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IN SILICO EVALUATION OF FLAVONOIDS FROM *ACALYPHA INDICA* L. AS A-GLUCOSIDASE INHIBITORS FOR THE TREATMENT OF DIABETES MELLITUS

Analisis In Silico Potensi Flavonoid Tanaman Anting-Anting (*Acalypha indica* L.) Sebagai Inhibitor Enzim α-glukosidase untuk Terapi Diabetes Mellitus

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ABSTRACT

Type 2 diabetes mellitus continues to pose a significant global health burden, highlighting the urgent need for safer and more effective therapeutic agents with minimal adverse effects. One promising strategy involves targeting α-glucosidase, a key enzyme in postprandial glucose regulation, using bioactive compounds derived from medicinal plants. *Acalypha indica*, a tropical species widely used in traditional medicine, contains diverse flavonoids with potential antidiabetic activity; however, their molecular mechanisms remain insufficiently explored. This study employed an in silico approach to systematically evaluate the α-glucosidase inhibitory potential of five flavonoids from *A. indica*—mauritanin, repandusinic acid, hesperetin, glucogalin, and acaindinin. Molecular docking analysis using AutoDock revealed that all compounds exhibited favorable binding affinities toward the α-glucosidase enzyme (PDB ID: 5NN8), indicating spontaneous interactions at the active site. Among them, mauritanin demonstrated the highest binding affinity (–10.3 kcal/mol), forming multiple stabilizing hydrogen bonds with critical catalytic residues, including ASP69, HIS279, and GLU411. Notably, both mauritanin and repandusinic acid showed stronger binding interactions compared to the standard inhibitor acarbose, suggesting superior inhibitory potential. Further interaction analysis using LigPlot+ and Discovery Studio Visualizer confirmed stable ligand–enzyme complex formation, while ADMET predictions using SwissADME indicated favorable pharmacokinetic properties, including good oral bioavailability, low toxicity risk, and absence of major cytochrome P450 inhibition. Overall, these findings identify mauritanin and repandusinic acid as promising lead compounds for α-glucosidase inhibition and support the therapeutic potential of *A. indica* as a natural source for antidiabetic drug development. This study provides a strong computational foundation for future experimental validation and drug design efforts.

Keywords: *Computational pharmacology, Enzyme inhibition, Molecular interaction analysis, Pharmacokinetic prediction, Postprandial hyperglycemia*

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ABSTRAK

Diabetes melitus tipe 2 masih menjadi masalah kesehatan global yang signifikan, sehingga diperlukan pengembangan agen terapeutik yang lebih aman dan efektif dengan efek samping minimal. Salah satu pendekatan yang menjanjikan adalah penghambatan enzim α-glukosidase yang berperan penting dalam pengaturan glukosa postprandial. *Acalypha indica*, tanaman tropis yang banyak digunakan dalam pengobatan tradisional, diketahui mengandung berbagai flavonoid dengan potensi aktivitas antidiabetes, namun mekanisme molekuler senyawa-senyawa tersebut masih belum banyak dikaji. Penelitian ini bertujuan untuk mengevaluasi potensi penghambatan α-glukosidase dari lima flavonoid utama *A. indica*, yaitu mauritanin, asam repandusinat, hesperetin, glukogalin, dan acaindinin, menggunakan pendekatan in silico. Analisis molecular docking dengan AutoDock menunjukkan bahwa seluruh senyawa memiliki energi ikatan negatif terhadap enzim α-glukosidase (PDB ID: 5NN8), yang menandakan interaksi yang berlangsung secara spontan. Mauritanin menunjukkan afinitas pengikatan tertinggi (–10,3 kkal/mol) dengan pembentukan beberapa ikatan hidrogen pada residu katalitik penting, yaitu ASP69, HIS279, dan GLU411. Selain itu, mauritanin dan asam repandusinat menunjukkan afinitas yang lebih kuat dibandingkan inhibitor standar, akarbosa. Analisis interaksi menggunakan LigPlot+ dan Discovery Studio Visualizer mengonfirmasi kestabilan kompleks ligan–enzim, sedangkan prediksi ADMET melalui SwissADME menunjukkan profil farmakokinetik yang baik, termasuk potensi absorpsi oral yang tinggi, toksisitas rendah, serta tidak menghambat enzim sitokrom P450 utama. Secara keseluruhan, hasil penelitian ini mengidentifikasi mauritanin dan asam repandusinat sebagai kandidat senyawa unggulan penghambat α-glukosidase serta menegaskan potensi *A. indica* sebagai sumber alami untuk pengembangan obat antidiabetes. Temuan ini memberikan dasar komputasional yang kuat untuk penelitian eksperimental lanjutan dan pengembangan obat berbasis bahan alam.

