Jurnal Pijar MIPA
https://jurnalfkip.unram.ac.id/index.php/JPM

ISSN 1907-1744 (Print)
ISSN 2460-1500 (Online)

Molecular Docking and Pharmacoinformatics Study of Bioactive Compounds in Jeringau (*Acorus calamus* L.) as Antidiabetic Agents Targeting α-Glucosidase

Rani Sakila Nasution[1], Indang Dewata[1], Nofri Yuhelman[1], Neny Sandrawati[2], Arif Juliari Kusnanda[1*]

[1]Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang, West Sumatra, Indonesia
[2]Department of Cosmetic Technology, Vocational School, Universitas Negeri Padang, West Sumatra, Indonesia
[*]e-mail: arifjuliari@fmipa.unp.ac.id

Received: May 8, 2025. Accepted: June 1, 2025. Published: June 26, 2025

Abstract: Diabetes mellitus (DM) is a metabolic disorder characterized by elevated blood glucose due to either insufficient amounts of insulin or the body's inability to use the produced insulin efficiently. The purpose of this article is to investigate the antidiabetic activity of bioactive compounds from Jeringau (*Acorus calamus* L.) in inhibiting α-glucosidase enzymes through a molecular docking simulation approach with the aim of predicting interactions that occur between enzyme targets and test compounds in finding new drug designs from natural ingredients as antidiabetics. Pharmacokinetic screening, toxicity prediction, and Lipinski's Rule of Five screening were conducted to assess the pharmacological suitability of the compounds, followed by molecular docking using MOE 2022 software. The results of the study showed that several compounds from Jeringau (*A. calamus* L.) as a galgravin have strong binding affinity to the α-glucosidase enzyme with a docking score of −8.40 kcal/mol. The pharmacokinetic prediction results indicate that the test compound exhibits good absorption and meets the criteria for drug-likeness. This study suggests that active compounds from Jeringau (*A. calamus* L.) have potential for development as natural-based antidiabetic agents. However, this research is limited to computational analysis without experimental data support, and compound selection is based on GC-MS results without further isolation or characterization. Further studies through in vitro and in vivo testing, as well as molecular dynamics simulations are required to validate these findings comprehensively.

Keywords: *Acorus calamus* L.; α-glukosidase; Antidiabetic; In Silico; Molecular Docking.

Introduction

Diabetes Mellitus (DM) is a metabolic disorder characterized by elevated blood glucose due to either insufficient amounts of insulin or the body's inability to use the produced insulin efficiently [1]. The International Diabetes Federation (IDF) confirmed that Indonesia ranks fifth in terms of the highest number of diabetes mellitus sufferers, reaching 19.5 million people. In addition, the IDF predicts that the number of diabetes mellitus sufferers in Indonesia will increase to around 28.57 million people by 2045[2][3].

Current treatment options for diabetes are still limited to lifestyle changes [4], insulin injection [5], and the use of antidiabetic drugs such as metformin [6], but when this medication is insufficient, other medications such as sulfonylureas, analogues, Glucagon Like Peptide-1 (GLP-1), Dipeptidyl Peptidase-IV (DPP-IV) inhibitors, SGLT2 inhibitors, thiazolidinediones, and a-glucosidase inhibitors may be added [7][8]. However, these drugs have been reported to cause side effects such as increased risk of cardiovascular disease, damage to the digestive tract, pancreatic cancer, thyroid cancer, infectious disorders, and severe joint pain [9][10][11]. Therefore, there is a need for safer, more effective, easy-to-use, and affordable treatments [6]. Traditional medicine approaches using antidiabetic compounds from various plants are gaining attention because natural medicines tend to have fewer side effects than synthetic drugs [5][12].

Jeringau (*Acorus calamus* L.) is a wild plant commonly found in several regions of Indonesia [13]. Generally, Jeringau is use as traditional medicine. These plants contain more than 40 types of secondary metabolites that have various benefits [14][15][16]. Its essential oil is rich in β-asarone, a compound that acts as a neuroprotective agent and insecticide [17]. In addition, there are sesquiterpenoids, diterpenoids, and alkaloids that have antioxidant and antimicrobial activities [18]. Ethyl acetate extract has also been reported to have potential as an antidiabetic agent, as this compound is able to significantly increase insulin sensitivity [19].

