HYDROGEN
JURNAL KEPENDIDIKAN KIMIA
https://e-journal.undikma.ac.id/index.php/hydrogen/index

October 2025. 13(5)
e-ISSN: 2656-3061
p-ISSN: 2338-6487
pp. 962-974

Molecular Docking of Anthraquinones from *Morinda citrifolia* Root as α-Glucosidase Inhibitors

Aldi Tobing[1], Masriani[1*], Ihsanul Arief[2]
[1] Chemistry Education Study Program, Faculty of Teacher Training and Education,Tanjungpura University, Pontianak, Indonesia
[2] Yarsi Academy of Pharmacy, Pontianak, Indonesia
[*] Corresponding Author e-mail: masriani@fkip.untan.ac.id

Article History
Received: 27-09-2025
Revised: 23-10-2025
Published: 19-11-2025

Keywords: Morinda citrifolia; anthraquinone derivatives; α-glucosidase; molecular docking; natural antidiabetic agents

Abstract
Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia and remains one of the major contributors to global morbidity and mortality. The development of safer and more effective antidiabetic agents from natural products has gained increasing attention due to the limitations of current synthetic drugs. Morinda citrifolia root has been reported to contain various anthraquinone derivatives with potential bioactivity. This study aimed to evaluate the inhibitory potential of 23 anthraquinone derivatives from Morinda citrifolia root against the α-glucosidase enzyme using an in silico molecular docking approach. Molecular docking was conducted using AutoDock Vina against α-glucosidase (PDB ID: 5ZCC) after protein preparation in UCSF Chimera. The docking targeted the catalytic site containing key residues (Arg411, Gln256, and Asp327) that interact with acarbose, and interaction patterns were analyzed using BIOVIA Discovery Studio Visualizer. The results demonstrated that several compounds exhibited stronger binding affinities than the standard inhibitor acarbose (-8.4 kcal/mol), while maintaining similar interaction patterns. In particular, compound 21 (-8.9 kcal/mol, H-bond with Gln256), compound 18 (-8.7 kcal/mol, H-bond with Arg411 and Gln256), and compound 15 (-8.3 kcal/mol, H-bond with Gln256 and Asp327) emerged as the most promising candidates. These findings suggest that anthraquinone derivatives from Morinda citrifolia root may serve as potential α-glucosidase inhibitors and warrant further pharmacokinetic and experimental validation.

How to Cite: Tobing, A., Masriani, M., & Arief, I. (2025). Molecular Docking of Anthraquinones from Morinda citrifolia Root as α-Glucosidase Inhibitors. Hydrogen: Jurnal Kependidikan Kimia, 13(5), 962–974. https://doi.org/10.33394/hjkk.v13i5.17725

https://doi.org/10.33394/hjkk.v13i5.17725

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia resulting from impaired insulin secretion or action, or both (Bakri et al., 2023; Wiyati et al., 2025). According to the International Diabetes Federation (IDF, 2021) report, the global prevalence of diabetes in 2021 exceeded 537 million people and is projected to rise to 643 million by 2030. This growing trend positions diabetes as one of the leading causes of global morbidity and mortality and imposes a substantial burden on healthcare systems and economy. The therapeutic strategy for managing type 2 diabetes is the inhibition of α-glucosidase, a key catalyst in the hydrolysis of complex carbohydrates to glucose, thereby influencing postprandial blood glucose levels (Liu et al., 2021). α-Glucosidase inhibitors, such as acarbose, miglitol, and voglibose, are effective in lowering postprandial blood glucose (BG) levels. However, their use is frequently associated with gastrointestinal side effects, including flatulence and diarrhea (Febriyanti et al., 2024), prompting the search for safer alternative inhibitors derived from natural products.

Medicinal plants are defined as plants with therapeutic properties and are generally classified into three main categories: traditional, modern, and potential (Rahman, 2023). In addition to

providing compounds with potential biological activity, medicinal plants offer advantages such as relatively low toxicity, wide availability, and cost-effective production (Humairo et al., 2024). They have long been recognized as an important source of bioactive compounds with antidiabetic properties. One promising species is *Morinda citrifolia* (*Noni*). Traditionally, *M. citrifolia* has been used to treat wounds, infections, menstrual cramps, digestive disorders, diabetes, hypertension, and as a natural laxative (Nerurkar et al., 2015). Such ethnomedicinal practices underscore the pharmacological potential of *M. citrifolia* and support ongoing scientific research aimed at identifying the specific bioactive compounds responsible for its therapeutic effects.

One of the classes of secondary metabolites present in the roots of *M. citrifolia* is anthraquinones. Anthraquinone derivatives are known to possess a broad spectrum of pharmacological activities, including laxative, anticancer, anti-inflammatory, anti-arthritic, antifungal, antibacterial, and antiviral properties. In addition, they have also been reported to exert antiplatelet and neuroprotective activities, as well as potential therapeutic applications in malaria and multiple sclerosis (Malik & Müller, 2016), along with insecticidal and antioxidant properties (Khan, 2019), anthraquinone compounds derived from *M. citrifolia* exhibit potential antiseptic and antibacterial activities (Abnaz & Levita, 2018). Previous studies have demonstrated that anthraquinones can inhibit α-glucosidase activity, thereby contributing to the reduction of postprandial blood glucose levels. Among these, alaternin, a specific anthraquinone derivative, has been reported to exhibit strong potential as an α-glucosidase inhibitor, with an IC_{50} value of 3.45 µM, while showing no cytotoxic effects on hepatocellular (HepG2) cells at concentrations up to 50 µM (Dirir et al., 2022). These findings highlight the promising role of anthraquinones from *M. citrifolia* roots as safe and effective natural candidates for α-glucosidase inhibition.

Nevertheless, limited studies have explored the binding mechanism of anthraquinones *from M. citrifolia* with α-glucosidase at the molecular level. *In silico* molecular docking can be employed to elucidate the molecular basis of these interactions by predicting binding affinities, identifying key active-site residues, and assessing the inhibitory potential of the compounds based on the strength and suitability of the interactions (Vidal-Limon et al., 2022). Thus, molecular docking serves as an essential approach to complement experimental data and support the development of anthraquinone-based natural antidiabetic agents. Accordingly, this study investigates the inhibitory potential of anthraquinone derivatives from *M. citrifolia* roots against α-glucosidase and compares their binding activity with the standard inhibitor, acarbose. This work provides new insights into the molecular interaction profiles of *M. citrifolia*-derived anthraquinones, which have not been previously characterized in detail, thereby advancing understanding of their inhibitory mechanisms and highlighting their potential as promising lead compounds for α-glucosidase inhibition.

METHOD

Instruments and Material

This study used hardware in the form of an Asus laptop running Microsoft Windows 11. The laptop is equipped with an Intel(R) Core(TM) i3-1005G1 CPU @ 1.20 GHz, with a frequency of 1190 MHz, 2 cores, 4 logical processors, and 4.00 GB of RAM. The laptop is also connected to an AC/DC adapter and the internet, and is used to support the molecular docking process. The software used in this study includes ChemDraw Professional version 16.0.1.4 (77), Microsoft Excel 2021, Chimera 1.16, PyRx-Python Prescription 0.8, and Discovery Studio Visualizer 2021 v21.1.0.20298. Additionally, the study utilized the Protein Data Bank (RCSB PDB).