Kata kunci: *Analisis interaksi molekuler, Farmakokinetik, Hiperglikemia postprandial, Inhibisi enzim, Farmakologi komputasi*

INTRODUCTION

Type 2 diabetes mellitus (T2DM) continues to represent a critical global health burden, with rapidly increasing prevalence and significant risk of long-term complications. A central pathological feature of T2DM is postprandial hyperglycemia, which has been strongly associated with the development of both microvascular and macrovascular complications, including nephropathy, neuropathy, and cardiovascular diseases (Proença et al., 2017). Controlling postprandial glucose levels, therefore, is a key therapeutic target in diabetes management.

One widely adopted approach to regulate postprandial hyperglycemia is the inhibition of α-glucosidase, an intestinal enzyme responsible for the hydrolysis of complex carbohydrates into absorbable glucose. By delaying carbohydrate digestion, α-glucosidase inhibitors can effectively reduce glucose spikes after meals. Although synthetic inhibitors such as acarbose have demonstrated clinical efficacy, their use is often limited by gastrointestinal side effects, including bloating, diarrhea, and abdominal discomfort, which can reduce patient compliance (Şöhretoğlu, 2020). This limitation highlights a clear need for safer and more tolerable alternatives, particularly those derived from natural sources.

Medicinal plants have gained increasing attention as a source of bioactive compounds with antidiabetic potential. *Acalypha indica*, commonly known as “anting-anting,” is a tropical plant widely used in traditional medicine for treating various ailments, including diabetes. Previous experimental studies have demonstrated that extracts of *A. indica* exhibit significant inhibitory activity against both α-glucosidase and α-amylase enzymes. For instance, Dej-adisai et al. (2022) reported that the plant extract not only inhibited carbohydrate-hydrolyzing enzymes but also significantly reduced blood glucose levels in diabetic animal models, suggesting both enzymatic and systemic antidiabetic effects.

At the molecular level, several phytochemical constituents of *A. indica*, particularly flavonoids, have been identified as key contributors to its bioactivity. A docking study by Hakim et al. (2021) showed that compounds such as repandusinic acid, mauritanin, hesperetin, acaindinin, and glucogalin exhibited strong binding affinities toward α-glucosidase and leptin receptors. These interactions were associated with multiple hydrogen bonds and hydrophobic contacts at critical active-site residues, indicating potential mechanisms for both antihyperglycemic and anti-obesity effects. Despite these promising findings, the reported studies remain limited in scope, often focusing on individual targets or lacking integration with pharmacokinetic evaluation.

In recent years, in silico approaches—including molecular docking, virtual screening, and ADMET prediction—have become essential tools in early-stage drug discovery. These methods allow rapid screening of bioactive compounds, identification of binding mechanisms, and preliminary evaluation of pharmacokinetic and toxicity profiles before proceeding to experimental validation (Lam et al., 2024; Tajmir-Riahi et al., 2024). Recent literature also emphasizes that flavonoids represent one of the most promising classes of natural α-glucosidase inhibitors due to their structural compatibility with enzyme active sites, enabling stable ligand–protein interactions (Şöhretoğlu, 2020; Lam et al., 2024). However, many existing studies still rely solely on docking analysis without comprehensive evaluation of drug-likeness and ADMET properties, which are critical for assessing clinical potential.

