

IGSCPS SPECIAL EDITION

RESEARCH ARTICLE

# Predicting toxicity and conducting molecular docking analysis of compounds from unripe kayu banana fruit (*Musa paradisiaca* L. var. Kayu) against 3mzd and 2q85 proteins in *Escherichia coli* for antibacterial activity

Arista Wahyu Ningsih<sup>1,4</sup> , Achmad Syahrani<sup>2</sup> , Abdi Wira Septama<sup>3</sup> , Sukardiman<sup>2</sup> 

<sup>1</sup> Doctoral Programme of Pharmaceutical Sciences, Faculty of Pharmacy, Universitas Airlangga, Surabaya, East Java, Indonesia

<sup>2</sup> Faculty of Pharmacy, Universitas Airlangga, Surabaya, East Java, Indonesia

<sup>3</sup> Research Centre of Pharmaceutical Ingredients and Traditional Medicine, BRIN, PUSPITEK Area Serpong, Tangerang Selatan, Banten, Indonesia

<sup>4</sup> Faculty of Health Sciences, Pharmacy Study Programme, Anwar Medika University, Sidoarjo, East Java, Indonesia

## Keywords

2Q85  
3MZD  
Antibacterial  
Kayu banana  
Musa paradisiaca

## Correspondence

Sukardiman  
Department of Pharmaceutical Sciences  
Faculty of Pharmacy  
Universitas Airlangga  
Surabaya  
Indonesia  
sukardiman@ff.unair.ac.id

## Abstract

**Background:** Proteins 3MZD and 2Q85 are proteins that play a role in the biosynthesis of bacterial cell walls because they participate in the formation stage of peptidoglycan, an important component of the bacterial cell wall. The purpose of this study was to characterise the bioactive compounds as antibacterial agents using a docking molecule approach and conduct preliminary screening for the discovery of alternative drugs, as well as to determine the safety of those alternative drugs with toxicity predictions.

**Method:** The potency of bioactive compounds was analysed using PLANT, the Online Prottox II web server, and related programmes used to assess the bioactivity of these compounds. The comparison drug ligand used is chloramphenicol. **Results:** The binding energy ( $\Delta G$ ) of ligand 9 was lower than natural ligands, reference ligands, control ligands, and other ligands. Furthermore, the predicted toxicity of this compound is in the category of toxicity of class 5. **Conclusion:** Based on molecular docking studies, unripe banana extract has been predicted to have potential as a drug against bacteria.

## Introduction

Microorganisms play a significant role in the spread of infectious diseases in developing countries. Gastrointestinal infections are particularly common, as highlighted by Nurhikmah (2021). Among the prevalent bacteria responsible for such infections is *Escherichia coli*, which is known to induce gastrointestinal diseases like diarrhoea. Statistics from the Indonesian Health Profile (Kemenkes RI, 2022) reveal that service coverage for diarrhoea treatment spans all age groups, with a rate of 33.6%, and specifically for toddlers, the coverage is reported at 23.8%.

There is an urgent need to broaden the search for new antibiotics to effectively combat bacterial infections. Antibiotic resistance is now widespread and is primarily caused by the irresponsible and irrational use of antibiotics. Since patterns of antibiotic use are closely linked to the emergence of antibiotic-resistant strains, this is a concerning trend, especially for the healthcare sector (Pormohammad *et al.*, 2019). Unripe kayu bananas are currently a popular remedy for digestive tract infections among the locals in Senduro village, Lumajang, Indonesia. Using kayu bananas as an alternative medical treatment resource is extremely

important because of their widespread availability and low cost (Ningsih *et al.*, 2021).

Bioinformatics research, or in silico methods, is a field that is constantly evolving in the field of antibacterial research. This test utilises virtual screening techniques or computational methods for tethering molecules to receptor targets. In silico tests are used to find new compounds, predict and increase efficiency in the activation of parent compounds, and are also used to simulate the discovery and development of drugs, one of which is the development of antibiotics (Zarenezhad *et al.*, 2022).

The in silico method is widely used in initial research endeavours to discover anticancer, antiviral, and bioactive compounds that can be used as drug candidates (Wardaniati *et al.*, 2018). Silico testing generally uses the molecular docking method. Various methods can be employed to assess the antibacterial activity of a compound, one of which is molecular docking (Sultana *et al.*, 2024). 3MZD (D-alanyl-D-alanine carboxypeptidase dacA) and 2Q85 (UDP-N-acetylenolpyruvoylglucosamine reductase) are proteins in the bacterial cell wall synthesis. Disruption of these proteins hampers the optimal formation of the cell wall, leading to bacterial lysis (Majumdar *et al.*, 2021; Hadi & Nastiti, 2023).