The in silico method is a computational approach used to predict and analyze molecular interactions [20], included in the search for antidiabetic compounds. Previous research [13], it has been reported that the active compounds of the ant nest plant (*Myrmecodia* Sp.) have potential as α-glucosidase enzyme inhibitors. The compound luteolin showed the strongest affinity with a docking score of -15.88 kcal/mol. In another study, [21], reported that rutin and quercetin 3-O-neohesperidoside compounds from soursop leaves (*Annona muricata Linn*) have the highest affinity in inhibiting α-glucosidase and α-amylase enzymes with docking scores of -11.14 kcal/mol and -10.91 kcal/mol, respectively. The primary target in this study is the α-

How to Cite:
R. S. Nasution, I. Dewata, N. Yuhelman, N. Sandrawati, and A. J. Kusnanda, "Molecular Docking and Pharmacoinformatics Study of Bioactive Compounds in Sweet Flag (Acorus calamus L.) as Antidiabetic Agents Targeting α-Glucosidase", *J. Pijar.MIPA*, vol. 20, no. 4, pp. 598–604, Jun. 2025. https://doi.org/10.29303/jpm.v20i4.8994

glucosidase enzyme, as it plays a role in breaking down carbohydrates into glucose, and its inhibition can help control blood sugar levels in diabetic patients. In recent research [13] has conducted in silico screening of active compounds from Jeringau (*Acorus calamus* L.) as α-glucosidase enzyme inhibitors, and demonstrated potential antidiabetic activity.

Secondary metabolites with good drug activity are contained in Jeringau (*A. calamus* L.) extract, including alkaloids, terpenoids, phenolics, and flavonoids are considered good in inhibiting hyperglycemia [15][16][14]. This study aims to evaluate the antidiabetic potential of bioactive compounds derived from Jeringau (*A. calamus* L.) by assessing their inhibitory activity against α-glucosidase enzymes through molecular docking simulations. The investigation is intended to predict the molecular interactions between the target enzyme and test compounds as a preliminary step in the discovery of novel antidiabetic agents from natural sources.

Research Methods

Tools

The hardware used is a Desktop-9IDKVEL with Windows 10 Pro 64-bit specifications, an Intel (R) Celeron (R) N4020 CPU (2 CPUs) ~1.1 GHz, and 4096MB RAM. The software used includes the moe 2022 application, Biovia Discovery Studio, PreADMET, PDB, and PubChem.

Ligand and Protein Preparation

A total of 20 compounds in the Jeringau plant obtained from literature studies were used as ligands, obtained in SMILE code form from the PubChem database via https://pubchem.ncbi.nlm.nih.gov/, as well as a comparative compound, acarbose, which has been clinically tested in α-glucosidase inhibition. The structure of the ligand was minimized before use and stored in *.mdb format [22]

The protein structure used as a receptor was downloaded in 3D format from the Protein Data Bank, namely α-glucosidase (PDB ID: 7P07) [23]. https://www.rcsb.org/structure/7P07 stored in *.pdb format. This structure was prepared by removing water molecules, correcting the structure, removing the original ligand, and searching for the active site of the protein.

Pharmacokinetic Studies

Predictions of pharmacokinetics and toxicity were performed using the PreADMET program accessed via http://preadmet.bmdrc.org/ [24].

Lipinski's Rule of Five Screening

The active compounds of Jeringau were analyzed based on Lipinski's Rule of Five to evaluate whether the compounds meet the chemical characteristics to be used as drugs. The parameters used include molecular weight <500 g/mol, lipophilicity (Log P) <5, number of hydrogen bond donors <5, number of hydrogen bond acceptors <10, and molar refractivity within the range of 40–130. This analysis was performed by uploading the compound structure in .sdf format to the website http://www.scfbio-iitd.res.in/software/drugdesign/lipinski.jsp to determine whether the compound complies with Lipinski's rules before the docking process is carried out [25].