The materials used in this study consisted of 23 anthraquinone derivatives identified in the roots of *Morinda citrifolia*, namely 1,2-dihydroxy-3-methoxy-anthraquinone **(1)**, 1,3,6-trihydroxy-2-methylanthraquinone **(2)**, 1,3-dihydroxy-2-methoxy-anthraquinone **(3)**, 1,3-dimethoxy-2-methoxymethylanthraquinone **(4)**, 1-hydroxy-2-methyl-9,10-anthraquinone **(5)**, 1-hydroxy-2-methylol-anthraquinone **(6)**, 1-methoxy-3-hydroxyanthraquinone **(7)**, 1-methyl-3-hydroxy-anthraquinone **(8)**, 2-ethoxy-1-hydroxyanthraquinone **(9)**, 2-formyl-1-hydroxyanthraquinone **(10)**, 2-formylanthraquinone **(11)**, 2-methoxy-1,3,6-trihydroxyanthraquinone **(12)**, 2-methoxy-3-methyl-anthraquinone **(13)**, 2-methyl-4-hydroxy-5,7-dimethoxyanthraquinone **(14)**, 3-hydroxy-2-hydroxymethyl-anthraquinone **(15)**, alizarin **(16)**, alizarin-1-methyl ether **(17)**, aloe-emodin **(18)**, damnacanthal **(19)**, emodin **(20)**, fridamycin E **(21)**, rubiadin **(22)**, and tectoquinone **(23)** (Hou et al., 2025).

The three-dimensional structure of the α-glucosidase receptor was retrieved from the Protein Data Bank (PDB) (https://www.rcsb.org/) with PDB ID: 5ZCC, while acarbose was used as the reference ligand and downloaded in (.pdb) file format.

Ligand Preparation

A total of 23 anthraquinone derivatives were selected as test ligands in this study. The chemical structures of these compounds were drawn using ChemDraw Professional and subsequently subjected to geometry optimization (energy minimization) to obtain stable conformations. The optimized structures were then saved in Structure Data File (SDF) format. Next, the ligands were prepared by adding missing hydrogen atoms using Chimera 1.16, and atomic charges were assigned. The prepared ligands were finally saved in PDBQT format for use in the molecular docking process. This process ensures that the three-dimensional conformation of the compounds is properly optimized to achieve spatial compatibility with the stereochemistry of the receptor's active site, thereby enabling efficient molecular interactions (Buannata et al., 2024).

Macromolecule Preparation

The receptor used in this study was the α-glucosidase protein with PDB ID 5ZCC, obtained from the Protein Data Bank (https://www.rcsb.org/). The receptor structure was prepared by removing water molecules, the native ligand, and any non-standard residues that could interfere with interactions with the test ligands. Hydrogen atoms were then added, and charges were assigned to stabilize the receptor structure. The prepared receptor file was saved in PDB format for subsequent molecular docking (Pattar et al., 2020; Yohana et al., 2024).

Native Ligand Preparation

The native ligand bound to the receptor was also isolated and prepared to serve as a reference control in the docking studies. Preparation involved removing solvents, non-standard residues, and protein components from the macromolecule, leaving only the ligand. Hydrogen atoms were added, and charges were assigned to ensure an optimized ligand structure. The prepared native ligand was saved in PDB format for further analysis (Yohana et al., 2024).

Molecular Docking

Molecular docking was performed using PyRx 0.8 with AutoDock Vina as the calculation engine to predict binding free energies between ligands and the receptor (Sulong et al., 2022). The receptor's active site was defined by setting a grid box, and docking parameters were established based on validation results. Docking quality was evaluated using root mean square deviation (RMSD), with a success criterion of RMSD ≤ 2 Å (Rasyid et al., 2024; Zheng et al., 2022). Docking simulations were carried out for each ligand, and the predicted binding affinity values were reported in kcal/mol. Ligands exhibiting the lowest binding energies were selected for further analysis, and the resulting receptor-ligand complexes were saved in PDB format.

Analysis and Visualization

Docking results were visualized using BIOVIA Discovery Studio Visualizer 2021. Interactions between ligands and amino acid residues in the receptor's active site were analyzed, including hydrogen bonds, electrostatic interactions, and hydrophobic contacts, to determine the contribution of each residue to ligand binding. The interaction data were exported as tables and visualized in both two-dimensional (2D) and three-dimensional (3D) formats for detailed interpretation (Kumar et al., 2020; Rasyid et al., 2023).

RESULTS AND DISCUSSION

With the progression of computational technologies, virtual screening of compounds has emerged as a crucial strategy in the discovery of antidiabetic drugs. This approach has demonstrated efficacy in rapidly and cost-effectively identifying potential inhibitors that target key enzymes involved in glucose metabolism, such as α-glucosidase (Prahayati & Rusdi, 2023). Virtual screening is particularly advantageous for developing drug candidates aimed at alleviating hyperglycemia in diabetes mellitus. In this study, the crystal structure of α-glucosidase (PDB ID: 5ZCC) was selected as the target protein, with acarbose serving as a reference to guide the virtual screening process (Bhaumik et al., 2024). A total of 23 anthraquinone derivatives (Hou et al., 2025), were assessed using molecular docking to predict their binding affinities with the active site of α-glucosidase. The docking results (Table 1), which include docking scores, types of interactions (hydrogen bonds and hydrophobic interactions), and binding affinities in kcal/mol, revealed varying levels of inhibitory potential. Hydrogen bonding and hydrophobic interactions are essential for stabilizing ligand-protein complexes.

Table 1. Docking Results of Anthraquinone Derivatives from *M.citrifolia* Roots and Standard Compound with α-Glucosidase

Compound Code	kcal/mol	Amino Acid Residues Involved In Hydrogen Bonds	Hydrophobic Amino Acid Residues
0 (Acarbose)	-7.7	Arg411, Gln256, Asp327	His326, Arg197, Asp199, Phe163, Ala200, His203, Phe225, Thr409, Ile143, Phe144, Met385, Gly410, Ser145, Tyr388, Asn387, Gly384, Trp288, Gln328, Phe282, Asn258
1	-8.3	Asn258, Gln256, Asp199	Phe225, Phe282, His203, Phe163, His326, Arg197, Tyr63, Ala200, Asp327, Arg411, Phe144, Ile143
2	-7.9	Arg411	Phe144, Tyr63, His326, Arg197, Phe163, Asp199, Gln256, Ala200, Asp327, His203, Ile143, Asn258, Phe282, Phe225
3	-7.7	-	Ile143, Phe144, Asp327, Ala200, Arg411, Phe163, His103, Asp199, Gln256, Phe282, Asn258
4	-7.3	Arg411	Phe144, Asp382, Gly384, Met385, Thr409, Phe225, Phe282, Ile143, Ala200, Asn258, His203, Gln256, Phe163, Asp327
5	-8.5	Asp60	Tyr63, Gln167, Ala200, His103, Asp199, Phe163, Gln256, Asp327, Asn258, Phe282, Ile143, Phe144, Arg411

