Edubiotik : Jurnal Pendidikan, Biologi dan Terapan
ISSN 2528-679X (print), ISSN 2597-9833 (online)
Vol. 10, No. 02, November 2025, 11. 496 – 506

Available online at:
https://ejurnal.uibu.ac.id/index.php/edubiotik

Research Article

OPEN ACCESS

In silico analysis of bioactive compounds from *Strobilanthes crispus* as MurE inhibitors in *Escherichia coli*

Yoga Aria Aditama [1,a], Indah Rakhmawati Afrida [1,b,*], Kukuh Munandar [1,c], Riyanto [2,d]

[1] Biology Education Program, Universitas Muhammadiyah Jember, Jember, Indonesia
[2] Biology Education Department, Insan Budi Utomo University, Malang, Indonesia
Email: yhogaaja1123@gmail.com [1,a], indahrakhmawatiafrida@unmuhjember.ac.id [1, b, *], kukuhmunandar@unmuhjember.ac.id [1, c], riyanto@uibu.ac.id [2,d]
* Corresponding author

Article Information

Article History:
Submitted: 2025-06-23
Revised: 2025-11-12
Accepted: 2025-12-30
Published: 2025-12-30

Keywords:
Escherichia coli;
molecular docking;
MurE enzyme;
Strobilanthes crispus;
urinary tract infection

ABSTRACT

Urinary Tract Infection (UTI) is one of the most common infectious diseases, predominantly caused by *Escherichia coli*. Increasing antibiotic resistance has driven the search for new antibacterial agents from natural sources. This study aims to evaluate the potential of bioactive compounds from *Strobilanthes crispus* as inhibitors of the *E. coli MurE* enzyme using an in-silico approach. Molecular docking, toxicity prediction, and pharmacokinetic analysis were performed. The docking results demonstrated that apigenin 7-O-beta-D-glucuronide exhibited the highest binding affinity toward MurE with a binding energy of -9,5 kcal/mol, followed by acteoside (-9,4 kcal/mol) and isoacteoside (-9,2 kcal/mol), outperforming ciprofloxacin (-7,1 kcal/mol). Pharmacokinetic analysis indicated that all tested compounds showed good solubility and acceptable safety profiles, althought they exhibited los gastrointestinal absorption and poor oral bioavailability. These findings suggest that *S. crispus* bioactive compounds possess promising potential as MurE inhibitors and warrant further optimization and experimental validation as antibacterial candidates against *E. coli*.

Publisher
Biology Education Department, Insan Budi Utomo University, Malang, Indonesia

How to Cite
Aria Aditama , Y., Rakhmawati Afrida , I., Munandar, K., & Riyanto. (2026). In silico analysis of bioactive compounds from Strobilanthes crispus as MurE inhibitors in Escherichia coli. Edubiotik : Jurnal Pendidikan, Biologi Dan Terapan, 10(02). https://doi.org/10.33503/ebio.v10i02.1721

INTRODUCTION

Urinary tract infection (UTI) remains a major global public health issue, with *Escherichia coli* (*E. coli*) recognized as the primary causative pathogen. UTI commonly affects the kidneys, ureters, bladder, and urethra, and disproportionately occurs among women of reproductive age (Brookes-Howell et al., 2019; Sher et al., 2024). In Indonesia, the estimated incidence reaches 90-100 cases per 100,000 population per year, underscoring the need for effective therapeutic strategies in both global and local contexts. Risk factors for UTI include poor personal hygiene, sexual activity, urinary catheterization, and

comorbidities such as diabetes mellitus, which contribute to increased susceptibility and severity (Du et al., 2024; Sinha et al., 2025; Soiza et al., 2018).

Antibiotics remain the standard therapy for UTI; however, irrational and excessive antibiotic use has accelerated antimicrobial resistance (AMR), particularly in *E. coli*. Increasing resistance to commonly used antibiotics such as ciprofloxacin poses a major clinical challenge, making previously manageable infections difficult to treat. The World Health Organization (WHO, 2021) has identified AMR as a global health emergency, emphasizing the urgent need for alternative therapeutic agents with novel mechanisms of action.

Medicinal plants have gained significant attention as promising sources of new bioactive compounds due to their diverse pharmacological properties and relatively low side-effect profiles. *Strobilanthes crispus*, traditionally used in several Asian countries including Indonesia, exhibits various biological activities, including anti-inflammatory, anticancer (Baraya et al., 2022; Bataya et al., 2021; Ng et al., 2021), antioxidant (Tan et al., 2019), and antimicrobial effects (Adibi et al., 2017; Adriana et al., 2023; Ban et al., 2022; Dwi Pramesti et al., 2024). Bioactive constituents of *S. crispus*, such as flavonoids, phenolic compounds, saponins, and tannins, have demonstrated antibacterial potential against several pathogenic bacteria (Adriana et al., 2023; Suboh et al., 2022).