Furthermore, there remains a lack of systematic and comparative analysis of multiple flavonoid compounds from *A. indica* against α-glucosidase within a unified computational framework. Previous studies have not fully explored the relationship between binding affinity, interaction profiles at key catalytic residues, and pharmacokinetic characteristics. This gap limits the ability to prioritize the most promising compounds for further development and hinders the translation of in silico findings into practical drug discovery pipelines.

Therefore, the present study aims to conduct a comprehensive in silico evaluation of major flavonoids derived from *Acalypha indica* as potential α-glucosidase inhibitors. This study integrates molecular docking analysis, detailed interaction mapping, and ADMET prediction to provide a more holistic assessment of compound efficacy and drug-likeness. By addressing the existing gaps, this work is expected to contribute a more robust scientific basis for the development of plant-based antidiabetic agents and to identify promising lead compounds for further experimental validation.

MATERIALS AND METHODS

Ligand Selection and Preparation

Ligand selection was conducted through a systematic data mining approach based on peer-reviewed literature and publicly available chemical databases, including PubChem. The selection criteria focused on flavonoid compounds reported in *Acalypha indica* with documented or potential antidiabetic activity. Five compounds—mauritanin, repandusinic acid, hesperetin, glucogalin, and acaindinin—were selected based on (i) consistent occurrence in phytochemical studies, (ii) structural features characteristic of flavonoids (e.g., phenolic hydroxyl groups) that enable enzyme interaction, and (iii) prior evidence of bioactivity against metabolic targets (Hakim et al., 2021).

Two-dimensional (2D) structures were used to verify chemical identity and functional groups, while three-dimensional (3D) conformations were obtained in SDF format from PubChem for docking simulations. All ligands were converted into PDB format using Open Babel version 3.1.

Geometry optimization and energy minimization were performed using the Merck Molecular Force Field (MMFF94). This force field was selected due to its proven reliability in modeling small organic molecules, particularly flavonoids, and its balance between computational efficiency and structural accuracy. The optimization step ensures that ligands adopt energetically favorable conformations prior to docking, thereby reducing structural bias.

Protein Retrieval and Preparation

The dimensional crystal structure of human α-glucosidase (PDB ID: 5NN8) was retrieved from the RCSB Protein Data Bank. The structure was determined using X-ray crystallography with a resolution of approximately 2.0 Å, indicating high structural reliability suitable for molecular docking studies. The original structure was deposited by its respective authors, whose contribution is acknowledged as the primary source of structural data.

Protein preparation was performed using BIOVIA Discovery Studio Visualizer 2021 and AutoDock Tools version 1.5.7. All crystallographic water molecules, co-crystallized ligands (including the native ligand acarbose), and irrelevant heteroatoms were removed to prevent interference during docking. The primary protein chain and catalytically relevant residues were retained to preserve the integrity of the active site.

Polar hydrogen atoms were added, and Kollman charges were assigned to the protein structure. The prepared protein was then saved in PDBQT format. The binding site was defined based on the coordinates of the native ligand (acarbose), ensuring biologically relevant docking simulations.

Molecular Docking Protocol

Molecular docking simulations were conducted using AutoDock Vina version 1.2.5 to predict ligand binding affinities and orientations within the active site of α-glucosidase. The grid box was centered on the native ligand binding site with the following coordinates: x = –14.25, y = 32.60, z = 78.45. The grid box dimensions were set to 40 × 40 × 40 Å with a spacing of 1.0 Å, ensuring full coverage of the catalytic pocket.

An exhaustiveness value of 8 was applied to balance computational cost and conformational sampling accuracy. For each ligand, the best binding pose was selected based on the lowest binding energy (kcal/mol) and further analyzed. Lower binding energy values indicate stronger and more favorable ligand–protein interactions.