Compound Code	kcal/mol	Amino Acid Residues Involved In Hydrogen Bonds	Hydrophobic Amino Acid Residues
6	-8.4	Arg411, Gln167	Phe282, Asn258, Gln256, Asp327, Ala200, Phe163, Tyr63, Asp199, Asp60, His103, Phe144, Ile143
7	-7.8	-	Ala200, Phe163, Phe144, Asp327, Arg411, Ile143, Phe225, Asn258, Phe282, Gln256, Asp199, His103
8	-8.5	-	Asp327, Phe144, Arg411, Asp60, Gln167, His103, Asp199, Phe163, Tyr63, Ala200, Gln256, His203, Asn258, Phe282, Ile143
9	-8.1	Arg411, Asp327, Asn258	Phe144, Asp60, Tyr63, Gln167, Asp199, Phe163, His103, Ala200, Gln256, Phe282
10	-8.4	Asp60, Gln167, His103	Ile143, Phe144, Arg411, Tyr63, Asp199, Ala200, Phe163, Gln256, Asp327, Asn258, Phe282
11	-8.3	Arg411, His326	Phe144, Arg197, Tyr63, Asp327, Asp199, Gln256, Ala200, Phe163, His203, Ile143, Asn258, Phe225
12	-7.9	Asp60	Phe282, Phe225, Asn258, Gln256, Phe163, Asp199, His103, Ala200, Gln167, Tyr63, Arg411, Asp327, Phe144, Ile143
13	-7.9	-	Phe144, Arg411, Ile143, Asp199, Phe163, Ala200, Asp327, Gln256, Asn258, Phe282
14	-7.8	Asn258, Arg411	Asp327, Phe144, Ala200, His103, Asp199, Gln256, Phe163, His203, Phe282, Gln328, Trp288
15	-8.3	Gln256, Asp327, Arg197	Phe225, Asn258, His203, Ala200, Asp199, Tyr63, His327, Phe163, Arg411, Phe144, Ile143
16	-8.0	-	Phe225, Phe282, His203, Asn258, Gln256, Phe163, Asp199, His103, Asp60, Arg411, Ala200, Asp327, Phe144, Ile143
17	-7.8	Asn258, Asp199, Gln256	Phe144, Ile143, Arg411, Phe163, Asp60, Asp327, Arg197, Ala200, His203, Phe282, Phe225
18	-8.7	His203, Asn258, Gln256, Asp199, Arg411	Ile143, Phe225, Phe282, Arg197, Ala200, Tyr63, Arg415, His326, Asp60, Phe163, Asp327, Phe144
19	-7.8	Asn258	Phe282, Asp327, Gln256, Phe163, Ala200, His103, Asp199, Arg411, Ile143, Phe144
20	-8.7	Asn258, His203, Asp199, Asp60	Phe225, Ile143, Phe282, Phe163, Gln256, Arg197, Tyr63, Ala200, Arg415, Arg411, Asp327, Phe144
21	-8.9	Gln328, His326, Gln256,	Ile143, Arg411, Phe163, Phe144, Asp199, Arg197, Tyr63, Asp60, Asp327, Phe282, Met285, Tyr288, Thr409
22	-7.9	Arg411, Asn258	Phe282, His203, Ala200, Phe163, Asp199, Gln256, Phe144, Asp327
23	-8.1	-	Phe282, Asn258, Asp327, Gln256, Ala200, Phe163, Asp199, His203, Tyr63, Gln167, Asp60, Arg411, Phe144, Ile143

Docking analyses have demonstrated that anthraquinone derivatives from *M. citrifolia* exhibit a spectrum of binding affinities toward α-glucosidase, with docking scores ranging from -8.9

to -7.3 kcal/mol. This variation signifies the differential potential of these compounds to occupy and stabilize the enzyme's active site. A more negative binding affinity value indicates a more stable complex between the receptor protein and the compound, reflecting stronger binding interactions (Nur et al., 2023). In comparison, the reference ligand acarbose exhibited a binding affinity of -7.7 kcal/mol, suggesting that several of the tested compounds may possess a stronger binding potential than the control ligand.