Although previous studies have reported the antibacterial activity of *Strobilanthes crispus* extracts, the molecular mechanisms underlying its activity against *Escherichia coli*, particularly uropathogenic strains, remain poorly understood. Several essential bacterial enzymes, such as DNA gyrase, MurA, and penicillin-binding proteins, have been extensively investigated as antibacterial targets; however, these targets are frequently associated with the development of antibiotic resistance due to their long-term clinical use. In contrast, the MurE enzyme, a cytosolic ligase involved in the incorporation of meso-diaminopimelic acid into the peptidoglycan precursor, plays a critical role in bacterial cell wall biosynthesis and remains comparatively underexplored as a therapeutic target (Kumar et al., 2023; Sangshetti et al., 2017). Previous in silico studies on plant-derived antibacterials have largely focused on well-established targets or evaluated crude extracts without elucidating specific enzyme–ligand interactions.

Therefore, this study contributes a target-specific and mechanistic in silico investigation by evaluating the interaction of individual *S. crispus* bioactive compounds with the MurE enzyme. Moreover, this work integrates molecular docking with pharmacokinetic and toxicity predictions, providing a more comprehensive assessment than docking-only studies. By comparing the binding affinity of *S. crispus* compounds with a reference antibiotic, this study offers new insights into MurE inhibition and highlights the potential of *S. crispus* as a source of alternative antibacterial agents against *E. coli*. Advances in computational biology enable in silico approaches such as molecular docking to efficiently predict ligand-protein interactions and assess potential antibacterial activity (Afrida et al., 2021; Bullock et al., 2020; Paramita et al., 2024; Widhiastuti et al., 2024). This method provides insights into binding affinity and inhibition mechanisms and can be complemented by toxicity and pharmacokinetic analysis to evaluate drug-likeness properties.

Therefore, this study aims to assess the antibacterial potential of *S. crispus* bioactive compounds against the MurE enzyme of *E. coli* through molecular docking analysis, supported by toxicity and pharmacokinetic evaluation. The findings are expected to contribute to the early development of plant-based therapeutic candidates to address *E. coli*-associated UTI and the increasing burden of antibiotic resistance.

RESEARCH METHODS

This study employed an exploratory descriptive research design based on an in-silico approach to investigate the antibacterial potential of bioactive compounds from *S. crispus* against *E. coli*. The entire research process was conducted computationally without wet-laboratory experiments, utilizing bioinformatics software and publicly accessible online databases. The research workflow comprised several stages, including identification of bioactive compounds, selection and preparation of the target protein, molecular preparation of ligands, docking simulation, and pharmacokinetic and toxicity evaluation.

Bioactive compounds of *S. crispus* were identified from the PubChem database. The three-dimensional crystal structure of the MurE enzyme of *E. coli* (muramyl ligase; PDB ID: 7B9E) was retrieved from the Protein Data Bank and prepared by removing water molecules and non-essential heteroatoms, followed by the addition of polar hydrogen atoms. Ligand structures were energy-minimized prior to docking. Molecular docking simulations were performed using AutoDock Vina with a rigid receptor and flexible ligands. The docking grid box was defined as encompassing the MurE active site region to ensure coverage of key catalytic residues, and the exhaustiveness parameter was set to 8. Docking poses were ranked based on binding affinity values (kcal/mol), and the optimal binding conformation was selected according to the lowest binding energy and favorable protein–ligand interaction profiles.

The population in this study comprised all bioactive compounds reported from *S. crispus*. Five compounds were selected as samples based on a predicted antibacterial probability (Pa value) greater than 0.6. According to the PASS (Prediction of Activity Spectra for Substances) approach, compounds with Pa values above 0.5 are considered to have a meaningful probability of exhibiting biological activity; therefore, a Pa threshold of >0.6 was applied to prioritize compounds with promising antibacterial potential for exploratory in silico analysis (Filimonov et al., 2018). These compounds included *apigenin 7-O-β-D-glucuronide (CID: 5319484), acteoside (CID: 5281800), isoacteoside (CID: 6476333), quercetin 3-rutinoside (CID: 5280805)*, and *calceolarioside (CID: 11284950)*. *Ciprofloxacin (CID: 2764)* was used as a reference compound due to its well-established antibacterial activity against Gram-negative and Gram-positive bacteria.

Computational analyses were conducted using PyMOL for visualization and structure preparation, Discovery Studio 2024 for active site identification and interaction analysis, and PyRx integrated with AutoDock Vina for molecular docking simulations (Mawaddani et al., 2022). Pharmacokinetic properties and toxicity profiles of the top-ranked compounds were predicted using SwissADME and ProTox-II online platforms. Data collection involved retrieving compound and protein structures from public databases and generating molecular interaction data from docking simulations, including binding affinity values, hydrogen bond interactions, and key interacting residues. Data analysis employed a descriptive-comparative approach by comparing the molecular docking results and pharmacokinetic–toxicological profiles of the tested compounds with those of the reference compound (*ciprofloxacin*). The results were interpreted to evaluate the antibacterial potential and drug-likeness of *S. crispus* bioactive compounds based on their molecular interaction characteristics.

FINDING AND DISCUSSION

The muramyl ligase (MurE) enzyme is an essential component of the peptidoglycan biosynthesis pathway, which is vital for the survival of bacteria, including *E. coli* the main pathogen responsible for urinary tract infections (UTIs) (Hervin et al., 2023). MurE catalyzes the addition of meso-diaminopimelic acid (m-DAP) to the growing peptidoglycan precursor, a key step in bacterial cell wall synthesis (Rohde, 2019). Since this process does not occur in eukaryotic cells, MurE serves as a specific and strategic target

for the development of novel antibacterial agents. In this study, the bioactive compounds from *S. crispus* were evaluated for their potential antibacterial activity through inhibition of the *E. coli MurE* enzyme using an in silico molecular docking approach (Table 1).