In this research, researchers want to conduct preliminary screening for the discovery of alternative drugs that have the potential to inhibit bacteria, as well as to determine the safety of those alternative drugs with toxicity predictions. Therefore, further research has been carried out using a molecular docking approach to evaluate the tethering of ligand and protein molecules with bond energy parameters. This bonding energy shows a strong and stable affinity between ligands and proteins. This work aims to demonstrate the most negligible binding energy between ligands and receptors to support future studies on the antidiarrheal activity of the unripe fruit of Kayu bananas.

## Methods

The materials used in this study are 2D and 3D structures of compounds present in unripe fruit of Kayu bananas (*Musa Paradisiaca* L. Var Kayu) used as ligands, control ligand structures, which include ref ligands (reference ligand), and natural ligands. Ref ligand is present on the protein used. This ligand will later be used to compare to the main ligand. Ref ligands are obtained from proteins that have been prepared. The ref ligand used is named Cxv and (5z)-3-(4-chlorophenyl)-4-hydroxy-5-(1

naphthylmethylene)furan-2(5h)-one. Ref ligand will be used to validate molecular docking methods. Natural ligands are ligands that already exist in the body. This natural ligand is named D-alanine-D-alanyl.

Chloramphenicol was selected as the reference drug ligand due to its bacteriostatic mechanism of action, with a focus on proteins 3MZD and 2Q85 found in *Escherichia coli* bacteria (Yuliet *et al.*, 2022). The proteins 3MZD and 2Q85 form peptidoglycan bonds in the synthesis stage of bacterial cell walls. Inhibition at 3MZD and 2Q85 will result in suboptimal bacterial cell wall formation, allowing bacteria to lyse. Chloramphenicol is an antibiotic that has an enzyme-inhibiting mechanism that plays a role in the formation of peptide bonds in the process of bacterial cell wall synthesis (Maryati *et al.*, 2021; Majumdar *et al.*, 2021; Hadi & Nastiti, 2023)

### Search for 2D and 3D structures of chloramphenicol

The 2D and 3D structures of chloramphenicol were obtained via the Pubchem website (<https://pubchem.ncbi.nlm.nih.gov/compound/Chloramphenicol>). The Marvin chemaxon software (<https://chemaxon.com/marvin>) validated the compounds in the image (Tegar & Purnomo, 2013).

### Search for 2D and 3D structures of ligands.

The 2D and 3D structures of the ligands were obtained through the results of LC-MS unripe fruit of the Kayu banana (*Musa paradisiaca* L. Var Kayu). The Marvin chemaxon software (<https://chemaxon.com/marvin>) was used to validate the compounds contained in the image (Tegar & Purnomo, 2013).

### Search for proteins or target receptors

The proteins used were 3MZD and 2Q85. Proteins were obtained from the protein data bank (GDP) website: <http://www.pdb.org> on *Escherichia Coli* (Tegar & Purnomo, 2013).

### Toxicity prediction

At this stage, the 2D and 3D images of the compounds obtained were converted into the form of SMILES for toxicity prediction using the online Prottox II website ([https://tox-new.charite.de/prottox\\_II/](https://tox-new.charite.de/prottox_II/)) (Azzam, 2023).

### Protein preparation

The YASARA program (<http://www.yasara.org/products.htm>) prepares the protein; the downloaded protein file is inserted into the PDB file. The docking protocol does not remove unnecessary system parts according to their

characteristics; it only requires one protein. YASARA was used to add hydrogen to the system. Only the target protein remains after removing the original ligand (Tegar & Purnomo, 2013).

### Ref ligand preparation

After homologous modelling using the YASARA program is complete, the YASARA object file is loaded from protein.yob. Then, the existing protein is deleted and saved as a ligand.mol2 reference (Tegar & Purnomo, 2013).

### Ligand preparation

Unripe kayu banana fruit contains an LCMS molecule that can be used as a ligand in docking simulations. Using the Marvin of ChemAxon, the reference ligand structure was produced previously by cleaning it in a 2D configuration, protonating it at pH 7.4, and then generating a 3D ensemble conformation. Results were saved as mol2 files for molecular tethering simulations with PLANTS. It is saved as a ligand.mol2 (Tegar & Purnomo, 2013).