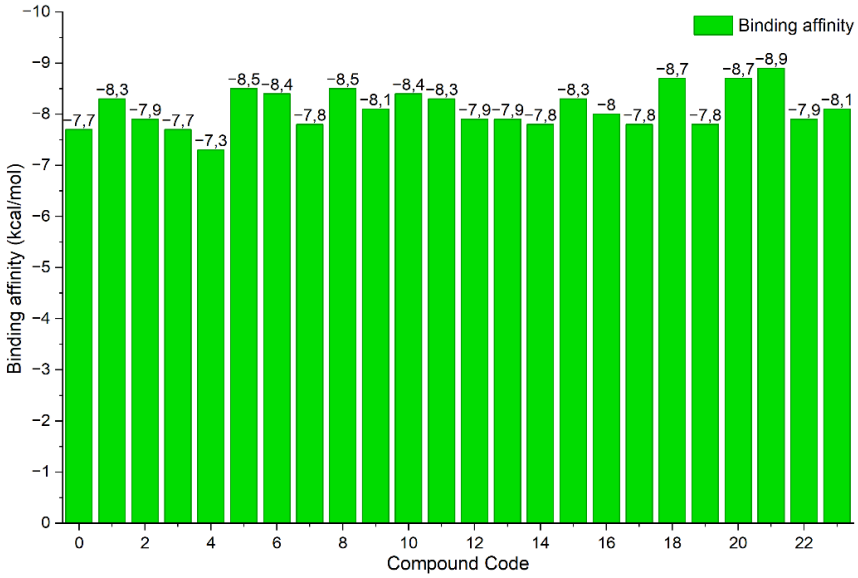
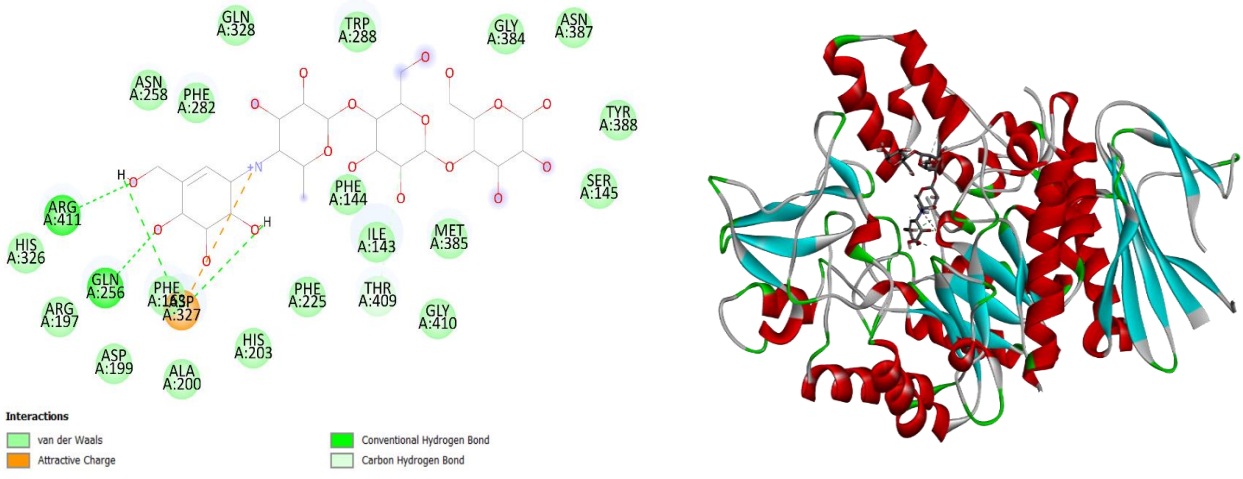
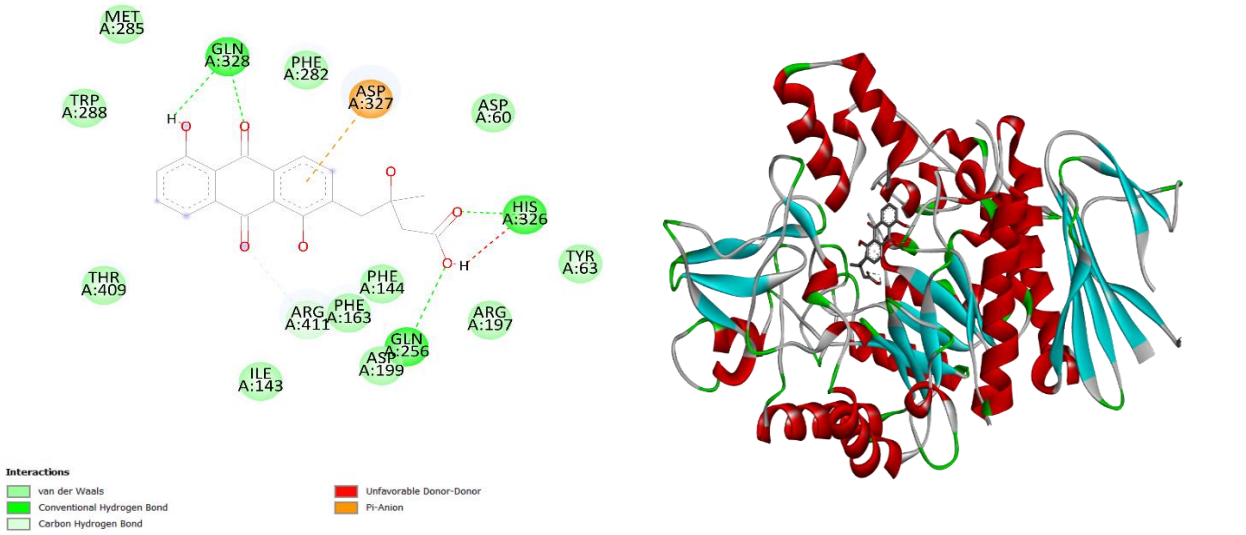


Figure 1. Comparison of binding affinity values of the tested compounds against α-glucosidase.

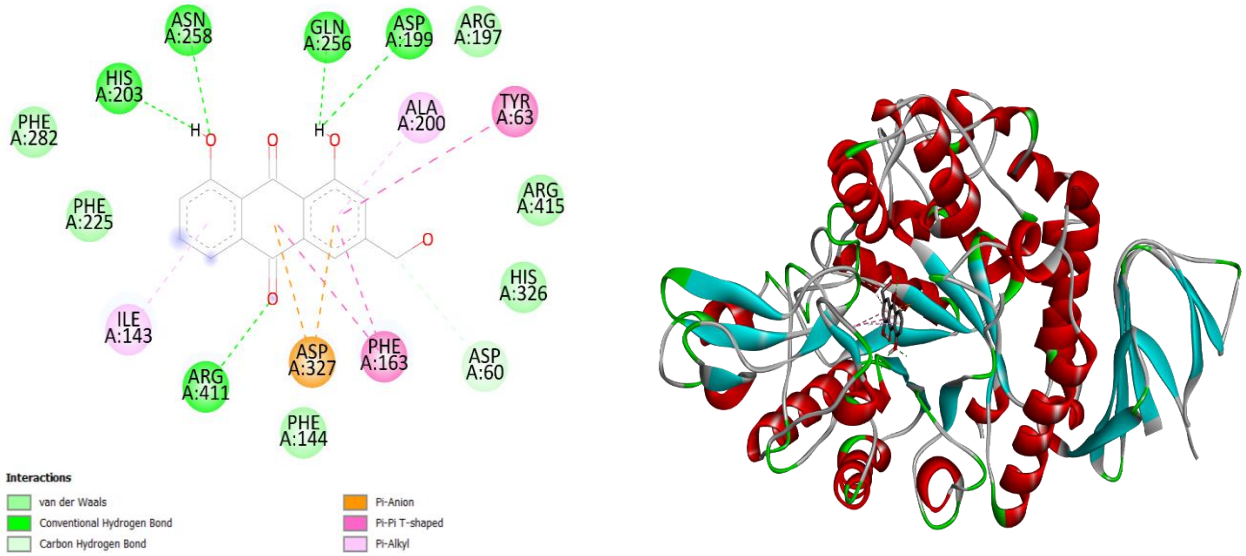
Beyond binding affinity, the nature of ligand-protein interactions is another critical aspect to consider. In this context, hydrogen bonding and electrostatic interactions with key active-site residues play vital roles in determining the inhibitory potential of the tested compounds against the α-glucosidase enzyme. Generally, a higher number of hydrogen bonds is associated with increased binding stability and lower (more negative) binding affinity values, indicating stronger interactions within the catalytic pocket. However, some compounds with high binding affinity formed only one hydrogen bond, suggesting that other noncovalent forces particularly hydrophobic and π-π stacking interactions also contribute significantly to the stabilization of the ligand-enzyme complex (Abuelizz et al., 2019; Bumulo et al., 2025). The combination of these various interactions collectively contributes to the effectiveness of ligand binding at the active site, ultimately influencing the binding affinity and inhibitory activity.