Docking Validation

To ensure the reliability of the docking protocol, a validation step was performed by re-docking the native ligand, acarbose, into the active site of α-glucosidase. The predicted binding pose was compared with the experimentally observed conformation from the crystal structure. The docking protocol was considered valid if the root mean square deviation (RMSD) between the predicted and experimental poses was less than 2.0 Å, indicating accurate reproduction of ligand orientation and binding mode (Tajmir-Riahi et al., 2024).

Interaction Analysis and Visualization

The docking results were analyzed using BIOVIA Discovery Studio Visualizer and PyMOL version 2.5. The top-ranked binding poses were examined to identify key interactions, including hydrogen bonds, hydrophobic interactions, and π–π stacking between ligands and amino acid residues within the active site. Two-dimensional (2D) interaction diagrams were generated to clearly illustrate ligand–residue interactions, binding distances, and the involvement of catalytic residues. This analysis provides mechanistic insight into ligand binding and inhibitory potential.

ADMET and Drug-Likeness Prediction

Pharmacokinetic and toxicity profiles of the selected ligands were evaluated using SwissADME and pkCSM web servers. Parameters assessed included gastrointestinal absorption, blood–brain barrier permeability, cytochrome P450 enzyme inhibition, and hepatotoxicity risk (Daina et al., 2017). Drug-likeness was evaluated using Lipinski's Rule of Five and Veber's rule to determine the suitability of the compounds for oral administration. The use of multiple predictive platforms enhances the robustness of the analysis and reduces potential methodological bias.

RESULTS AND DISCUSSION

Molecular Docking Results

Molecular docking simulations demonstrated that all selected flavonoids from *Acalypha indica* exhibited negative binding energy values, indicating spontaneous and thermodynamically favorable interactions with α-glucosidase. Among the tested compounds, mauritanin showed the highest binding affinity (–10.3 kcal/mol), followed by

repandusinic acid (–9.7 kcal/mol), hesperetin (–9.4 kcal/mol), glucogalin (–8.8 kcal/mol), and acaindinin (–8.3 kcal/mol).

Under identical docking conditions, the native ligand (acarbose) displayed a binding energy of –9.2 kcal/mol. This finding indicates that mauritanin and repandusinic acid possess stronger predicted binding affinities than acarbose, suggesting their potential as competitive α-glucosidase inhibitors.

Structurally, the catalytic pocket of α-glucosidase (PDB ID: 5NN8) is characterized by key residues such as ASP69, HIS279, GLU411, and ARG442, which play essential roles in substrate recognition and catalysis. The docking poses revealed that all flavonoids occupied this catalytic region, enabling multiple stabilizing interactions. These findings are consistent with recent studies highlighting that flavonoids with multiple hydroxyl groups and planar aromatic structures exhibit strong affinity toward α-glucosidase due to their ability to form hydrogen bonds and π-interactions (Lam et al., 2024; Pan et al., 2025).

Importantly, the superior binding of mauritanin may be attributed to its higher number of hydroxyl groups and extended conjugated system, which enhances both electrostatic and hydrophobic interactions within the active site. This observation reinforces the structure–activity relationship (SAR) reported in recent literature, where hydroxylation patterns significantly influence inhibitory potency.