Table 1. Binding affinity and amino acid residues between ligands and proteins

Complex	Binding Affinity (kcal/mol)	Interacting Residues	Interaction Types	Bond Distance (Å)
Apigenin 7-O-beta-D-glucuronide_MurE	-9.5	GLN370, PHE307, MET343, ASN308, ALA371, LYS367, THR121, LYS120, ARG342	Hydrogen bonds, electrostatic, hydrophobic interactions	2.7 – 4.1
Acteoside_MurE	-9.4	THR117, THR122, ASN118, ASN308, GLU357, LYS367, GLN370, ALA306, PHE307, ALA364, ALA371, ASP357, TYR358	Hydrogen bonds, electrostatic, hydrophobic, non-covalent	2.6 – 4.2
Isoacteoside_MurE	-9.2	SER29, ASN91, LEU27, VAL41, ASP28, ASP164, VAL163, THR26, MET25	Hydrogen bonds, electrostatic, hydrophobic interactions	2.7 – 4.1
Quercetin 3-Rutinoside_MurE	-9.0	THR143, THR121, MET347, ALA371, ARG342, LYS367, THR112, LYS120, GLY119, TYR358	Hydrogen bonds, electrostatic, hydrophobic, non-covalent	2.7 – 4.2
Calceolarioside_MurE	-8.2	ASP357, ARG342, THR121, ALA371, PHE307, ALA306, MET343, LYS367	Hydrogen bonds, electrostatic, hydrophobic interactions	2.7 – 4.1
Ciprofloxacin_MurE (control)	-7.1	THR122, ASN308, ALA368, LYS367, TYR358	Hydrogen bonds, electrostatic, hydrophobic interactions	2.2 – 4.1

The molecular docking results demonstrated that the *S. crispus* bioactive compounds were able to interact effectively with the active site of the *E. coli MurE* enzyme, forming hydrogen bonds, hydrophobic interactions, and electrostatic contacts with several amino acid residues. The binding affinity values ranged from –8.2 to –9.5 kcal/mol, reflecting varying binding strengths among the compounds. Apigenin 7-O-β-D-glucuronide exhibited the strongest interaction (–9.5 kcal/mol), forming hydrogen bonds with GLN370 and THR121, electrostatic interactions with LYS120 and ARG342, and hydrophobic contacts with MET343 and ALA371 (Figure 1). The short bond distances (2.7–4.1 Å) indicatea stable and energetically favorable ligand–protein complex. Similarly, acteoside and isoacteoside showed strong binding affinities of –9.4 kcal/mol and –9.2 kcal/mol, respectively. Acteoside interacted with 13 amino acid residues, including ASN118, GLU357, ASP357, and TYR358 (Figure 2), suggesting stable and synergistic binding, while isoacteoside formed hydrogen bonds with SER29 and THR26 and electrostatic interactions with ASP28 and ASP164 near the MurE active site (Figure 3). Quercetin 3-rutinoside also demonstrated a high binding potential (–9.0 kcal/mol), forming hydrogen and electrostatic interactions with ARG342, LYS367, and TYR358 (Figure 4), whereas calceolarioside exhibited a lower binding affinity (–8.2 kcal/mol) and interacted mainly with ASP357, ARG342, and LYS367 (Figure 5).

For comparison, ciprofloxacin formed key interactions with residues THR122, ASN308, ALA368, LYS367, and TYR358 at the MurE catalytic site (Figure 6), consistent with previous reports (Moreira da Silva et al., 2017; Rambaher et al., 2023). These findings suggest that ciprofloxacin, in condition to its

established inhibition of DNA gyrase and topoisomerase IV, may also interact with MurE, indicating potential drug repurposing effects against bacterial cell wall biosynthesis (Ogbuagu et al., 2022).

To further interpret these docking results, the involvement of MurE catalytic residues was analyzed based on recent structural studies. MurE is an ATP-dependent ligase responsible for the incorporation of D-glutamate into the UDP-N-acetylmuramoyl peptide during peptidoglycan biosynthesis. Structural and functional analyses have identified several conserved catalytic and substrate-binding residues in *E. coli* MurE, including ARG342, LYS367, ASP357, and TYR358, which play essential roles in ATP binding, substrate stabilization, and peptide bond formation. These residues are highly conserved among Gram-negative bacteria and absent in mammalian cells, making MurE an attractive antibacterial target. The direct interactions observed between *S. crispus* bioactive compounds, and these key catalytic residues suggest a plausible inhibitory mechanism through competitive occupation of the MurE active site, potentially disrupting ATP utilization and peptide ligation. Similar inhibitory patterns have been reported for flavonoids such as apigenin and quercetin, which exert antibacterial effects through enzyme inhibition and interference with bacterial metabolic pathways (Saqallah et al., 2022; Shamsudin et al., 2022).

