands from *Aframomum daneilli* and drugs used for the cure of typhoid fever.

S/N	Compounds	LIPINSKI	GHOSE	VEBER	EGAN	MUEGGE	PASSED
1	Alloaroma Adendrene	YES	YES	YES	YES	NO	PASSED
2	Carotol	YES	YES	YES	YES	NO	PASSED
3	Alpha Seliene	YES	YES	YES	YES	NO	PASSED
4	Caryophyllene oxide	YES	YES	YES	YES	NO	PASSED
	DRUGS						
5	Ciprofloxacin	YES	YES	YES	YES	YES	PASSED
6	Ceftriaxone	NO	NO	NO	NO	NO	FAILED
7	Ofloxacin	YES	YES	YES	YES	YES	PASSED
8	Cefixime	YES	NO	NO	NO	NO	FAILED



ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

Figure 1. 1TM2- Caryophyllene oxide interaction:

2D Schematic representation of main interaction of Charyophellen Oxide with 1TM2.

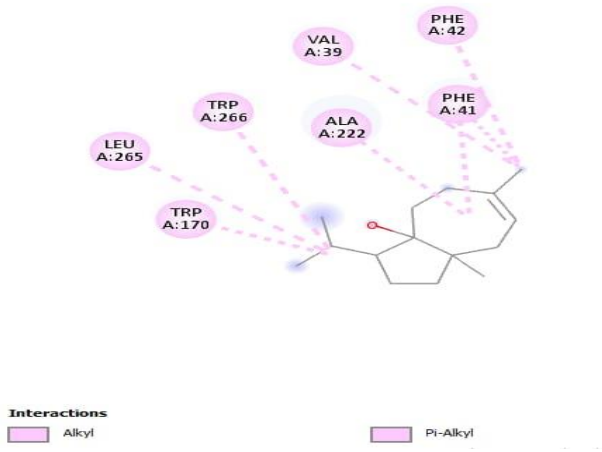


Figure 2. – interaction of 2TM2 - Carotol:

2D Schematic representation of main interaction of carotol with 2TM2.

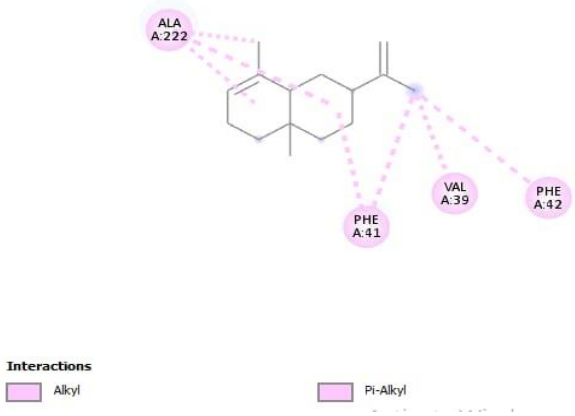


Figure 3. – Interaction 2TM2 – Alpha Seleine:

2D Schematic representation of main interaction of Alpha seleine with 2TM2

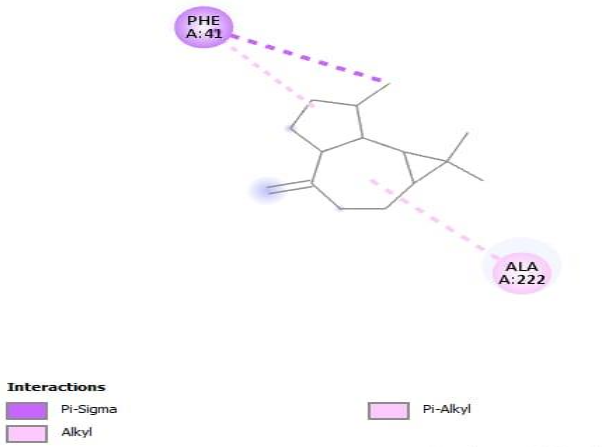


Figure 4. – Interaction 2TM2 – Alloaroma dendrene:

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

2D Schematic representation of main interaction of Alloaroma dendrene with 2TM2.