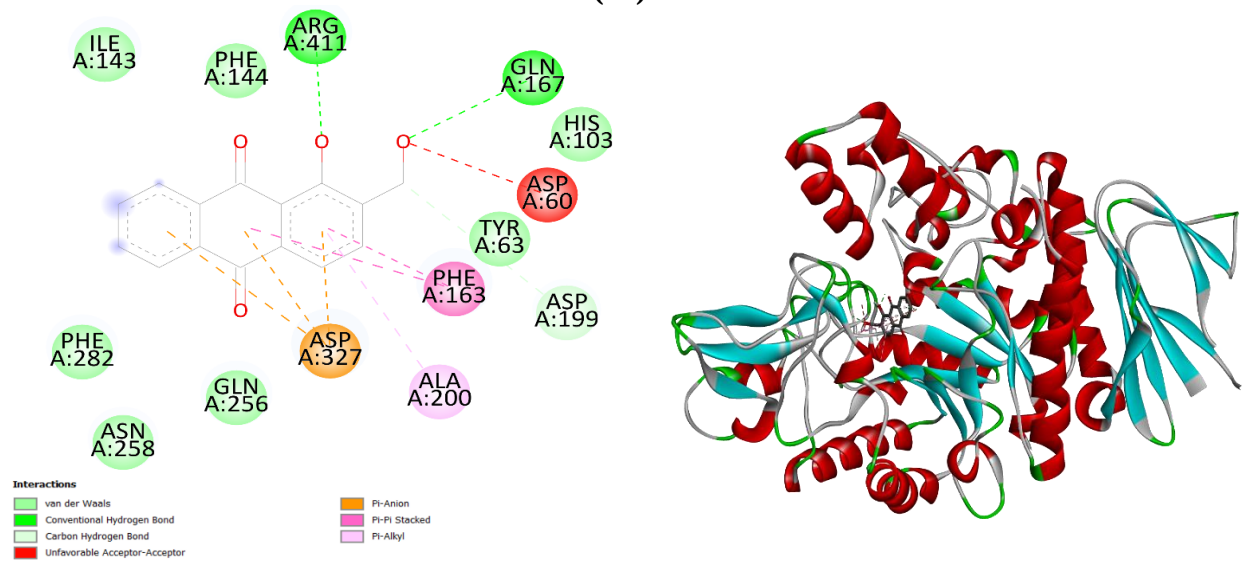
(0)


MET A:285
GLN A:328
PHE A:282
ASP A:327
TRP A:288
ASP A:60
HIS A:326
TYR A:63
THR A:409
PHE A:144
ARG A:411
PHE A:163
ARG A:197
GLN A:256
ASP A:199
ILE A:143
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Unfavorable Donor-Donor
Pi-Anion

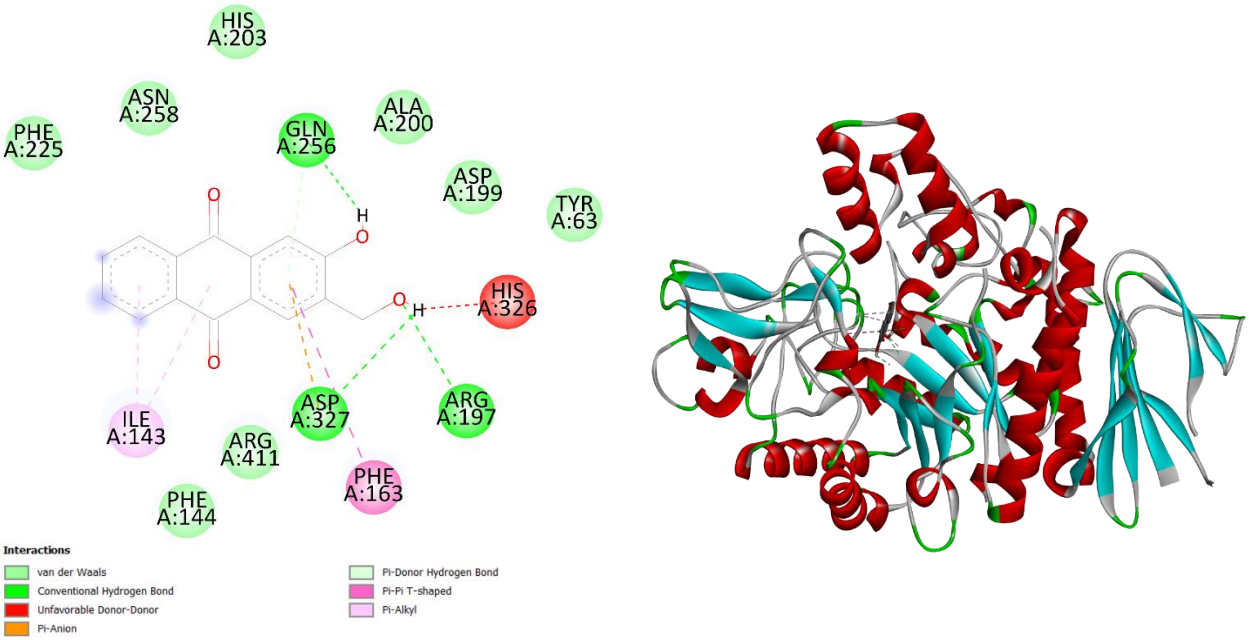
(21)


ASN A:258
GLN A:256
ASP A:199
ARG A:197
HIS A:203
PHE A:282
ALA A:200
TYR A:63
PHE A:225
ARG A:415
HIS A:326
ILE A:143
ASP A:327
PHE A:163
ASP A:60
ARG A:411
PHE A:144
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Anion
Pi-Pi T-shaped
Pi-Alkyl

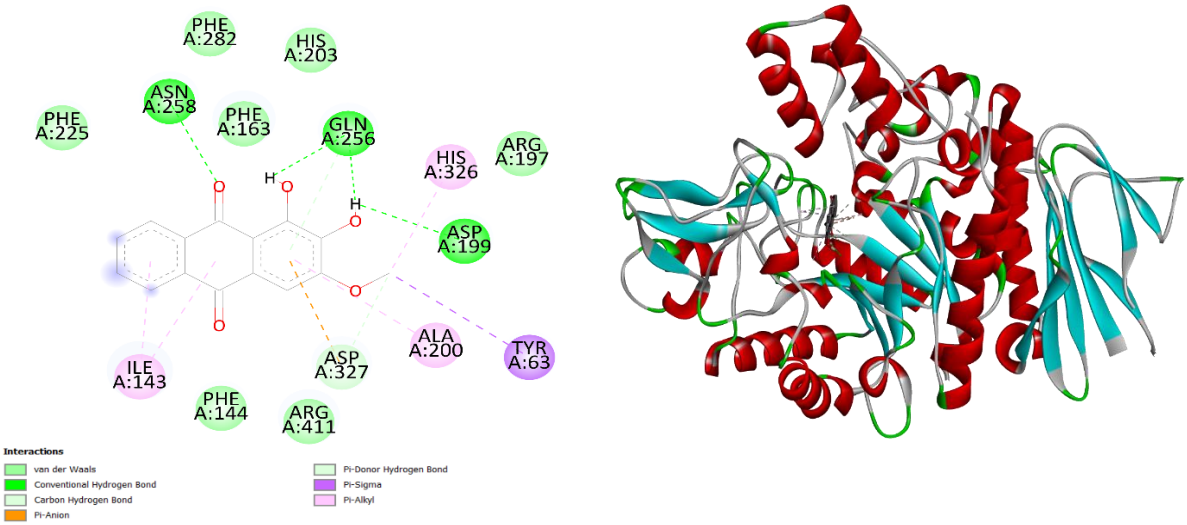
(18)


ILE A:143
ARG A:411
PHE A:144
GLN A:167
HIS A:103
ASP A:60
TYR A:63
PHE A:163
ASP A:199
PHE A:282
ASP A:327
GLN A:256
ALA A:200
ASN A:258
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Unfavorable Acceptor-Acceptor
Pi-Anion
Pi-Pi Stacked
Pi-Alkyl