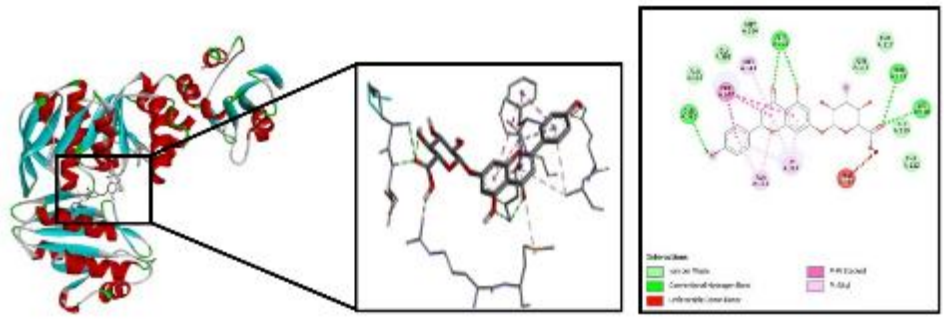

Figure 1. Interaction between the *apigenin 7-O-beta-D-glucuronide_MurE complex* and the amino acid residues

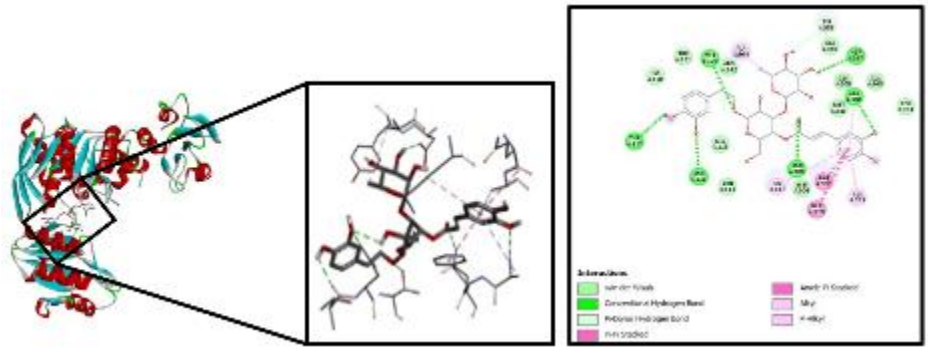

Figure 2. Interaction between the *acteoside_MurE complex* and the amino acid residues

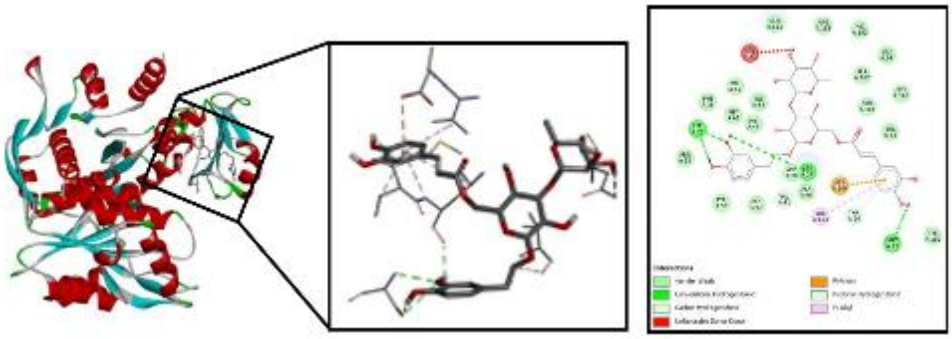

Figure 3. Interaction between the *isoacteoside_MurE* complex and amino acid residues

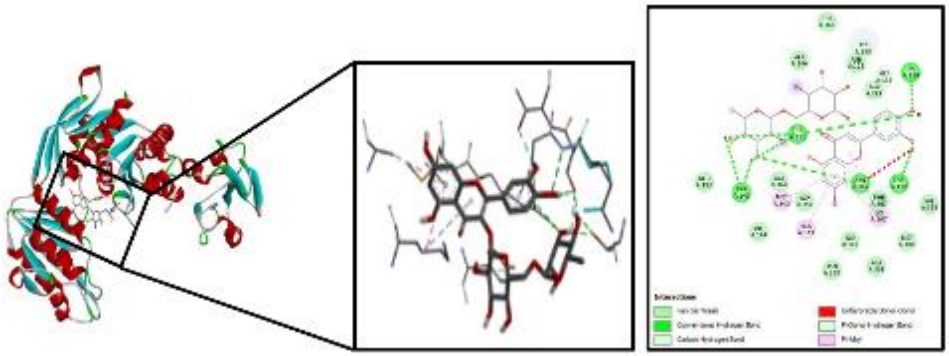

Figure 4. Interaction between the *quercetin 3-rutinoside_MurE* complex and the amino acid residues

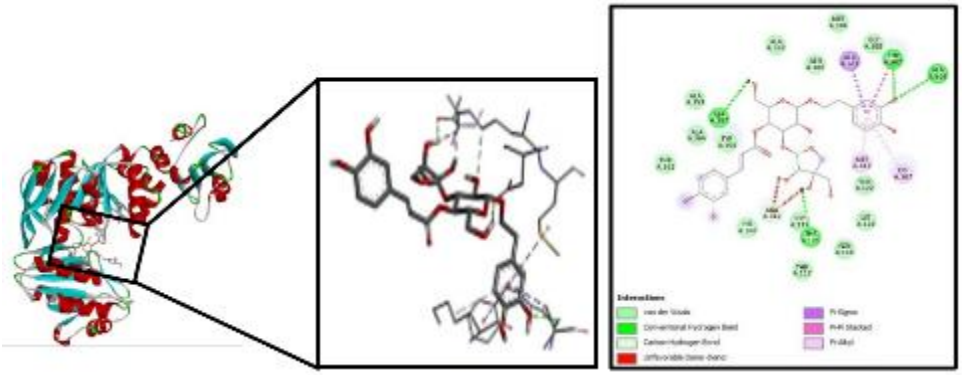

Figure 5. Interaction between the *calceolarioside_MurE* complex and the amino acid residues