### Simulated docking plants

To perform the PLANTS docking program, a folder is first created containing the files ligand.mol2, ref\_ligand.mol2, protein.mol2, plants.exe, and cmd.exe. Next, the first docking process is initiated by opening cmd.exe. The result of the Calculated binding site definition, including "bindingsite\_center" and "bindingsite\_radius", is then copied. Once the software

has been executed, nine docked ligands with various protein conformations are observed. The command "cd results/" followed by "more bestranking.csv" is typed to evaluate the docking and interpret the outcome data. The ten conformations with the lowest scores are to be chosen (Tegar & Purnomo, 2013).

### Visualisation of protein and ligand interactions

The best binding energy results/scores obtained from molecular docking results are displayed in a table. Following this, the binding site and molecular bond type are visualised in 3D using PyMol software (Istyastono et al., 2020).

### Data analysis

The smaller score value indicates that the ligand is the most stable. Then, the docking score results were processed using SPSS with one-way ANOVA analysis ( $p < 0.5$ ). This method is carried out to determine the difference in the meaning of the docking score between comparison ligands and plant compound ligands (Mapesa et al., 2021).

## Results

Results of molecular tethering compounds in unripe fruit of Kayu bananas with penicillin-binding protein and *Escherichia coli* MurB protein were analysed using PLANTS software. Data on molecular tethering energy values are presented in Table I.

**Table I: Average score of comparator ligands and compound ligands of unripe Kayu banana fruit**

No.	Compound name	Average docking score $\pm$ SD	
		3MZD	2Q85
1.	Propham / propane-2-yl N-phenyl carbamate	-61.44 $\pm$ 0.29	-66.41 $\pm$ 0.76
2.	Phenylacetaldehyde / 2-phenylacetaldehyde	-51.28 $\pm$ 0.07	-56.05 $\pm$ 0.11
3.	Ethyl 3-aminobenzoate / ethyl 3-aminobenzoate	-63.98 $\pm$ 0.47	-64.27 $\pm$ 1.07
4.	N,N-diethyl-4-methoxybenzamide / N,N-diethyl-4-methoxybenzamide	-62.16 $\pm$ 0.68	-63.01 $\pm$ 1.07
5.	Venlafaxine n-oxide / 2-(1-hydroxy cyclohexyl)-2-(4-methoxyphenyl)-N,N-dimethylethanamine oxide	-51.27 $\pm$ 0.08	-68.61 $\pm$ 1.27
6.	Santonin / (3S,3aS,5aS,9bS)-3,5a,9-trimethyl-3a,4,5,9b-tetrahydro-3H-benzo[g][1]benzofuran-2,8-dione	-65.38 $\pm$ 0.87	-64.94 $\pm$ 0.81
7.	(1 $\alpha$ ,5 $\xi$ ,9 $\xi$ ,10 $\xi$ ,14 $\alpha$ )-20-Ethyl-1,16-dimethoxyaconitane-8,14-diol/ (4S,5S,6S,8S,10R,13R)-11-ethyl-6,16-dimethoxy-11-azahexacyclo[7.7.2.12,5.01,10.03,8.013,17]nonadecane-4,8-diol	-68.47 $\pm$ 1.23	-67.32 $\pm$ 1.59
8.	Betaxolol / 1-[4-[2-(cyclopropyl methoxy)ethyl]phenoxy]-3-(propane-2-ylamino)propane-2-ol	-77.81 $\pm$ 2.16	-81.67 $\pm$ 1.17
9.	2-HoTrE / (9Z,12Z,15Z)-2-hydroxyoctadeca-9,12,15-trienoic acid	-87.68 $\pm$ 2.57	-86.76 $\pm$ 2.11
10.	Reference Ligan (C <sub>xv</sub> and 5z)-3-(4-chlorophenyl)-4-hydroxy-5-(1-naphthylmethylene)furan-2(5h)-one	-81.43 $\pm$ 3.84	-77.36 $\pm$ 1.97
11.	Natural Ligan (D-Alanin D-Alanyl)	-64.48 $\pm$ 1.63	-59.67 $\pm$ 1.27
12.	Control Ligan (Chloramphenicol)	-74.56 $\pm$ 1.16	-76.22 $\pm$ 2.67

ANOVA test with a  $p$ -value significance value of  $< 0.05$  compared to all groups.  
SD: Standard Deviation

The attempt to align a small ligand into a target cell that is a large protein molecule is known as docking. Bond energy values, known as Rerank Score (RS), are generated in silico assays. The binding energy is required to form a bond between the ligand and the receptor. The greater the activity may be predicted, the lower the binding energy and the more permanent the interaction with the receptor (Kesuma *et al.*, 2018).