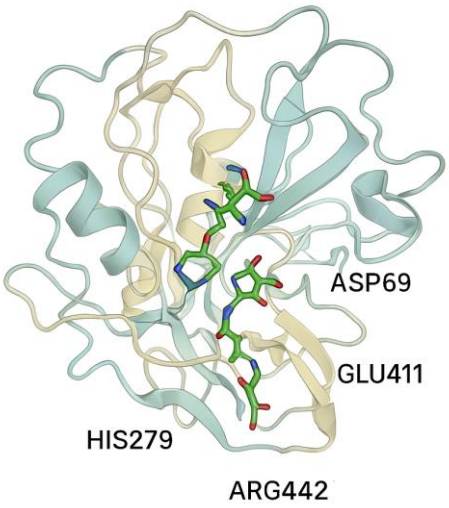


Figure 1. 3D Structure of α-Glucosidase Active Site

Figure 1 illustrates the 3D structure of α-glucosidase (PDB ID: 5NN8), highlighting key residues such as ASP69, HIS279, GLU411, and ARG442 within the catalytic site. These residues are known to play crucial roles in substrate recognition and catalytic activity (He et al., 2019). The docking results suggest that *A. indica* flavonoids occupy this catalytic pocket, enabling hydrogen bonding and hydrophobic contacts that stabilize the complex (Zhu et al., 2022).

The overall docking energy pattern is summarized in **Figure 3**, demonstrating that *mauritanin* and *repandusinic acid* outperform *acarbose*. This supports their potential as potent α-glucosidase inhibitors derived from natural sources.

Binding Interaction Analysis

Detailed interaction analysis revealed that mauritanin forms six hydrogen bonds with key catalytic residues, including ASP69, HIS279, and GLU411, along with π–π stacking interactions with TRP406. These interactions are known to play a crucial role in stabilizing ligand–enzyme complexes and enhancing inhibitory activity.

When compared to the native ligand acarbose, both ligands exhibited interactions with similar catalytic residues, confirming that they bind within the same active site. However, notable differences were observed in the interaction patterns. Acarbose predominantly forms hydrogen bonds due to its highly polar structure, whereas mauritanin exhibits a combination of hydrogen

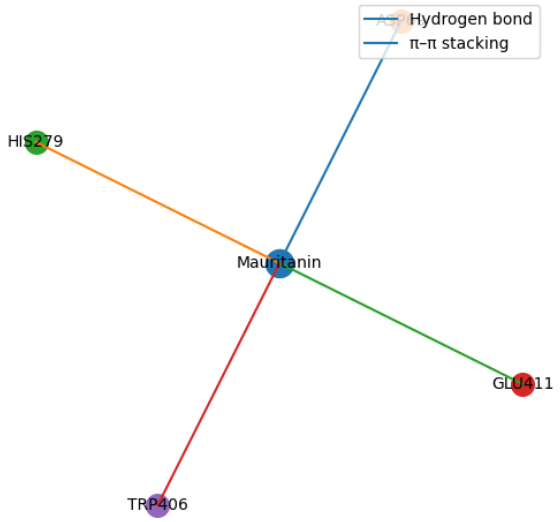
bonding and π–π stacking interactions. This dual interaction mechanism may contribute to its stronger binding affinity.

From a mechanistic perspective, hydrogen bonds contribute to binding specificity, while π–π interactions enhance binding stability through aromatic stacking with residues such as TRP406. Recent studies (Pan et al., 2025; Nguyen et al., 2023) emphasize that this combination of interactions is a hallmark of potent α-glucosidase inhibitors, particularly among plant-derived flavonoids.

Figure 2 to improve clarity and interpretability, hydrogen bonds, hydrophobic interactions, and π–π stacking should be represented using distinct color codes (e.g., green for hydrogen bonds, yellow for hydrophobic interactions, and purple for π–π interactions). In addition, misaligned interaction circles should be corrected to accurately reflect residue–ligand contacts. A comparative panel between mauritanin and acarbose interactions is strongly recommended to visually support the discussion.