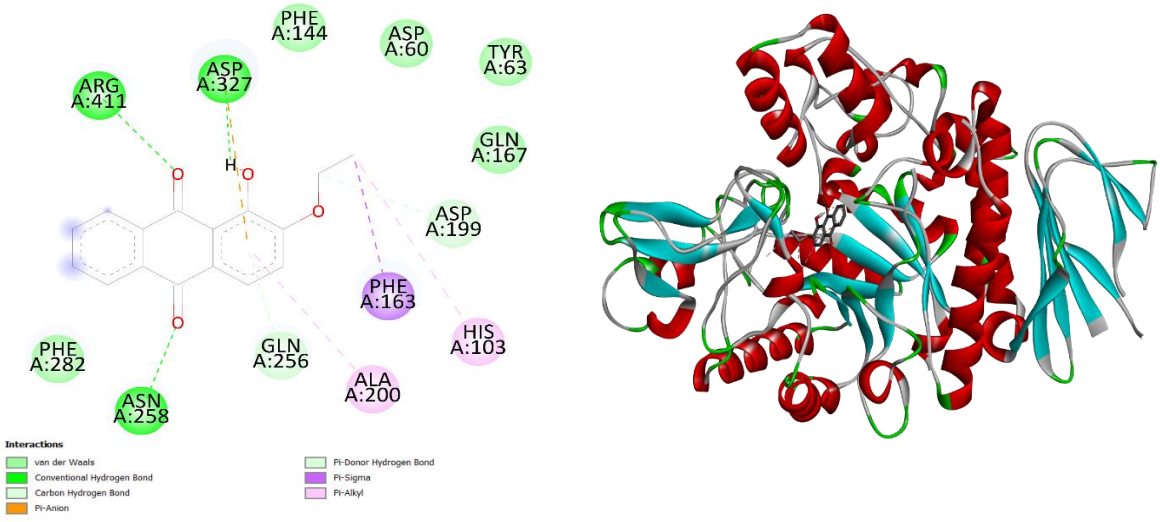
(6)


HIS A:203
ASN A:258
ALA A:200
PHE A:225
GLN A:256
ASP A:199
TYR A:63
HIS A:326
ARG A:197
ASP A:327
ILE A:143
ARG A:411
PHE A:163
PHE A:144
Interactions
van der Waals
Conventional Hydrogen Bond
Unfavorable Donor-Donor
Pi-Anion
Pi-Donor Hydrogen Bond
Pi-Pi T-shaped
Pi-Alkyl

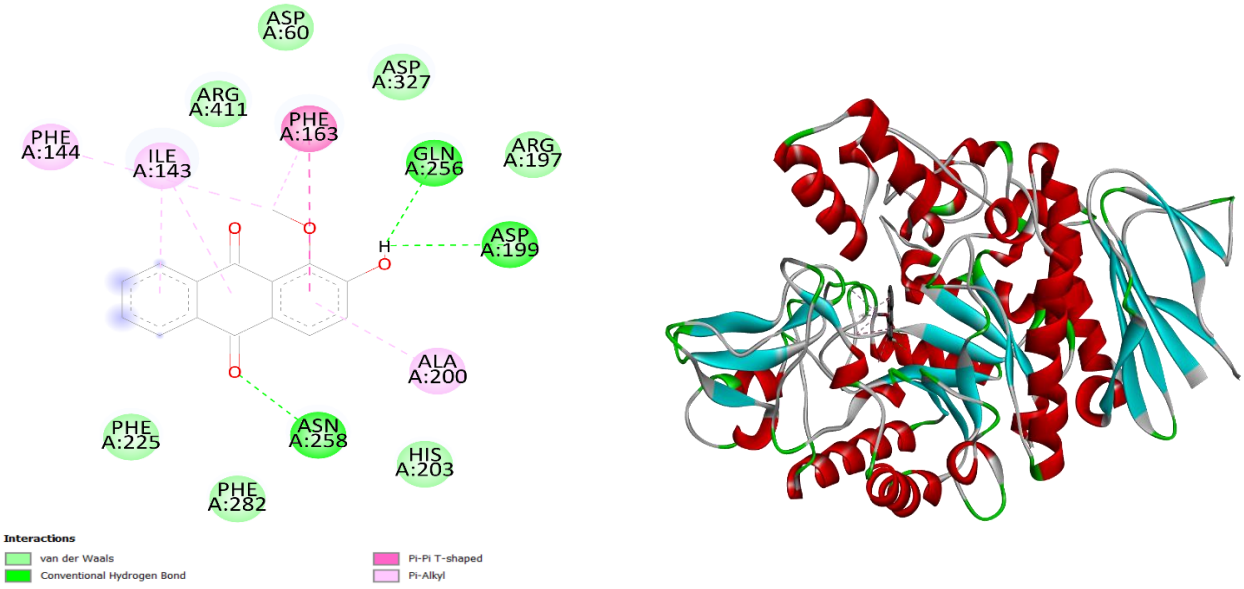
(15)


PHE A:282
HIS A:203
ASN A:258
PHE A:225
PHE A:163
GLN A:256
HIS A:326
ARG A:197
ASP A:199
ALA A:200
TYR A:63
ILE A:143
ASP A:327
PHE A:144
ARG A:411
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Anion
Pi-Donor Hydrogen Bond
Pi-Sigma
Pi-Alkyl

(1)


PHE A:144
ASP A:60
TYR A:63
ASP A:327
ARG A:411
GLN A:167
ASP A:199
PHE A:163
HIS A:103
PHE A:282
GLN A:256
ALA A:200
ASN A:258
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Anion
Pi-Donor Hydrogen Bond
Pi-Sigma
Pi-Alkyl

(9)



(17)

Figure 2. Visualization of 2D and 3D ligand-receptor interactions. **(0)** acarbose, **(21)** fridamycin E, **(18)** aloe-emodin, **(6)** 1-hydroxy-2-methylol-anthraquinone, **(15)** 3-hydroxy-2-hydroxymethyl-anthraquinone, **(1)** 1,2-dihydroxy-3-methoxy-anthraquinone, **(9)** 2-ethoxy-1-hydroxyanthraquinone, **(17)** alizarin-1-methyl ether.

Docking simulations revealed that acarbose interacts with several key residues within the active pocket of α-glucosidase, namely Arg411, Gln256, and Asp327. These residues function as critical anchoring points that stabilize the ligand enzyme complex, and their interactions serve as a benchmark for evaluating the biological relevance of the tested compounds (Puspita et al., 2022). In other words, the greater the similarity in hydrogen-bonding patterns between the test compounds and acarbose at these residues, the higher the likelihood that the compounds mimic the inhibitory mechanism of acarbose. Accordingly, interactions with Arg411, Gln256, and Asp327 constitute the primary basis for selecting the most promising candidates from the docking results.