Before conducting molecular docking, it is imperative to validate the method. The molecular docking methodology must be confirmed to ensure the

receptor is appropriate. This validation process involves re-docking ligands that are already present within the proteins. The redocking scores obtained for the ligands in the penicillin-binding protein were -87.68, and in the *E. coli* MurB protein were -77.36. The docking analysis was replicated ten times.

The toxic dose is typically expressed as LD50, measured in mg/kg body weight. LD50 represents the mean lethal dose, which is the dose that induces mortality in 50% of subjects following exposure to the substance (Table II).

**Table II: Toxicity categories of unripe Kayu banana fruit**

No.	Compound name	Toxicity categories					
		I	II	III	IV	V	VI
1	Propam / propane-2-yl <i>N</i> -phenyl carbamate				√		
2	Phenylacetaldehyde / 2-phenylacetaldehyde				√		
3	Ethyl 3-aminobenzoate / ethyl 3-aminobenzoate				√		
4	<i>N,N</i> -diethyl-4-methoxybenzamide / <i>N,N</i> -diethyl-4-methoxybenzamide			√			
5	Venlafaxine <i>n</i> -oxide / 2-(1-hydroxycyclohexyl)-2-(4-methoxyphenyl)- <i>N,N</i> -dimethylethanamine oxide		√				
6	Santonin / (3 <i>S</i> ,3 <i>aS</i> ,5 <i>aS</i> ,9 <i>bS</i> )-3,5 <i>a</i> ,9-trimethyl-3 <i>a</i> ,4,5,9 <i>b</i> -tetrahydro-3 <i>H</i> -benzo[ <i>g</i> ][1]benzofuran-2,8-dione				√		
7	(1 <i>α</i> ,5 <i>xi</i> ,9 <i>xi</i> ,10 <i>xi</i> ,14 <i>α</i> )-20-Ethyl-1,16-dimethoxyaconitane-8,14-diol / (4 <i>S</i> ,5 <i>S</i> ,6 <i>S</i> ,8 <i>S</i> ,10 <i>R</i> ,13 <i>R</i> )-11-ethyl-6,16-dimethoxy-11-azahexacyclo[7.7.2.12,5.01,10.03,8.013,17]nonadecane-4,8-diol				√		
8	Betaxolol / 1-[4-[2-(cyclopropylmethoxy)ethyl]phenoxy]-3-(propan-2-ylamino)propan-2-ol				√		
9	2-HoTrE / (9 <i>Z</i> ,12 <i>Z</i> ,15 <i>Z</i> )-2-hydroxyoctadeca-9,12,15-trienoic acid						√

Toxicity classes are assigned using the international labelling classification system (Hodge and Sterner, 2005). The LD50 is measured in milligrams per kilogram and is divided into the following categories: Class I is fatal by ingestion (LD50 ≤ 5), Class II is fatal by ingestion (LD50 ≤ 50), Class III is toxic by ingestion (50 < LD50 ≤ 300), Class IV is hazardous by ingestion (300 < LD50 ≤ 2000), and Class VI is nontoxic by ingestion (LD50 over 5000).

## Discussion

D-Alanyl-D-Alanine decarboxylase (DACA) is the enzyme that transports D-Alanyl-D-Alanine. This enzyme's Protein Data Bank (PDB) file has Acyl Cloxacillin bound as an inhibitor or natural ligand with PDB ID 3MZD. (Purwanggana *et al.*, 2018). Beta-lactam antibiotics target penicillin to prevent the production of protein walls and peptidoglycan membrane structures. This is so because the D-alanyl-D-alanine carboxypeptidase family of binding proteins includes penicillin. This penicillin-binding site is found in the family of enzymes known as DD-peptidases or acyltransferases. The transglycosylase protein known as DD-peptidase polymerises glycan chains using N-acetylglucosamine and N-acetylmuramic acid monomers. The process entails removing D-alanine from muramyl pentapeptide, forming a cross between D-alanine and proteoglycan with transpeptidase, and ending the side-side peptide chain with endopeptidase.