Table 6. ADMET Analysis Results of Alloaroma Dendrene

PROPERTY	**MODEL NAME**	**PREDICTED VALUE**
ABSORPTION (mol/L)	CACO-2 PERMEABILITY(CM\S)	-4.57
	PGP-INHIBITOR	NO
	PGP-SUBSTRATE	NO
	HUMAN INTESTINAL ABSORBTION	HIGH
DISTRIBUTION (L/kg)	VOLUME DISTRIBUTION	1.647
	BBB PENETRATION	YES
METABOLISM	CYPLA2 INHIBITOR	NO
	CYP2C19 INHIBITOR	YES
	CYP2C9 INHIBITOR	NO
	CYP3A4 INHIBITOR	YES
	CYP1A2 SUBSTRATE	NO
	CYP2C19 SUBSTRATE	YES
	CYP2C9 SUBSTRATE	NO
	CYP3A4 SUBSTRATE	NO
EXCRETION (mL/min/kg)	TOTAL CLEARANCE	13.563
	HALF-LIFE(T1/2CHOURS)	0.040
TOXICITY	HERG BLOCKERS	NO
	HUMAN HEPTOTOXICITY	NO
	DILI	NO
	AMES TOXICITY	NO
	RAT ORAL ACUTE TOXICITY	YES
	FDAMDD	NO
	CARCINOGENICITY	NO
	RESPIRATORY TOXICITY	YES

Table 7. Carotol

PROPERTY	**MODEL NAME**	**PREDICTED VALUE**
ABSORPTION (mol/L)	CACO-2 PERMEABILITY(CM\S)	4.303

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

	PGP-INHIBITOR	YES
	PGP-SUBSTRATE	NO
	HUMAN INTESTINAL ABSORBTION	NO
DISTRIBUTION (L/kg)	VOLUME DISTRIBUTION	5.306
	BBB PENETRATION	NO
METABOLISM	CYPLA2 INHIBITOR	NO
	CYP2C19 INHIBITOR	NO
	CYP2C9 INHIBITOR	NO
	CYP3A4 INHIBITOR	YES
	CYP1A2 SUBSTRATE	YES
	CYP2C19 SUBSTRATE	NO
	CYP2C9 SUBSTRATE	NO
	CYP3A4 SUBSTRATE	YES
EXCRETION (mL/min/kg)	TOTAL CLEARANCE	10.31
	HALF-LIFE(T1/2CHOURS)	0.09
TOXICITY	HERG BLOCKERS	NO
	HUMAN HEPTOTOXICITY	NO
	DILI	YES
	AMES TOXICITY	NO
	RAT ORAL ACUTE TOXICITY	YES
	FDAMDD	NO
	CARCINOGENICITY	YES
	RESPIRATORY TOXICITY	NO

Table 8. Caryophyllene oxide

PROPERTY	**MODEL NAME**	**PREDICTED VALUE**
ABSORPTION (mol/L)	CACO-2 PERMEABILITY(CM\S)	4.679
	PGP-INHIBITOR	**NO**
	PGP-SUBSTRATE	**NO**
	HUMAN INTESTINAL ABSORBTION	**NO**
DISTRIBUTION (L/kg)	VOLUME DISTRIBUTION	1.469

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

	BBB PENETRATION	YES
METABOLISM	CYPLA2 INHIBITOR	NO
	CYP2C19 INHIBITOR	NO
	CYP2C9 INHIBITOR	NO
	CYP3A4 INHIBITOR	NO
	CYP1A2 SUBSTRATE	NO
	CYP2C19 SUBSTRATE	YES
	CYP2C9 SUBSTRATE	YES
	CYP3A4 SUBSTRATE	NO
EXCRETION (mL/min/kg)	TOTAL CLEARANCE	15.503
	HALF-LIFE(T1/2CHOURS)	0.083
TOXICITY	HERG BLOCKERS	NO
	HUMAN HEPTOTOXICITY	NO
	DILI	NO
	AMES TOXICITY	NO
	RAT ORAL ACUTE TOXICITY	NO
	FDAMDD	NO
	CARCINOGENICITY	NO
	RESPIRATORY TOXICITY	YES