Among the 23 anthraquinone derivatives evaluated, several compounds exhibited strong potential as α-glucosidase inhibitors. Compound 21 stood out with a binding affinity of -8.9 kcal/mol, surpassing acarbose, while simultaneously forming a hydrogen bond with Gln256. This interaction indicates that compound 21 may stabilize the enzyme-ligand complex more efficiently, a highly desirable property for a candidate inhibitor. Likewise, compound 18 (-8.7 kcal/mol) displayed an even more favorable pattern by simultaneously forming hydrogen bonds with Arg411 and Gln256, the primary anchoring residues of acarbose. Such multiple interactions are expected to enhance binding energy contributions and prolong ligand retention within the active pocket, thereby yielding stronger inhibitory activity than acarbose (Nur et al., 2023). Similarly, compound 15 (-8.3 kcal/mol) emerged as another promising candidate, engaging two key residues, Gln256 and Asp327, which may facilitate a broader hydrogen-bonding network within the active site. This dual interaction provides a mechanistic advantage compared to compounds forming only a single hydrogen bond. A distinctive interaction pattern was observed for compound 9 (-8.1 kcal/mol), which bound to Arg411 and Asp327 a less common but potentially synergistic residue combination.

Interestingly, several other compounds with moderately strong affinities, such as compound 6 (-8.4 kcal/mol), compound 1 (-8.3 kcal/mol), and compound 17 (-7.8 kcal/mol), remain relevant despite engaging only a single key residue. Their shared hydrogen-bonding interactions with acarbose suggest the possibility of biological activity, albeit with relatively

lower stability. Taken together, these findings highlight that inhibitory effectiveness is not solely dictated by more negative binding affinities but also by the extent of multiple anchoring interactions that closely mimic the binding mechanism of acarbose. Compounds that exhibit broader or stronger interactions than acarbose at these key residues are therefore expected to demonstrate enhanced inhibitory activity, as stronger and more extensive hydrogen-bonding networks generally contribute to greater enzyme-ligand complex stability and inhibitory potency (Shahzad et al., 2025).

When compared to the control ligand (acarbose), the advantages of certain anthraquinone derivatives-particularly compounds 21, 18, and 15 lie in their combination of stronger binding affinities and multiple key residue engagements. This suggests that these compounds may not only replicate but potentially surpass the inhibitory mechanism of acarbose, either by enhancing complex stability or by exploiting a broader hydrogen-bonding network within the active site. Pharmacologically, this is highly significant, as ligand stability within the α-glucosidase pocket directly correlates with the duration and potency of inhibitory effects in the context of antidiabetic therapy (Abuelizz et al., 2019).

Nevertheless, it must be emphasized that docking outcomes remain predictive in nature. While high binding affinities and acarbose-like interaction patterns provide strong preliminary indicators, the actual inhibitory efficacy of these compounds must be validated through pharmacokinetic (ADMET) profiling, including absorption, distribution, metabolism, elimination, and toxicity assessments. Subsequent in vitro and in vivo experiments will also be essential to confirm whether high-affinity ligands not only exhibit robust binding but also possess adequate bioavailability and acceptable safety profiles for therapeutic application. Thus, the integration of in silico predictions with experimental validation is crucial for refining the selection of the most promising α-glucosidase inhibitor candidates.

CONCLUSION

This study demonstrated that several anthraquinone derivatives from *Morinda citrifolia* root exhibited strong inhibitory potential against α-glucosidase, with binding affinities comparable to or exceeding that of the standard inhibitor, acarbose. The ability of key compounds particularly compounds **(21)** fridamycin E, **(18)** aloe-emodin, **(15)** 3-hydroxy-2-hydroxymethyl-anthraquinone to form hydrogen bonds with critical residues (Arg411, Gln256, and Asp327) highlights their mechanistic resemblance to acarbose, suggesting a promising inhibitory effect on the enzyme's catalytic activity. The novelty of this study lies in the first comprehensive molecular docking evaluation of 23 anthraquinone derivatives from *M. citrifolia* roots, providing new molecular insights into their α-glucosidase inhibitory mechanisms. These findings not only expand current understanding of the bioactive potential of *M. citrifolia* but also offer valuable leads for the development of safer, plant-based antidiabetic agents. Further pharmacokinetic and experimental validation is warranted to confirm their therapeutic applicability.

RECOMMENDATIONS

Future research should focus on validating the inhibitory activity of the most promising anthraquinone derivatives particularly compounds **(21)** fridamycin E, **(18)** aloe-emodin, **(15)** 3-hydroxy-2-hydroxymethyl-anthraquinone hrough in vitro enzymatic assays and in vivo models to confirm their biological efficacy against α-glucosidase. In addition, pharmacokinetic and toxicity evaluations are essential to determine their safety profile and drug-likeness properties.

BIBLIOGRAPHY

Abnaz, Z. D., & Levita, J. (2018). Review : Buah Mengkudu (Morinda citrifolia L.), dan Biji Jinten Hitam (Nigella sativa L.) dan Teori Uji Toksisitas. *Farmaka*, *16*(1).

Abuelizz, H. A., Iwana, N. A. N. I., Ahmad, R., Anouar, E. H., Marzouk, M., & Al-Salahi, R. (2019). Synthesis, biological activity and molecular docking of new tricyclic series as α-glucosidase inhibitors. *BMC Chemistry*, *13*(3). https://doi.org/10.1186/s13065-019-0560-4

Bakri, A. H., Bamahry, A., Pratama, A. A., Bima, I. H., & Yanti, A. K. E. (2023). Hubungan Usia, Jenis Kelamin dan Indeks Massa Tubuh (IMT) dengan Kadar HbA1c di Rumah Sakit Ibnu Sina Makassar. *Jurnal Mahasiswa Kedokteran*, *3*(9).

Bhaumik, S., Sarkar, A., Debnath, S., Debnath, B., Ghosh, R., Zaki, M. E. A., & Al-Hussain, S. A. (2024). α-Glucosidase inhibitory potential of Oroxylum indicum using molecular docking, molecular dynamics, and in vitro evaluation. *Saudi Pharmaceutical Journal*, *32*(6). https://doi.org/10.1016/j.jsps.2024.102095

Buannata, J., Wijianto, B., & Arief, I. (2024). Molecular docking study of modified isoniazid compounds on mycolic acid synthase in the cell wall of mycobacterium tuberculosis. *Acta Chimica Asiana*, *7*(2), 471–477. https://doi.org/10.29303/aca.v7i2.173

Bumulo, N., Aman, L. O., Kilo, J. La, La Kilo, A., Salimi, Y. K., & Arviani, A. (2025). In Silico Study of the Potential of Moringa oleifera Secondary Metabolites as α-Glucosidase Inhibitors. *Indonesian Journal of Pharmaceutical Education*, *5*(1). https://doi.org/10.37311/ijpe.v5i1.28749

Dirir, A. M., Daou, M., Yousef, A. F., & Yousef, L. F. (2022). A review of alpha-glucosidase inhibitors from plants as potential candidates for the treatment of type-2 diabetes. In *Phytochemistry Reviews* (Vol. 21, Issue 4, pp. 1049–1079). Springer Science and Business Media B.V. https://doi.org/10.1007/s11101-021-09773-1