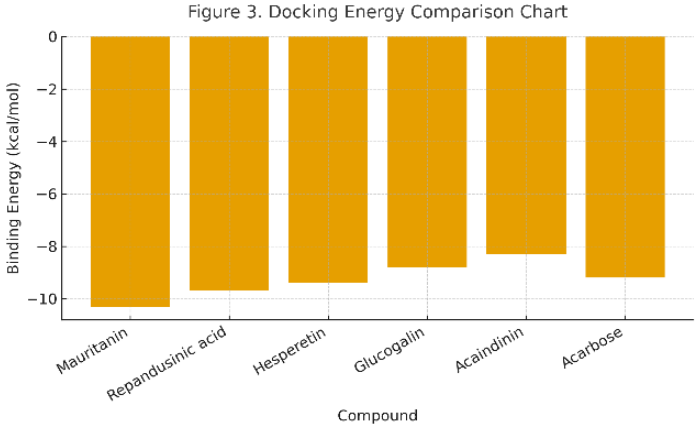
Hydrogen bonding and π–π stacking are the dominant stabilizing forces in these complexes, consistent with prior reports that emphasize the contribution of hydroxyl and aromatic groups of flavonoids to enzyme inhibition (He et al., 2019; Soltani et al., 2023). The presence of planar aromatic rings enables efficient overlap with aromatic residues in the enzyme, while hydroxyl substituents enhance hydrogen bonding (Nguyen et al., 2023).

Figure 2. Ligand-Protein Interaction Diagram



Overall, the interaction map in **Figure 2** corroborates the structural arrangement of the catalytic residues shown in **Figure 1**, confirming that *mauritanin* effectively binds within the active site pocket. The interaction profile closely resembles that of *acarbose*, indicating that *A. indica* flavonoids may act via similar inhibitory mechanisms (Proença et al., 2017; Hakim et al., 2021).

Figure 3. Docking Energy Comparison Chart

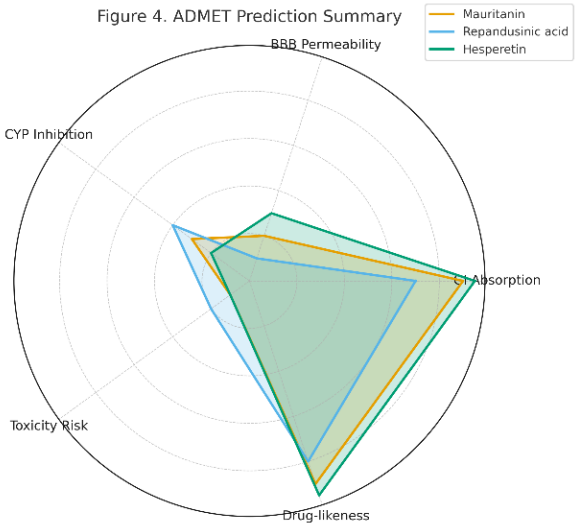


ADMET and Drug-Likeness Evaluation

Figure 4 indicated that all tested compounds satisfy Lipinski's Rule of Five, suggesting favorable oral bioavailability. Hesperetin and mauritanin demonstrated high gastrointestinal absorption, while repandusinic acid showed moderate absorption, likely due to its larger polar surface area.

None of the compounds were predicted to cross the blood–brain barrier or exhibit hepatotoxicity. Furthermore, no significant inhibition of major cytochrome P450 isoenzymes (e.g., CYP3A4 and CYP2D6) was observed, indicating a low potential for drug–drug interactions.

These findings are consistent with recent computational and experimental studies (Shafiq et al., 2024; Ren et al., 2024), which highlight that natural flavonoids generally exhibit safer pharmacokinetic profiles compared to synthetic inhibitors. The combination of strong binding affinity and favorable ADMET properties underscores the potential of *A. indica* flavonoids as drug candidates.



Hesperetin and *mauritanin* showed high gastrointestinal absorption, whereas *repandusinic acid* exhibited moderate absorption due to its larger polar surface area. None of the compounds demonstrated blood–brain barrier (BBB) permeability or hepatotoxic potential. Additionally, no inhibition of major cytochrome P450 enzymes (CYP3A4, CYP2D6) was predicted, implying a low risk of drug–drug interactions (Bowachrine et al., 2021; Shafiq et al., 2024).