Table 9. Alpha-Seliene

PROPERTY	**MODEL NAME**	**PREDICTED VALUE**
ABSORPTION (mol/L)	CACO-2 PERMEABILITY(CM\S)	-4.471
	PGP-INHIBITOR	**NO**
	PGP-SUBSTRATE	**NO**
	HUMAN INTESTINAL ABSORBTION	**HIGH**
DISTRIBUTION (L/kg)	VOLUME DISTRIBUTION	3.277
	BBB PENETRATION	YES
METABOLISM	CYPLA2 INHIBITOR	NO

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

	CYP2C19 INHIBITOR	YES
	CYP2C9 INHIBITOR	NO
	CYP3A4 INHIBITOR	NO
	CYP1A2 SUBSTRATE	YES
	CYP2C19 SUBSTRATE	YES
	CYP2C9 SUBSTRATE	YES
	CYP3A4 SUBSTRATE	NO
EXCRETION(mL/min/kg)	TOTAL CLEARANCE	13.979
	HALF-LIFE(T1/2CHOURS)	0.064
TOXICITY	HERG BLOCKERS	NO
	HUMAN HEPTOTOXICITY	NO
	DILI	NO
	AMES TOXICITY	NO
	RAT ORAL ACUTE TOXICITY	NO
	FDAMDD	NO
	CARCINOGENICITY	NO
	RESPIRATORY TOXICITY	NO

Table 10. ADMET analysis results of ciprofloxacin

PROPERTY	**MODEL NAME**	**PREDICTED VALUE**
ABSORPTION (mol/L)	CACO-2 PERMEABILITY(CM\S)	-5.269
	PGP-INHIBITOR	YES
	PGP-SUBSTRATE	NO
	HUMAN INTESTINAL ABSORBTION	HIGH
DISTRIBUTION (L/kg)	VOLUME DISTRIBUTION	2.342
	BBB PENETRATION	NO
METABOLISM	CYPLA2 INHIBITOR	NO
	CYP2C19 INHIBITOR	NO
	CYP2C9 INHIBITOR	NO
	CYP3A4 INHIBITOR	NO

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

	CYP1A2 SUBSTRATE	NO
	CYP2C19 SUBSTRATE	NO
	CYP2C9 SUBSTRATE	NO
	CYP3A4 SUBSTRATE	NO
EXCRETION(mL/min/kg)	TOTAL CLEARANCE	3.241
	HALF-LIFE(T1/2CHOURS)	0.056
TOXICITY	HERG BLOCKERS	NO
	HUMAN HEPTOTOXICITY	YES
	DILI	YES
	AMES TOXICITY	NO
	RAT ORAL ACUTE TOXICITY	NO
	FDAMDD	YES
	CARCINOGENICITY	NO
	RESPIRATORY TOXICITY	YES

DISCUSSION AND CONCLUSION

Discusion

Typhoid fever, caused by the Gram-negative bacterium *Salmonella enterica* serovar Typhi (*S. Typhi*), continues to pose significant health challenges in many parts of the world, especially in developing nations with limited access to clean water and antibiotics. The emergence of multidrug-resistant strains has necessitated a shift in research focus towards identifying novel, plant-derived therapeutic agents with potent antibacterial activity (Hurley et al., 2014; Orish et al., 2014). In this study, the potential of phytochemicals from *Aframomum danielli*, a plant renowned for its antimicrobial properties, was investigated through computational methods targeting four crucial proteins associated with typhoid pathogenesis: DNA Gyrase B (1TM2), DNA Gyrase A (5ZTJ), L-lactate dehydrogenase (1LDJ), and OmpF porin (4KR4).

Molecular docking revealed promising interactions between several of the fourteen (14) phytocompounds and the four protein targets. DNA Gyrase B (1TM2), an essential enzyme for DNA replication in bacteria, served as the primary focus due to its established role in bacterial survival and its validation as a drug target. Compounds such as Alloaromadendrene, Carotol, Caryophyllene oxide and Alpha-selinene exhibited strong binding affinities to 1TM2, in some cases outperforming standard antibiotics like Ceftriaxone and Cefixime in docking scores.

This high binding affinity suggests potential inhibitory activity against DNA Gyrase B, which could disrupt DNA supercoiling and replication in *S. Typhi*, leading to bacterial cell death. Similar interactions were observed with 5ZTJ and 1LDJ, implicating the selected compounds in the inhibition of energy metabolism and cell membrane permeability, given the role of L-lactate dehydrogenase and porins in bacterial physiology.