Molecular Docking Studies

Docking of the α-glucosidase enzyme with pdb code 7P07 using MOE software. Docking simulations were performed through the Dock menu, with Site on Ligand Atoms if the protein had a natural ligand, otherwise Site was performed with Site Finder. The docking process was performed using Triangle Matcher placement with the London dG score function and 10 poses, followed by Refinement using the Rigid Receptor method with the GBVI/WSA dG score function and 1 pose. The docking results were saved in the output column in .mdb format. The completed docking process generates a data table containing the Docking Score (S) and Root Mean Square Deviation (RMSD), which are displayed in the Database Viewer window. The ligand position for each pose is displayed by opening the browse window in the database menu in the Database Viewer window. The docking results include a visualization of the ligand–α-glucosidase enzyme interaction and a Docking Score (S) that reflects the binding energy required for receptor–ligand interaction. This score serves as an indicator for predicting the antidiabetic potential of bioactive compounds from Jeringau (*A. calamus* L.)[24].

Results and Discussion

Pharmacokinetic Screening and Lipinski Rule of Five

The parameters used in the ADMET study are Caco-2 values, HIA (Human Intestinal Absorption), and Plasma Protein Binding. The Caco-2 parameter plays a role in determining the permeability of compounds. HIA (Human Intestinal Absorption) is used to predict the percentage of drug absorption in the human intestine, and Plasma Protein Binding measures the percentage of compounds that bind to plasma proteins [26]. Previous literature has reported various pharmacological activities of the Jeringau plant (*A. calamus* L.), which shows potential biological activity as an antioxidant and antidiabetic agent [27][13]. In this study, pharmacokinetic and toxicity screening were conducted on several active compounds from Jeringau, with the results shown in Table 1.

Based on the results of pharmacokinetic and toxicity predictions in Table 1, the active compounds in Jeringau show that all test compounds have medium permeability to Caco-2 cells (4–70 nm/sec). This range indicates that the test compounds can pass through the intestinal epithelial cell barrier. The Human Intestinal Absorption (HIA) parameter is good in the range of 70–100%, and the majority of the test compounds have good HIA values. These findings indicate that the compounds possess high absorption potential In addition, the Plasma Protein Binding (PBB) percentage parameter shows that some test compounds have strong bonds with plasma proteins because they are in the range of >90% [26]. Compounds included in this category include α-asarone, apigenin, galgravin, ganschisandrin, methyl eugenol, and veraguensin. Furthermore, based on the toxicity

predictions shown in Table 1, almost all compounds in Jeringau show toxic potential. However, the toxic potential of a compound does not always indicate a health hazard, as some natural compounds have been shown to have selective toxicity to cancer cells without damaging normal cells. In addition, toxicity also depends on the concentration and duration of exposure [28]

The drug-likeness analysis of Jeringau (*A. Calamus L).* compounds were conducted to assess their suitability for oral administration, focusing on pharmacokinetic parameters such as absorption and distribution. Compounds that fulfil Lipinski's Rule of Five are considered to have favorable characteristics as oral drug candidates. The criteria established by Lipinski's Rule of Five include the physicochemical properties of the compound based on molecular weight, log P, the number of hydrogen bond donors and acceptors, and molar refractivity [29][30]. The data on the application of Lipinski's rule can be seen in Table 2.

Table 1. Results of Pharmacokinetic Predictions and Toxicity

Compounds	Pharmacokinetic prediction			Toxicity		
	Caco-2 (nm/sec)	HIA (%)	PPB (%)	Ames test	Carcinoma mouse	Carcino rots
α-acarone	58.09	100	93.39	Mutagen	+	+
Acarone	26.06	99.52	84.88	Mutagen	+	+
Apigenin	10.54	88.12	97.25	Mutagen	+	+
Ferulic acid	21.11	90.60	50.41	Mutagen	-	+
Galgravin	54.57	97.49	93.78	Mutagen	-	+
Ganschisandrin	57.14	98.37	99.44	Mutagen	-	+
Methyl eugenol	58.09	100	100	Mutagen	+	+
Tataroside	10.68	24.51	37.32	Mutagen	+	-
Veraguensin	54.57	97.50	93.79	Mutagen	-	+
Quinones	17.45	97.80	85.19	Mutagen	+	+
Acarbose (control)	9.444	-	-	Non-mutagenic	-	-