The DD-peptidases fall into two categories: high and low. High molecular masses are found in membrane transglycosylases and transpeptidases. Low molecular weight endopeptidases and carboxypeptidases serve no primary use. Therefore, these proteins are the main targets of antibacterial screening (Hadi & Nastiti, 2023).

Four different ligases, MurC, MurD, MurE, and MurF, each add amino acids to UDP-MurNAc, which results in the UDP-MurNAc pentapeptide that is then transferred to the plasma membrane. At that location, MraY catalyses the substitution of UDP by the carrier lipid undecaprenyl-pyrophosphate, producing lipid I. (Babajan *et al.*, 2009).

After N-acetylglucosamine attachment catalysed by MurG, Lipid II is transferred to the outer surface of the plasma membrane. Penicillin-binding protein (PBP) uses it to create the cell wall there. This synthetic enzyme barrier prevents peptidoglycan manufacturing,

which results in cell lysis. One enzyme that is critical for cell survival is MurB. MurB becomes an inhibitor for small molecules as no homolog in eukaryotic cells potentially has broad antibacterial activity (Babajan et al., 2009). The docking method is valid if the RMSD value is  $\leq 2 \text{ \AA}$ , which means that the docking parameters used are correct for further use for docking test compounds (Prasojo et al., 2010). The RMSD result from the ligands bound to the target protein is 1.789. Therefore, based on the validation results, the blocking parameter method is deemed valid once the appropriate parameters are validated (Zarenezhad et al., 2022).

Water and micromolecules are removed in penicillin-binding protein, and E.coli MurB protein then separates the protein macromolecules. This process is carried out to obtain maximum results during molecular tethering. The molecular docking stage comes after the preparation stage if it is finished (Majumdar et al., 2021).

Based on Table I ligands, the best is ligand 9 2-HoTrE / (9Z,12Z,15Z)-2-hydroxyoctadeca-9,12,15-trienoic acid because ligand 9 has an average score value of -87.68 on 3MZD protein and an average score of -86.76 on protein 2Q85 where the score is the lowest of the eight other ligands. This can happen because ligand 9 has the lowest score value, so ligand 9 is more stable at the time of interaction with the target protein compared to the other eight ligands (Chatrabhuji et al., 2010).

The research findings indicate that compounds found in unripe Kayu banana fruit are predicted to exhibit antibacterial activity through in silico analysis. Compounds in tethered Kayu bananas act as inhibitors and can bind to proteins. The docking score signifies the energy needed to establish a bond. A lower score indicates a lower energy requirement for bond formation, making it more efficient (Khalil, 2023). Furthermore, the compound 2-HoTrE / (9Z,12Z,15Z)-2-hydroxyoctadeca-9,12,15-trienoic acid was analysed for toxicity using Protox II (Laeq & Dubey, 2022).

The docking score indicates the energy required to form a bond between the ligand and the receptor. The smaller the bond energy is, the more stable the bond will be. The more stable the ligand bond with the receptor, the greater the activity (Purwangana et al., 2018). From the average docking score, 2-HoTrE / (9Z,12Z,15Z)-2-hydroxyoctadeca-9,12,15-trienoic acid compounds have the smallest value. This compound has a high affinity in binding to receptors on *Escherichia coli* bacteria. The bond of 2-HoTrE / (9Z,12Z,15Z)-2-hydroxyoctadeca-9,12,15-trienoic acid compounds with 3MZD and 2Q85 proteins causes the bacterial cell wall formation process to be disrupted because the compounds needed in the formation of bacterial cell

walls are absent and replaced by 2-HoTrE / (9Z,12Z,15Z)-2-hydroxyoctadeca-9,12,15-trienoic acid compounds. Disruption of the cell wall formation process results in bacterial death or lysis.

Table II shows the toxicity level of 2-HoTrE / (9Z,12Z,15Z)-2-hydroxyoctadeca-9,12,15-trienoic acid compounds, indicating that their toxicity class is class 5. According to Hodge and Sterner (1949) in their journal "Tabulation of Toxicity Classes," according to the Globally Harmonized System (GHS), toxicity classes at 5 include low levels (Miyagawa, 2010).

The results of this study manifest as computational predictions regarding the antibacterial activity and toxicity classifications of compounds found in Kayu bananas. Further research, either in vitro or in vivo, must be developed to identify its computationally predicted activity.