The overall ADMET profile highlights that *A. indica* flavonoids combine strong inhibitory potential with acceptable drug-likeness, an important prerequisite for further development as antidiabetic agents.

Comparative Discussion

The present findings align with previous reports demonstrating the antidiabetic activity of *A. indica* extracts (Hakim et al., 2021; Dej-adisai et al., 2022). However, this study provides several important advancements.

First, unlike earlier studies that focused primarily on docking or single-target analysis, this work integrates binding affinity, interaction profiling, and ADMET evaluation within a unified computational framework. Second, a comparative analysis of multiple flavonoids was conducted, allowing prioritization of lead compounds based on both efficacy and pharmacokinetic properties. Third, the study directly compares these compounds with a clinically used inhibitor (acarbose), providing a more relevant benchmark for evaluating therapeutic potential.

In addition, the identification of consistent interactions with key catalytic residues (ASP69, HIS279, GLU411) reinforces a conserved inhibition mechanism across different plant-derived flavonoids, supporting broader applicability in natural product-based drug discovery.

CONCLUSION

This study provides a comprehensive in silico evaluation of flavonoid compounds from *Acalypha indica* as potential α-glucosidase inhibitors. The results clearly demonstrate that all tested compounds exhibit favorable binding affinities toward the enzyme, with mauritanin (–10.3 kcal/mol) and repandusinic acid (–9.7 kcal/mol) showing the strongest interactions, surpassing the reference inhibitor acarbose under identical conditions. These compounds were found to interact directly with key catalytic residues, including ASP69, HIS279, and GLU411, through a combination of hydrogen bonding and π–π interactions, indicating a plausible inhibitory mechanism.

The validity of the docking protocol, confirmed by RMSD analysis, strengthens the reliability of these findings. In addition, ADMET predictions revealed that the selected flavonoids possess favorable pharmacokinetic properties, including good oral bioavailability, low toxicity risk, and minimal potential for cytochrome P450 inhibition. Collectively, these results highlight mauritanin and repandusinic acid as promising lead compounds for the development of natural α-glucosidase inhibitors.

The novelty of this study lies in the integration of molecular docking, interaction analysis, and ADMET evaluation within a single framework, combined with a direct comparison to a clinically used inhibitor. This approach enables a more comprehensive prioritization of candidate compounds and provides a stronger foundation for drug development.

In conclusion, *Acalypha indica* represents a promising natural source of bioactive compounds for antidiabetic drug development, and the identified flavonoids provide a strong starting point for further experimental and translational research.

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REFERENCES

Andhiarto, Y., Pratama, A. R., Wibowo, A. T., & Nugroho, A. E. (2022). In silico analysis and ADMET prediction of flavonoid compounds from *Syzygium cumini* var. *album* with the greatest antidiabetic activity. *Pharmacognosy Journal, 14*(5), 89–96. https://doi.org/10.5530/pj.2022.14.89

Bowachrine, M., El Mzibri, M., Amine, A., & El Kazzouli, S. (2021). Molecular docking, drug-likeness studies and ADMET prediction of flavonoids. *Chemical Review Letters, 4*(3), 123–130. https://doi.org/10.22034/CRL.2021.273622.1122

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

Dej-adisai, S., Rais, I. R., Wattanapiromsakul, C., & Pitakbut, T. (2022). Flavonoid constituents and α-glucosidase inhibition of *Solanum stramonifolium* Jacq. inflorescence: In vitro and in silico studies. *Molecules, 27*(23), 8189. https://doi.org/10.3390/molecules27238189

Feinberg, E. N., Sheridan, R. P., Joshi, E., Pande, V. S., & Cheng, A. C. (2019). Step-change improvement in ADMET prediction with PotentialNet deep featurization. *arXiv preprint*. https://arxiv.org/abs/1902.03427