Table 2. Results of the Linpinski Rule of Five screening

Compounds	Lipinski's parameter				
	Molecular weight (<500 g/mol)	Proton donor (<5)	Proton acceptor (<10)	Log P (<5)	Molar Refractivity 40-130
α-acarone	208	0	3	2.65	56.39
Acarone	236	0	2	3.71	76.54
Apigenin	270	3	5	0.95	61.89
Ferulic acid	194	2	4	0.55	45.35
Galgravin	372	0	5	4.54	103.93
Ganschinsandrin	372	0	5	4.54	103.93
Methyl eugenol	178	0	2	2.49	49.45
Tataroside	444	0	0	0	0.00
Veraguensin	372	0	5	4.54	103.93
Quinones	108	0	2	0.38	23.72
Acarbose (control)	645	14	18	2.13	145.01

As shown in Table 2, all active compounds satisfy the criteria of Lipinski's Rule of Five, suggesting their potential as antidiabetic agents based on molecular weight, the number of hydrogen bond donors and acceptors, and lipophilicity (log P) values. Compounds with a molecular weight greater than 500 g/mol tend to have difficulty penetrating biological membranes, which slows down the absorption process. Meanwhile, the log P value reflects the hydrophobicity and lipophilicity of a compound, which affects its ability to penetrate cell membranes and interact with target receptors [31]. The results of this analysis show that all tested compounds comply with Lipinski's Rule of Five, indicating good potential for further development. By meeting these criteria, the compounds can be further evaluated through in silico simulations of their interactions with the α-glucosidase enzyme.

Analysis of Molecular Docking Results

Molecular docking is a computational method used to predict the interaction between compounds and a target protein in this case, the α-glucosidase enzyme, which plays a key role in the hydrolysis of disaccharides into glucose in the small intestine. By inhibiting the activity of this enzyme, postprandial blood glucose spikes can be reduced, making it an effective strategy in diabetes therapy. This technique aims to evaluate the potential of active compounds from Jeringau (*A. calamus* L) as enzyme inhibitors, with the expectation that they may serve as antidiabetic agents. Docking analysis is conducted by focusing on two main parameters: Binding Affinity (S score) and Root Mean Square Deviation (RMSD). A more negative S score indicates a stronger binding affinity between the ligand and the receptor [32]. Meanwhile, the RMSD value is used to assess the conformity of the ligand's conformation relative to its reference position, with the optimal value being ≤ 2 Å [33]. An RMSD value between 2–3 Å is still considered acceptable; however, values greater than 3 Å are generally regarded as less valid [34].

Based on the results of the molecular docking simulation shown in Table 3, the binding affinity between

the ligands and the α-glucosidase protein receptor can be observed. Several compounds, such as veraguensin, galgravin, ganschisandrin, and tataroside, exhibit strong interaction with the α-glucosidase enzyme. These four tested compounds meet the criteria in terms of pharmacokinetics and toxicity, as well as comply with Lipinski's Rule of Five. The results of the best ligand screening against the α-glucosidase enzyme are presented in Table 3.

Table 3. Results of Molecular Docking of Active Compounds from Jeringau (*A. Calamus* L) Against α-Glucosidase Enzyme

Compounds	S score (kcal/mol)	RMSD (Å)	Amino acid residue	Distance (Å)	Type of bond
α-acarone	-5.77	1.29	Asp348	1.64	Hydrogen bond
Acarone	-6.22	2.15	Asp71	2.70	Hydrogen bond
Apigenin	-5.80	0.93	Arg214	2.51	Hydrogen bond
Ferulic acid	-5.51	1.87	Trp463	3.98	Hydrogen bond
Galgravin	-8.40	1.54	Asp71	1.85	Hydrogen bond
			His114	2.40	Hydrogen bond
			Tyr74	2.85	Hydrogen bond
			Asp348	2.90	Hydrogen bond
			Arg214	2.27	Hydrogen bond
Ganschinsandrin	-8.35	1.62	Trp463	4.29	Hydrogen bond
Methyl eugenol	-5.41	1.17	Met72	5.03	Hydrogen bond
Tataroside	-7.40	1.77	His347	2.54	Hydrogen bond
Quinones	-4.64	2.19	Ile38	4.72	Hydrogen bond
Veraguensin	-8.37	1.89	His83	2.33	Hydrogen bond
Acarbose (control)	-6.16	1.53	Arg440	2.17	Hydrogen bond
			Asp71	3.23	Hydrogen bond
			Glu247	3.04	Hydrogen bond