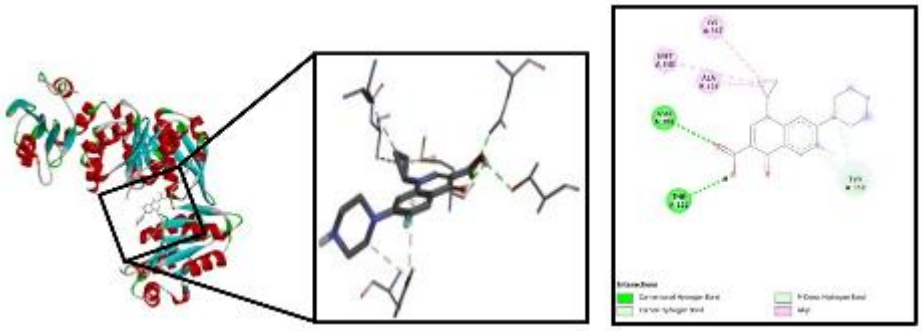

Figure 6. Interaction between the *ciprofloxacin_MurE* complex and the amino acid residues

Following the molecular docking analysis, pharmacokinetic evaluation was conducted to assess the drug-likeness of the tested compounds (Table 2). The pharmacokinetic profiles revealed notable differences between *ciprofloxacin* and the five *S. crispus* bioactive compounds. Ciprofloxacin exhibited the lowest molecular weight (331.34 g/mol) and the smallest topological polar surface area (TPSA: 74.57 Å²), supporting its high gastrointestinal absorption, optimal bioavailability, and high solubility (Moradpour et al., 2023). It also complied with all major drug-likeness rules (Lipinski, Ghose, Veber, Egan, and Muegge) and achieved the highest bioavailability score (0.55), indicating an ideal oral drug profile. Conversely, all *S. crispus* compounds had high molecular weights (>446 g/mol) and large TPSA values (>187 Å² to 289.43 Å²), limiting membrane permeability and gastrointestinal absorption. Consequently, these compounds violated two or more oral drug-likeness criteria and showed low bioavailability scores (0.11–0.17). The low consensus logP values (–1.51 to 0.29) reflected strong hydrophilicity, favoring solubility but restricting membrane diffusion.

Table 2. Results of pharmacokinetic analysis of test compounds

Parameter	Apigenin 7-O-beta-D-Glucuronide	Acteoside	Isoacteoside	Quercetin 3-rutinoside	Calceolarioside	Ciprofloxacin
Molecular Weight (g/mol)	446.36	624.59	624.59	610.52	610.56	331.34
TPSA (Å²)	187.12	245.29	245.29	289.43	245.29	74.57
LogP (Consensus)	0.29	-0.60	-0.49	-1.51	-0.84	1.25
Solubility Class (ESOL)	soluble	soluble	soluble	soluble	soluble	very soluble
GI Absorption	Low	Low	Low	Low	Low	High
Lipinski's Violation	2	3	3	3	3	0
Ghose's Violation	0	4	4	4	4	0
Veber Violation	1	2	2	1	2	0
Egan's Violation	1	1	1	1	1	0
Muegge's Violation	3	4	4	4	4	0
Bioavailability Score	0.11	0.17	0.17	0.17	0.17	0.55
PAINS Alert	0	1 alert (catechol_A)	1 alert (catechol_A)	1 alert (catechol_A)	1 alert (catechol_A)	0
Brenk Alert	0	3 alerts	2 alerts	1 alert	2 alerts	0
Leadlikeness	did not pass	did not pass	did not pass	did not pass	did not pass	passed

Several *S. crispus* compounds also triggered PAINS and Brenk alerts, including *acteoside, isoacteoside*, and *calceolarioside*, suggesting the presence of structural motifs that may cause assay interference or chemical instability (Capuzzi et al., 2017). Although these characteristics indicate potential limitations for direct oral administration, they do not preclude the possibility that these compounds may act as potential *MurE* inhibitors. Instead, formulation optimization strategies, such as nanoparticle encapsulation, prodrug desain, or chemical modification may enhance their pharmacokinetic behavior and biological performance (Ogbuagu et al., 2022; Saqallah et al., 2022).

To complement the pharmacokinetic analysis, toxicity predictions were performed to estimate the safety profiles of the tested compounds (Table 3). The results indicated that all *S. crispus* bioactive compounds exhibited lower predicted acute toxicity than ciprofloxacin. Each of the five compounds showed a predicted LD_{50} value of 5000 mg/kg body weight, corresponding to toxicity class 5 under the Globally Harmonized System (GHS), which suggests a low risk of acute toxicity based on computational models. In comparison, ciprofloxacin displayed a predicted LD_{50} value of 2000 mg/kg (class 4). The toxicity prediction models yielded confidence levels above 70% for all compounds, indicating acceptable reliability of the predictions; however, experimental validation is required to confirm these findings.