The interaction profiles, particularly with amino acid residues like Phe41, Ala222, Val164, Trp170, and Lys35 on 1TM2, highlight the structural compatibility of these ligands with the active site of the enzyme. The presence of hydrogen bonds and hydrophobic interactions, as seen in figures 4.1–4.4, reinforces the stability of these

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

complexes. These interactions suggest a competitive inhibition mechanism and confirm that the binding is not merely superficial but may interfere with the protein's function.

After the docking analysis, the compounds were subjected to drug-likeness filtering based on Lipinski's Rule of Five and other filters like Veber, Egan, Ghose, and Muegge via SwissADME. The majority of the lead compounds passed the criteria, suggesting favorable oral bioavailability and physicochemical properties suitable for drug development. Notably, Alloaromadendrene, Carotol, Caryophyllene oxide and Alpha-selinene met these criteria, while reference antibiotics like Ciprofloxacin and Ofloxacin also passed, but with occasional rule violations in Ceftriaxone and Cefixime.

Passing these drug-likeness filters is crucial, as it predicts that these compounds have molecular weights, lipophilicity (logP), and hydrogen bonding potential within acceptable ranges for absorption and systemic distribution. These properties suggest that, if developed into drugs, the compounds could effectively reach their targets in the human body after oral administration.

Pharmacokinetic properties such as intestinal absorption, blood-brain barrier (BBB) permeability, P-glycoprotein interaction, and cytochrome P450 (CYP) metabolism were assessed using ADMET analysis. The selected lead compounds demonstrated high gastrointestinal absorption, implying suitability for oral administration. This is an important therapeutic advantage, especially in low-resource settings where oral dosage forms are preferred for ease of use and compliance.

BBB permeability was generally low, which is a desirable property for drugs targeting enteric bacteria like *S. Typhi*, as central nervous system (CNS) penetration is not required and may lead to off-target effects. The compounds also exhibited minimal inhibition of P-glycoprotein, reducing the risk of rapid efflux and enhancing their intracellular retention.

Furthermore, several of the compounds were identified as potential substrates and inhibitors of major CYP enzymes such as CYP1A2, CYP2C19, CYP2C9, and CYP3A4. This duality has significant pharmacological implications: while metabolic transformation is essential for bioactivation or clearance, CYP inhibition could lead to potential drug–drug interactions. Thus, further in vitro and in vivo studies would be necessary to refine dosing regimens and evaluate toxicity.

The toxicity predictions, including acute oral toxicity and AMES mutagenicity, revealed that most compounds were non-mutagenic and exhibited low toxicity (Category III or IV). However, Carotol showed mild toxicity alerts, indicating the need for caution in their development. The absence of carcinogenicity and AMES toxicity in most of the compounds supports their candidacy as safe therapeutic agents.

The findings from this in silico investigation support the potential of *Aframomum danielli* compounds as scaffolds for new anti-typhoid drugs. The compounds not only displayed significant interactions with multiple bacterial targets but also passed drug-likeness and ADMET filters, indicating good pharmacokinetic and safety profiles. Such multi-target action is particularly promising in overcoming bacterial resistance, which often arises due to mutations in a single target protein. A multi-site mechanism reduces the likelihood of resistance development.

Moreover, the study validates the traditional use of *Aframomum danielli* in ethnomedicine for treating microbial infections and aligns with the global shift towards natural product-based drug discovery. These compounds could be further optimized through medicinal chemistry to enhance potency, reduce toxicity, and improve selectivity.

Conclusion

In conclusion, Alloaromadendrene, Carotol, Alpha-selinene, and Caryophyllene oxide stand out as promising candidates. They should be prioritized for in vitro validation against *S. Typhi* strains, cytotoxicity testing in mammalian cell lines, and eventual in vivo efficacy studies. The integration of computational and experimental pharmacology will be essential in transitioning these leads from virtual screening to clinical application.