Hou, S., Ma, D., Wu, S., Hui, Q., & Hao, Z. (2025). Morinda citrifolia L.: A Comprehensive Review on Phytochemistry, Pharmacological Effects, and Antioxidant Potential. In *Antioxidants* (Vol. 14, Issue 3). Multidisciplinary Digital Publishing Institute (MDPI). https://doi.org/10.3390/antiox14030295

Humairo, S., Pribadi, T. J. P., & Supriyatna, A. (2024). Inventarisasi Tumbuhan Obat Di Kawasan Hutan Kota Babakan Siliwangi Bandung. *Botani : Publikasi Ilmu Tanaman Dan Agribisnis*, *1*(3), 14–26. https://doi.org/10.62951/botani.v1i3.74

IDF. (2021). IDF Diabetes Atlas 10th edition. *Https://Diabetesatlas.Org/Idfawp/Resource-Files/2021/07/IDF_Atlas_10th_Edition_2021.Pdf*. www.diabetesatlas.org

Khan, N. T. (2019). ANTHRAQUINONES-A Naturopathic Compound. *Journal of New Developments in Chemistry*, *2*(2), 25–28. https://doi.org/10.14302/issn.2377-2549.jndc-18-2569

Kumar, S. P., Smiline Girija, A. S., & Priyadharsini, J. V. (2020). Targeting NM23-H1-mediated Inhibition of Tumour Metastasis in Viral Hepatitis with Bioactive Compounds from Ganoderma lucidum: A Computational Study. *Indian Journal of Pharmaceutical Sciences*, *82*(2), 300–305. http://www.rcsb.org/pdb

Liu, S. K., Hao, H., Bian, Y., Ge, Y. X., Lu, S., Xie, H. X., Wang, K. M., Tao, H., Yuan, C., Zhang, J., Zhang, J., Jiang, C. S., & Zhu, K. (2021). Discovery of New α-Glucosidase Inhibitors: Structure-Based Virtual Screening and Biological Evaluation. *Frontiers in Chemistry*, *9*. https://doi.org/10.3389/fchem.2021.639279

Malik, E. M., & Müller, C. E. (2016). Anthraquinones As Pharmacological Tools and Drugs. In *Medicinal Research Reviews* (Vol. 36, Issue 4, pp. 705–748). John Wiley and Sons Inc. https://doi.org/10.1002/med.21391

Nerurkar, P. V., Hwang, P. W., & Saksa, E. (2015). Anti-diabetic potential of noni: The Yin and the Yang. In *Molecules* (Vol. 20, Issue 10, pp. 17684–17719). MDPI AG. https://doi.org/10.3390/molecules201017684

Nur, M. S., Yudiandani, R. E., & Solikah, A. N. (2023). Potensi Senyawa Chromodoris sebagai Pengikat Reseptor SARS-CoV-2 secara In Silico. *Sains Dan Matematika*, *7*(2), 70–76. https://doi.org/10.26740/sainsmat.v7n2.p70-76

Pattar, S. V., Adhoni, S. A., Kamanavalli, C. M., & Kumbar, S. S. (2020). In silico molecular docking studies and MM/GBSA analysis of coumarin-carbonodithioate hybrid derivatives divulge the anticancer potential against breast cancer. *Beni-Suef University Journal of Basic and Applied Sciences*, *9*(1). https://doi.org/10.1186/s43088-020-00059-7

Prahayati, S., & Rusdi, B. (2023). Uji In Silico Aktivitas Senyawa Kumarin Turunannya Terhadap Enzim Alfa Glukosidase Antidiabetes. *Jurnal Riset Farmasi*, *1*, 9–16. https://doi.org/10.29313/jrf.v3i1.2343

Puspita, P. J., Liliyani, N. P. P., & Ambarsari, L. (2022). *In Silico Analysis of Active Compounds of Avocado Fruit (Persea americana Mill.) as Tyrosinase Enzyme Inhibitors*. *9*(2), 73–87.

Rahman, A. (2023). Studi Doking Molekuler Perbandingan Evektivitas Senyawa Dari Buah Morinda Citrifolia L. Sebagai Antikanker Molecular Docking Studies Of Comparison The Effectiveness Compounds From Morinda Citrifolia L. Fruits As An Anticancer. *CHEMVIRO: Jurnal Kimia Dan Ilmu Lingkungan*, *1*(2), 56–64. http://lilab.ecust.edu.cn

Rasyid, H., Asmirah, Firdausiah, S., Bahrun, Arief, I., & Soekamto, N. H. (2024). The Potential of Paku Gajah (Angiopteris evecta) as Antitumor Through In Vitro and In Silico Studies. *Molekul*, *19*(2), 296–308. https://doi.org/10.20884/1.jm.2024.19.2.10644

Rasyid, H., Mardiyanti, R., Arief, I., & Saputri, W. D. (2023). An Insight of Cryptocarya Secondary Metabolites as Anticancer P388: Study of Molecular Docking ADMET Properties Molecular Dynamic Simulation. *Molekul*, *18*(1), 89–97. https://doi.org/10.20884/1.jm.2023.18.1.6364

Shahzad, A., Liu, W., Hussain, S., Ni, Y., Cui, K., Sun, Y., Liu, X., Duan, Q., Xia, J., Zhang, J., Xu, Z., Sai, B., Zhu, Y., Zhang, Q., & Yang, Z. (2025). Integrated in vitro, in silico, and in vivo approaches to elucidate the antidiabetic mechanisms of Cicer arietinum and Hordeum vulgare extract and secondary metabolites. *Scientific Reports*, *15*(1). https://doi.org/10.1038/s41598-025-89642-5

Vidal-Limon, A., Aguilar-Toalá, J. E., & Liceaga, A. M. (2022). Integration of Molecular Docking Analysis and Molecular Dynamics Simulations for Studying Food Proteins and Bioactive Peptides. In *Journal of Agricultural and Food Chemistry* (Vol. 70, Issue 4, pp. 934–943). American Chemical Society. https://doi.org/10.1021/acs.jafc.1c06110

Wiyati, E. P., Alfitroh, I., & Hardini, T. (2025). Docking Molekular Elatin (Flavonoid) Dari Daun Kopasanda (Chromolaena odorata L.) Sebagai Anti Diabetes Melitus Tipe 2. *Jurnal Review Pendidikan Dan Pengajaran*, *1*.

Yohana, V., Wijianto, B., & Arief, I. (2024). Molecular Docking Study of Epigallocatechin Gallate (EGCG) as A Therapy for Type 2 Diabetes Mellitus. In *Jurnal Kimia Riset* (Vol. 9, Issue 1). http://www.rcsb.org/pdb/

Zheng, L., Meng, J., Jiang, K., Lan, H., Wang, Z., Lin, M., Li, W., Guo, H., Wei, Y., & Mu, Y. (2022). Improving protein–ligand docking and screening accuracies by incorporating a scoring function correction term. *Briefings in Bioinformatics*, *23*(3). https://doi.org/10.1093/bib/bbac051