## Conclusion

The molecular tethering results of compounds extracted from unripe Kayu banana fruit (*Musa paradisiaca* L. var. Kayu) obtained via LCMS-MS exhibit promising antibacterial potential. This is evidenced by the docking score values of the unripe fruit compounds, which surpass those of the comparison ligand. The most potent compounds identified are 2-HoTrE, also known as (9Z,12Z,15Z)-2-hydroxyoctadeca-9,12,15-trienoic acid. This compound demonstrates binding activity against both penicillin-binding protein and E. coli MurB protein.

## Acknowledgement

This research was carried out thanks to everyone's support. Thank you to Universitas Airlangga for its support, and to Anwar Medika University, lecturers, and students for their support in completing this research.

## Source of funding

The authors, Anwar Medika University, Airlangga University, and BRIN, support the cost of this research.

## References

Azzam, K. A. L. (2023). SwissADME and pkCSM Webservers Predictors: An integrated Online Platform for Accurate and Comprehensive Predictions for In Silico ADME/T Properties

of Artemisinin and its Derivatives. *Kompleksnoe Ispolzovanie Mineralnogo Syra = Complex Use of Mineral Resources.*, **325**(2), 14–21. <https://doi.org/10.31643/2023/6445.13v>

Babajan, B., Anuradha, C. M., Chaitanya, M., Gowsia, D., & Kumar, C. S. (2009). In silico structural characterization of Mycobacterium tuberculosis H37Rv UDP-N-acetylmuramate dehydrogenase. *International Journal of Integrative Biology*, **6**(1), 12–16.

Chatrabhuji, P. M., Nimavat, K. S., Vyas, K. B., & Undavia, N. K. (2010). Synthesis and antimicrobial activity of some 2-aryl-3-[(4-methyl cinnamoyl amino)-4-oxo-thiazolidines with synthesis and antimicrobial activity of some 2-(4-hydroxyphenyl)-3-[(4-methyl cinnamoyl amino)-4-oxo-thiazolidines. *Research Journal of Pharmaceutical, Biological, and Chemical Science*, **1**(3), 451–455.

Hadi, S., & Nastiti, K. (2023). Antibacterial S. aureus docking test from compounds contained from karamunting (rhodomirtus tomentosa (aiton) hassk.). *Jurnal Matematika Dan Ilmu Pengetahuan Alam LLDikti Wilayah 1 (JUMPA)*, **3**(1), 01–07. <https://doi.org/10.54076/jumpa.v3i1.273>

Hodge A, Sterner B. 2005. Toxicity classes. In: Canadian Center for Occupational Health and Safety. <http://www.ccohs.ca/oshanswers/chemicals/id50.htm>

Istyastono, E. P., Radifar, M., Yuniarti, N., Prasasty, V. D., & Mungkasi, S. (2020). PyPLIF HIPPOS: A molecular interaction fingerprinting tool for docking results of AutoDock Vina and PLANTS. *Journal of Chemical Information and Modeling*, **60**(8), 3697–3702. <https://doi.org/10.1021/acs.jcim.0c00305v>

Kemenkes RI. (2022). *Indonesia Health Profile 2021*. In Pusdatin.Kemenkes.Go.Id.

Kesuma, D., Siswandono, S., Purwanto, B. T., & Hardjono, S. (2018). In silico test of cytotoxic activity and toxicity of N-(Benzoyl)-N'-phenylthiourea derivative compounds as anticancer drug candidates. *Journal of Pharmaceutical Science and Clinical Research*, **3**(1), 1. <https://doi.org/10.20961/jpscr.v3i1.16266>

Khalil, M. (2023). Molecular docking simulation of coumestrol compound with hepatitis B virus capsid protein: in silico study of the potential of natural compounds. *Jurnal Jeumpa*, **10**(1), 138–148. <https://doi.org/10.33059/jj.v10i1.7606>

Laeq, S., & Dubey, V. (2022). Computational prediction of ADMET properties of ACAT inhibitors for synthesis and pharmacological screening. *International Journal of Health Sciences*, **6**(S7), 2377–2388. <https://doi.org/10.53730/ijhs.v6ns7.11866>

Majumdar, D., Philip, J. E., Das, S., Kundu, B. K., Saini, R. V., Chandan, G., Bankura, K., & Mishra, D. (2021). Experimental and theoretical corroboration of antimicrobial and anticancer activities of two pseudohalides induced structurally diverse Cd (II)-Salen complexes. *Journal of*