Overall, the integrated in silico analysis combining molecular docking, pharmacokinetic profiling, and toxicity prediction suggests that *S. crispus* bioactive compounds particularly *apigenin 7-O-beta-D-glucuronide* and *acteoside* may act as potential *MurE* inhibitors in *E. coli*. *MurE* plays a critical role in the ATP-dependent ligation of *D*-glutamate to UDP-*N*-acetylmuramoyl-*L*-alanine, a key step in the formation of the peptide stem that ultimately incorporates meso-diaminopimelic acid (m-DAP) during bacterial peptidoglycan biosynthesis. Disruption of this pathway can compromise cell wall integrity and bacterial viability.

Table 3. Analysis of predicted toxicity of test compounds

	Apigenin 7-O-beta-D-Glucuronide	Acteoside	Isoacteoside	Quercetin 3-rutinoside	Calceolarioside	Ciprofloxacin
Predicted LD_{50}	5000	5000	5000	5000	5000	2000
Predicted Toxicity	5	5	5	5	5	4
Average Similarity	74.11%	100%	100%	100%	99.1%	100%
Prediction Accuracy	69.26%	100%	100%	100%	72.9%	100%

The docking results demonstrated that these compounds interact strongly with conserved catalytic and substrate-binding residues within the *MurE* active site, including ARG342, LYS367, ASP357, and TYR358, which are known to be essential for ATP utilization and peptide bond formation in the m-DAP–dependent peptidoglycan synthesis pathway. The observed high binding affinities, together with favorable predicted toxicity profiles, suggest that these compounds may competitively occupy the *MurE* catalytic pocket and interfere with the ligation process required for proper cell wall assembly. Although their predicted oral bioavailability is limited, these findings highlight the potential of *S. crispus* bioactive compounds as lead molecules for further optimization and development of natural product–based antibacterial agents targeting the *m-DAP–MurE* axis in *E. coli*.

CONCLUSION

This study conceptually supports the potential of *S. crispus* bioactive compounds (*apigenin 7-O-beta-D-glucuronide, acteoside, isoacteoside, quercetin 3-rutinoside*, and *calceolarioside*) as potential antibacterial agents against *E. coli* through inhibition of the MurE enzyme, a crucial catalyst in bacterial cell wall biosynthesis. The molecular docking results revealed that these compounds formed stable interactions with the active residues of MurE, suggesting their ability to interfere with its catalytic function. Toxicological analysis indicated that all compounds belong to toxicity class 5 (predicted LD_{50} = 5000 mg/kg), reflecting lower predicted acute toxicity compared to ciprofloxacin (class 4). However, pharmacokinetic evaluation showed limitations related to high molecular weight, large polar surface area, and low gastrointestinal absorption, which may restrict oral bioavailability. Importantly, this study contributes to the development of herbal-based antibacterial candidates by providing an integrated in silico framework that links bioactive compound selection, MurE-targeted mechanistic analysis, and preliminary safety evaluation to support early-stage screening of natural products. Overall, these findings provide a conceptual basis for the development of *S. crispus*-derived antibacterial agents as natural product leads, while further in vitro and in vivo validation, as well as formulation optimization (e.g., nanoparticle or prodrug strategies), are recommended to enhance their pharmacological effectiveness and clinical applicability.

ACKNOWLEDGEMENT

The author would like to thank the LPPM of Universitas Muhammadiyah Jember for the funding provided for the implementation of this research with contract number 469/II.3.AU/LPPM/Riset/2024 dated December 9, 2024.

REFERENCES

Adibi, S., Nordan, H., Ningsih, S. N., Kurnia, M., Evando, E., & Rohiat, S. (2017). Aktivitas antioksidan dan antibakteri ekstrak daun *Strobilanthes crispus* Bl (keji beling) terhadap *Staphylococcus aureus* dan *Escherichia coli*. *Alotrop: Jurnal Pendidikan dan Ilmu Kimia*, 1(2), 148–154). https://doi.org/10.33369/atp.v1i2.3547

Adriana, L., Dewi, C., & Nasir, N. H. (2023). Uji aktivitas antibakteri ekstrak etanol daun keji beling (*Strobilanthes crispa* Bl) terhadap pertumbuhan bakteri *Staphylococcus epidermidis* dan *Pseudomonas aeruginosa*. *Jurnal Pharmacia Mandala Waluya*, *2*(3), 162–174). https://doi.org/10.54883/jpmw.v2i3.82

Afrida, I. R., Fatchiyah, F., Widodo, N., Amin, M., & Djati, M. S. (2021). Shogaol, bisdemethoxycurcumin, and curcuminoid: Potential zingiber compounds against covid-19. *Biointerface Research in Applied Chemistry*, *11*(5), 12869–12876. https://doi.org/10.33263/BRIAC115.1286912876

Ban, W. K., Fong, I. L., Khong, H. Y., & Phung, J. H. Y. (2022). Wound healing, antimicrobial and antioxidant properties of *Clinacanthus nutans* (Burm.f.) Lindau and *Strobilanthes crispus* (L.) Blume extracts. *Molecules*, *27*(5), 1722–1740. https://doi.org/10.3390/molecules27051722