REFERENCES

1. Abioye, A. I., Akinyemi, K. O., & Isawumi, M. A. (2017). Understanding the adaptive physiological role of fever: A review. Journal of Clinical Pathology and Laboratory Medicine, 2(1), 18–26.
2. Akinmoladun, F. O., Akinrinlola, B. L., Komolafe, T. O., & Farombi, E. O. (2020). Phytochemical screening and biological activities of Aframomum danielli. Journal of Medicinal Plants Research, 14(3), 112–119. https://doi.org/10.5897/JMPR2020.6981
3. Bhargava, A., & Chandra, P. (2016). Typhoid fever: Clinical and laboratory characteristics in an urban hospital. International Journal of Infectious Diseases, 45, 24–29. https://doi.org/10.1016/j.ijid.2016.03.004
4. Chandrasekaran, A., Natarajan, J., & Sekar, K. (2018). In silico pharmacokinetic and molecular docking studies of phytochemicals against key molecular targets of cardiovascular diseases. Journal of Molecular Modeling, 24(4), 103. https://doi.org/10.1007/s00894-018-3622-6
5. 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, 42717. https://doi.org/10.1038/srep42717
6. Hurley, D., McCusker, M. P., Fanning, S., & Martins, M. (2014). Salmonella–host interactions–modulation of the host innate immune system. Frontiers in Immunology, 5, 481. https://doi.org/10.3389/fimmu.2014.00481
7. Ibrahim, M. A., Ismail, S., & Salau, A. M. (2020a). Computational docking studies on phytochemicals as inhibitors of bacterial DNA gyrase. Journal of Pharmaceutical Research International, 32(10), 1–12. https://doi.org/10.9734/jpri/2020/v32i1030604
8. Inegbenebor, U., Okosun, O., & Mordi, R. (2009). Antimicrobial activity of ethanolic extract of Aframomum danielli (Alligator pepper). Nigerian Journal of Health and Biomedical Sciences, 8(2), 16–20.
9. Kim, S., Chen, J., Cheng, T., Gindulyte, A., He, J., He, S., ... & Bolton, E. E. (2021). PubChem in 2021: new data content and improved web interfaces. Nucleic Acids Research, 49(D1), D1388–D1395. https://doi.org/10.1093/nar/gkaa971
10. Kourlaba, G., Sypsa, V., Kalomenidis, I., & Costopoulos, C. (2016). Mechanisms of action and resistance of DNA gyrase inhibitors. Chemotherapy Research and Practice, 2016, 1–9. https://doi.org/10.1155/2016/4038795
11. Lei, Y., Wang, Y., Zhang, H., & Fan, W. (2019). ADMET evaluation in drug discovery: 15 rule-based filters for drug-likeness. Drug Discovery Today, 24(7), 1461–1468. https://doi.org/10.1016/j.drudis.2019.04.009
12. Morris, G. M., Huey, R., Lindstrom, W., Sanner, M. F., Belew, R. K., Goodsell, D. S., & Olson, A. J. (2009). AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. Journal of Computational Chemistry, 30(16), 2785–2791. https://doi.org/10.1002/jcc.21256
13. Mulu, W., Asnake, S., & Gelaw, A. (2021). Prevalence, antimicrobial susceptibility pattern and associated risk factors of Salmonella enterica serovar typhi infections among febrile patients in Ethiopia. BMC Infectious Diseases, 21, 273. https://doi.org/10.1186/s12879-021-05941-1
14. Nwachukwu, I. N., Nworgu, Z. A. M., & Ezugwu, C. O. (2019). Characterization and antimicrobial potential of Aframomum danielli. African Journal of Biotechnology, 18(23), 513–519. https://doi.org/10.5897/AJB2019.16845
15. Orish, C. N., Olanrewaju, F. O., & Ekong, M. B. (2014). Pathogenesis and control of typhoid fever: An update. European Journal of Experimental Biology, 4(2), 139–147.
16. Wibisono, F. J., Puspitasari, I. M., & Wibowo, H. (2020). Typhoid fever diagnostic challenges in resource-limited settings: A review of available tools and approaches. Tropical Medicine and Health, 48, 76. https://doi.org/10.1186/s41182-020-00257-4
17. Xiong, G., Wu, Z., Yi, J., Fu, L., Yang, Z., Hsieh, C., ... & Jiang, Z. (2021). ADMETlab 2.0: An integrated online platform for accurate and comprehensive predictions of ADMET properties. Nucleic Acids Research, 49(W1), W5–W14. https://doi.org/10.1093/nar/gkab255