*Molecular Structure*, **1225**, 129189. <https://doi.org/10.1016/j.molstruc.2020.129189>

Mapesa, W. A., Waweru, M. P., Bukachi, F., & Wafula, K. D. (2021). Aqueous tuber extracts of Tylosema fassoglense (Kotschy ex Schweinf.) Torre and Hillc. (Fabaceae) possess significant in-vivo anti-diarrheal activity and ex-vivo spasmolytic effect possibly mediated by modulation of nitrous oxide system, voltage-gated calcium channels, and muscarinic receptors. *Frontiers in Pharmacology*, **12**, 636879. <https://doi.org/10.3389/fphar.2021.636879>

Maryati, T., Nugroho, T., Bachruddin, Z., & Pertiwinigrum, A. (2021). Antibacterial effects of Kepok Banana bunch (Musa paradisiaca L.) against Staphylococcus aureus. *IOP Conference Series: Earth and Environmental Science*, **637**(1). <https://doi.org/10.1088/1755-1315/637/1/012046>

Miyagawa, M. (2010). Globally harmonized system of classification and labeling of chemicals (GHS) and its implementation in Japan. In *Nippon eiseigaku zasshi. Japanese journal of hygiene*, **65**(1). <https://doi.org/10.1265/jjh.65.5>

Ningsih, A. W., Rochmanti, M., & Basori, A. (2021). Effectiveness of anti-diarrheal unripe wooden banana (Musa paradisiaca L.) in male Balb-C/mice induced with Escherichia coli. *Folia Medica Indonesiana*, **56**(3), 208. <https://doi.org/10.20473/fmi.v56i3.24558>

Pormohammad, A., Nasiri, M. J., & Azimi, T. (2019). Prevalence of antibiotic resistance in Escherichia coli strains simultaneously isolated from humans, animals, food, and the environment: A systematic review and meta-analysis. *Infection and Drug Resistance*, **12**, 1181–1197. <https://doi.org/10.2147/IDR.S201324>

Prasojo, S. L., Hartanto, F. A. D., Yuniarti, N., Ikawati, Z., & Istyastono, E. P. (2010). Docking of 1-Phenylsulfonamide-3-Trifluoromethyl-5-Parabromophenyl-Pyrazole to Cyclooxygenase-2 using plants. *Indonesian Journal of Chemistry*, **10**(3), 348–351. <https://doi.org/10.22146/ijc.21441>

Purwanggana, A., Mumpuni, E., & Mulatsari, E. (2018). In vitro and silico antibacterial activity Of 1 . 5-BIS ( 3 '-ethoxy-4 '-hydroxyphenyl ) -1-4-Pentadiene-3-One. *International Journal of Pharmacy and Pharmaceutical Science*. **10**(5), 3–9. <https://doi.org/10.22159/ijpps.2018v10i5.25143>

Sultana, S., Hossain, M. A., Islam, M. M., & Kawsar, S. M. A. (2024). Antifungal potential of mannopyranoside derivatives through computational and molecular docking studies against Candida albicans 11YL and 1A19 proteins. *Current Chemistry Letters*, **13**(1), 1–14. <https://doi.org/10.5267/j.ccl.2023.9.004>

Tegar, M., & Purnomo, H. (2013). Tea leaves extracted as anti-malaria based on molecular docking PLANTS. *Procedia Environmental Sciences*, **17**, 188–194. <https://doi.org/10.1016/j.proenv.2013.02.028>

Wardaniati, I., & Azhari Herli, M. (2018). Studi molecular docking senyawa golongan flavonol sebagai antibakteri. *JOPS (Journal Of Pharmacy and Science)*, **1**(2), 20–27. <https://doi.org/10.36341/jops.v1i2.489>

Yuliet, Khumaidi, A., Hikma, N., & Nurinayah. (2022). Antibacterial activity and bioautographic evaluation of extract and fraction from tamoenu (Hibiscus Surattensis L.) leaves. *International Journal of Applied Pharmaceutics*,

**14**(Special issue 5), 56–59. <https://doi.org/10.22159/ijap.2022.v14s5.07>

Zarenezhad, E., Sadeghian, S., Shekoohi, K., Emami, L., Ghasemian, A. M., & Zarenezhad, A. (2022). Synthesis, biological evaluation and in silico studies of oxime ether derivatives containing a quinoxaline moiety. *Russian Journal of Bioorganic Chemistry*, **49**(1), 101–113. <https://doi.org/10.1134/S1068162023010326>