Baraya, Y. S. aibu, Wee, C. L., Mustapha, Z., Wong, K. K., & Yaacob, N. S. (2022). *Strobilanthes crispus* elicits anti-tumor immunogenicity in in vitro and in vivo metastatic breast carcinoma. *PLoS ONE*, *17*(8), e0271203. https://doi.org/10.1371/journal.pone.0271203

Bataya, Y. S., Yankuzo, H. M., & Wong, K. K. (2021). *Strobilanthes crispus* bioactive subfraction inhibits tumor progression and improves hematological and morphological parameters in mouse mammary carcinoma model. *Science Direct Elsevier*, *267*(1), 113522–113530. https://doi.org/https://doi.org/10.1016/j.jep.2020.113522

Brookes-Howell, L., Thomas-Jones, E., Bates, J., Bekkers, M. J., Brugman, C., Coulman, E., Francis, N., Hashmi, K., Hood, K., Kirby, N., Llor, C., Little, P., Moore, M., Moragas, A., Rumsby, K., Verheij, T., & Butler, C. (2019). Challenges in managing urinary tract infection and the potential of a point-ofcare test guided care in primary care: An international qualitative study. *BJGP Open*, *3*(2), 1–12. https://doi.org/10.3399/bjgpopen18X101630

Bullock, J., Luccioni, A., Hoffman Pham, K., Sin Nga Lam, C., & Luengo-Oroz, M. (2020). Mapping the landscape of artificial intelligence applications against COVID-19. *Journal of Artificial Intelligence Research*, *69*(2020), 807–845. https://doi.org/10.1613/jair.1.12162

Capuzzi, S. J., Muratov, E. N., & Tropsho, A. (2017). Phantom PAINS: Probems with the utility of alerts for pan-assay interference compounds. *Journal of Chemical Information and Modeling*, *57*(3), 417–427. https://doi.org/10.1021/acs.jcim.6b00640

Du, Y., Sui, X., Bai, Y., Shi, Z., Liu, B., Zheng, Z., Zhang, Z., Zhao, Y., Wang, J., Zhang, Q., Zhu, Y., Liu, Q., Wang, M., Sun, H., & Shao, C. (2024). Dietary influences on urinary tract infections: unraveling the gut microbiota connection. *Food & Function*, *15*(19), 10099–10109. https://doi.org/10.1039/d4fo03271c

Pramesti, D. A., Harlita, T. D., & Aina, G. Q. (2024). Efektivitas antibakteri kombinasi ekstrak daun binahong (*Anredera cordifolia* (Ten.) Steenis) dan keji beling (*Strobilanthes crispus* Blume) terhadap *Escherichia* coli pada ulkus diabetikum. *JI-KES (Jurnal Ilmu Kesehatan)*, *8*(1), 67–75. https://doi.org/10.33006/jikes.v8i1.790

Filimonov, D. A., Druzhilovskiy, D. S., Lagunin, A. A., Gloriozova, T. A., Rudik, A. V., Dmitriev, A. V., Pogodin, P. V., & Poroikov, V. V. (2018). Computer-aided prediction of biological activity spectra for chemical compounds: Opportunities and limitations. *Biomedical Chemistry: Research and Methods*, *1*(1). https://doi.org/10.18097/BMCRM00004

Hervin, V., Roy, V., & Agrofoglio, L. A. (2023). Antibiotics and antibiotic resistance: Mur ligases as an antibacterial target. *Molecules*, *28*(24), 1–24. https://doi.org/10.3390/molecules28248076

Kumar, D., Sarkar, N., Roy, K. K., Bisht, D., Kumar, D., Mandal, B., Rajagopal, M., & Dey, Y. Na. (2023). The potential of Mur enzymes as targets for antimikrobial drug discovery. *Current Drug Targets*, *24*(8), 627–647. https://doi.org/10.2174/1389450124666230608150759

Mawaddani, N., Sutiyanti, E., Widyananda, M. H., Kharisma, V. D., Turista, D. D. R., Tamam, M. B., Jakhmola, V., Syamsurizal, Fajri, B. R., Ghifari, M. R., Albari, M. T., Ghifari, M. A., Lubis, A. P., Novaliendry, D., Putri, D. H., Fitri, F., Sari, D. P., Nugraha, A. P., Ansori, A. N. M., & Zainul, R. (2022). In silico study of entry inhibitor from *Moringa oleifera* bioactive compounds against SARS-CoV-2 infection. *Pharmacognosy Journal*, *14*(5), 565–574. https://doi.org/10.5530/pj.2022.14.137

Moradpour, J., Shajarizadeh, A., Id, J. C., Chit, A., & Id, P. G. (2023). The impact of national income and vaccine hesitancy on country-level COVID-19 vaccine uptake. *PLoS ONE*, *18*(11), 1–16. https://doi.org/10.1371/journal.pone.0293184

Moreira da Silva, R. C. R., de Oliveira Martins Júnior, P., Gonçalves, L. F., de Paulo Martins, V., de Melo, A. B. F., Pitondo-Silva, A., & de Campos, T. A. (2017). Ciprofloxacin resistance in uropathogenic *Escherichia coli* isolates causing community-acquired urinary infections in Brasília, Brazil. *Journal of Global Antimicrobial Resistance*, *9*(June), 61–67. https://doi.org/10.1016/j.jgar.2017.01.009