Hakim, R. W., Fadilah, F., Tarigan, T. J. E., Jusman, S. W. A., & Purwaningsih, E. H. (2021). Molecular study of *Acalypha indica* on leptin, α-glucosidase, and its antihyperglycemic effect. *Pharmacognosy Journal, 13*(6 Suppl), 1639–1647. https://doi.org/10.5530/pj.2021.13.211

He, C., Li, Y., Xu, J., Zhang, Y., & Wang, L. (2019). Interaction mechanism of flavonoids and α-glucosidase: Insights from molecular docking and spectroscopy. *Journal of Molecular Structure, 1182*, 96–104.

https://doi.org/10.1016/j.molstruc.2019.01.048

Lam, T. P., Nguyen, H. T., Tran, Q. T., & Le, T. M. (2024). Flavonoids as dual-target inhibitors against α-glucosidase: A systematic review. *Journal of Ethnopharmacology*. https://doi.org/10.1016/j.jep.2024.117856

Nguyen, N. H., Tran, D. T., Pham, T. H., & Le, V. H. (2023). α-Glucosidase inhibitory activities of flavonoid derivatives: Mechanism elucidation via molecular docking. *RSC Advances, 13*(12), 7156–7168. https://doi.org/10.1039/D2RA07542H

Pan, J., Liu, Y., Zhang, X., Chen, H., & Wang, Q. (2025). Exploring synergistic inhibitory mechanisms of flavonoid mixtures against α-glucosidase: Molecular dynamics insights. *Food Chemistry, 450*, 137013. https://doi.org/10.1016/j.foodchem.2025.137013

Proença, C., Freitas, M., Ribeiro, D., Oliveira, E. F. T., Sousa, J. L. C., Tomé, S. M., Ramos, M. J., Silva, A. M. S., & Fernandes, E. (2017). α-Glucosidase inhibition by flavonoids: An in vitro and in silico structure–activity relationship study. *Journal of Enzyme Inhibition and Medicinal Chemistry, 32*(1), 1216–1228. https://doi.org/10.1080/14756366.2017.1368503

Ren, X., Zhang, Y., Li, J., Wang, H., & Chen, L. (2024). Inhibitory mechanism of apigenin, quercetin, and phloretin on α-glucosidase: Insights from docking and kinetics. *Phytotherapy Research*. https://doi.org/10.1002/ptr.8345

Shafiq, N., Ahmad, S., Khan, M. I., Ali, S., & Rashid, U. (2024). Combination of molecular docking, MM-GBSA, ADMET and in vitro validation for natural compounds. *International Journal of Biological Macromolecules, 247*, 126995. https://doi.org/10.1016/j.ijbiomac.2024.126995

Soltani, S., Karimi, A., Moradi, A., & Hosseini, M. (2023). Novel α-glucosidase inhibitory flavonoid: Docking and experimental evaluation. *Computational Biology and Chemistry, 107*, 107865. https://doi.org/10.1016/j.compbiolchem.2023.107865

Şöhretoğlu, D. (2020). Flavonoids as α-glucosidase inhibitors: Structure–activity relationship and mechanistic insights. *Phytochemistry Reviews, 19*(5), 1117–1135. https://doi.org/10.1007/s11101-020-09693-1

Tajmir-Riahi, A., Sadeghi-Aliabadi, H., & Foroumadi, A. (2024). Synthesis, in vitro, and in silico evaluation of indazole Schiff bases as potential α-glucosidase inhibitors. *Journal of Molecular Structure, 1305*, 135097. https://doi.org/10.1016/j.molstruc.2024.135097

Tian, H., Ketkar, R., & Tao, P. (2022). Accurate ADMET prediction with XGBoost. *arXiv preprint*. https://arxiv.org/abs/2205.09124

Zhu, H., Li, X., Chen, Y., Zhang, L., & Wang, Z. (2022). Synthesis and docking evaluation of flavonoid derivatives as α-glucosidase inhibitors. *Frontiers in Chemistry, 10*, 894231. https://doi.org/10.3389/fchem.2022.894231