Ng, M. G., Ng, C. H., Ng, K. Y., Chye, S. M., Ling, A. P. K., & Koh, R. Y. (2021). Review anticancer properties of *Strobilanthes crispus*: A review. *Processes*, *9*(8), 1370–1388. https://doi.org/10.3390/pr9081370

Ogbuagu, O. O., Mbata, A. O., Balogun, O. D., Oladapo, O., Ojo, O. O., & Muonde, M. (2022). Novel phytochemicals in tranditional medicine: Isolation and pharmalogical profiling of bioactive compounds. *International Journal of Medical and All Body Health Research*, *03*(01), 63–71. https://doi.org/10.1080/07391102.2021.1989040

Paramita, S. S., Afrida, I. R., & Usman, A. (2024). Potensi anti-inflamasi galangin dan beta pinene senyawa *Alpinia purpurata* K.Schum terhadap *Candida albicans*. *BIO-CONS: Jurnal Biologi Dan Konservasi*, *6*(2), 395–401. https://doi.org/10.31537/biocons.v6i2.1883

Rambaher, M. H., Zdovc, I., Glavač, N. K., Gobec, S., & Frlan, R. (2023). Mur ligase F as a new target for the flavonoids quercitrin, myricetin, and (–)-epicatechin. *Journal of Computer-Aided Molecular Design*, *37*(12), 721–733. https://doi.org/10.1007/s10822-023-00535-z

Rohde, M. (2019). The Gram-positive bacterial cell wall chapter: The Gram-positive bacterial cell wall. *Microbiology Spectrum*, *7*(3), 1–45. https://doi.org/10.1128/microbiolspec.GPP3-0044-2018.10.1128/microbiolspec.gpp3-0044-2018

Sangshetti, J. N., Josi, S. S., Patil, R. H., Moloney, M. G., & Shinde, D. B. (2017). Mur ligase inhibitors as antibacterial: A comprehensive review. *Current Drug Targets*, *23*(21), 3164–3196. https://doi.org/10.2174/1381612823666170214115048

Saqallah, F. G., Hamed, W. M., Talib, W. H., Dianita, R., & Wahab, H. A. (2022). Antimicrobial activity and molecular docking screening of bioactive components of *Antirrhinum majus* (snapdragon) aerial parts. *Heliyon*, *8*(8), e10391. https://doi.org/10.1016/j.heliyon.2022.e10391

Shamsudin, N. F., Ahmed, Q. U., Mahmood, S., Shah, S. A. A., Khatib, A., Mukhtar, S., Alsharif, M. A., Parveen, H., & Zakaria, Z. A. (2022). Antibacterial effects of flavonoids and their structure-activity relationship study: A comparative interpretation. *Molecules*, *27*(4), 1149–1192. https://doi.org/10.3390/molecules27041149

Sher, E. K., Džidić-Krivić, A., Sesar, A., Farhat, E. K., Čeliković, A., Bećа-Zećo, M., Pinjic, E., & Sher, F. (2024). Current state and novel outlook on prevention and treatment of rising antibiotic resistance in urinary tract infections. *Pharmacology and Therapeutics*, *261*(7), 108688–108705. https://doi.org/10.1016/j.pharmthera.2024.108688

Sinha, S., Yadav, M., Verma, R. K., Afaq, N., & Srivastava, D. (2025). Prevalence of urinary tract infection and the molecular characterization with special reference to fim h gene uropathogenic *E.coli* isolated from urine samples at a tertiery hospital. *Journal of Neonatal Surgery*, *14*(18s), 676–688.

Soiza, R. L., Donaldson, A. I. C., & Myint, P. K. (2018). Vaccine against arteriosclerosis: an update. *Therapeutic Advances in Vaccines*, *9*(6), 259–261. https://doi.org/10.1177/2042098618769568

Suboh, S. F., Mahat, A. M., Yusof, M. H., & Razak, W. R. W. A. (2022). Antimicrobial activity of *Strobilanthes crispus* leaves aqueous extract and green biosynthesis iron oxide nanoparticles against selected human pathogens. *Asia-Pacific Journal of Molecular Biology and Biotechnology*,

30(4), 20–32. https://doi.org/10.35118/apjmbb.2022.030.4.03

Tan, S.-A., Lim, S., Law, C., Yue, C., Poh, T., Saad, W., Ismail, S., Yusoff, K., & Loke, C. (2019). Antioxidative and photocytotoxic effects of standardized *Clinacanthus nutans* and *Strobilanthes crispus* extracts toward HepG2 liver cells. *Pharmacognosy Magazine*, *15*(65), 613–620. https://doi.org/10.4103/pm.pm_84_19

Widhiastuti, R., Afrida, I. R., & Usman, A. (2024). Potensi antibakteri senyawa 1-acetoxyeugenol acetate dan galanal B senyawa *Alpinia purpurata* K.Schum terhadap *Salmonella typhi*. *BIO-CONS: Jurnal Biologi Dan Konservasi*, *6*(2), 425–431. https://doi.org/10.31537/biocons.v6i2.2040