Based on the results of molecular docking against the α-glucosidase enzyme presented in Table 3, the test compound galgravin showed the best binding affinity value (S), with an S value of -8.40 kcal/mol. This value is significantly lower than acarbose as a reference compound (-6.16 kcal/mol) and better than other test compounds. This difference shows that galgravin compounds are able to bind more strongly and stably to the active site of the enzyme, which can strengthen their effectiveness in inhibiting the α-glucosidase enzyme. These results are supported by previous studies [26][35], which reported that the binding energy range of acarbose (control) was between -6.16 and -7.5 kcal/mol. The binding energy of galgravin is lower than that of acarbose, both in this study and in previous studies. Thus, it reinforces its potential as a more effective α-glucosidase inhibitor in lowering blood glucose levels [26].

Method docking validation was performed by re-docking the original ligand into the active site of the enzyme receptor to evaluate the accuracy of the ligand position prediction algorithm. The RMSD (Root Mean Square Deviation) parameter was used to describe the extent of protein conformation deviation before and after the docking process. Based on the literature, an acceptable RMSD value to show valid molecular interactions is <2 Å [32]. The docking simulation results show that all tested compounds have RMSD values below the threshold. In particular, galgravin exhibit low RMSD values, which further support the validity of the predicted ligand conformations within the enzyme's active site. The S-score, RMSD, and the amino acid residues involved in hydrogen bonding interactions between the test compounds and the α-glucosidase enzyme, including a comparison with the compound acarbose, are presented in Figure 1.

The two-dimensional (2D) and three-dimensional (3D) visualizations of the binding site illustrate the interactions between the compounds galgravin, and the control acarbose with the α-glucosidase enzyme receptor. The 3D visualization shows the ligand's position within the enzyme's active site, while the 2D visualization clearly depicts the amino acid residues involved in hydrogen bonding, marked by dashed lines. In Figure 1(a), galgravin demonstrates good affinity toward the receptor by forming five hydrogen bonds. These interactions involve the residues Asp 71 (1.85 Å), His 114 (2.40 Å), Tyr 74 (2.85 Å), Asp 348 (2.90 Å), and Arg 214 (2.27 Å). The number of hydrogen bonds indicates that galgravin effectively occupies the enzyme's active site, which may competitively inhibit the activity of the α-glucosidase enzyme [24]. Meanwhile, in Figure 1(b) the control acarbose compound, which is well-known as an α-glucosidase inhibitor, forms three hydrogen bonds involving the residues Arg 440 (2.17 Å), Asp 71 (3.23 Å), and Glu 247 (3.04 Å). This confirms that acarbose interacts effectively with the enzyme's active site, making it a relevant comparator.

From these interaction results, it can be concluded that galgravin compounds have promising potential as α-glucosidase inhibitors because they form stronger hydrogen interactions compared to other compounds, including acarbose. The combination of high binding energy, stable interaction conformation, and good pharmacokinetic profile based on ADMET and Lipinski's Rule of Five screening results, strengthens the compound's potential to be developed as an oral antidiabetic agent. The advantage of galgravin lies not only in its interaction affinity but also in its drug-likeness characteristics that support its oral bioavailability. This provides promising therapeutic prospects, especially as a natural alternative to acarbose. However, these results are still predictive based on computational docking methods, so further validation through in vitro and in vivo tests, or advanced molecular dynamics simulations is needed to

confirm the biological activity of these compounds in the context of diabetes treatment.

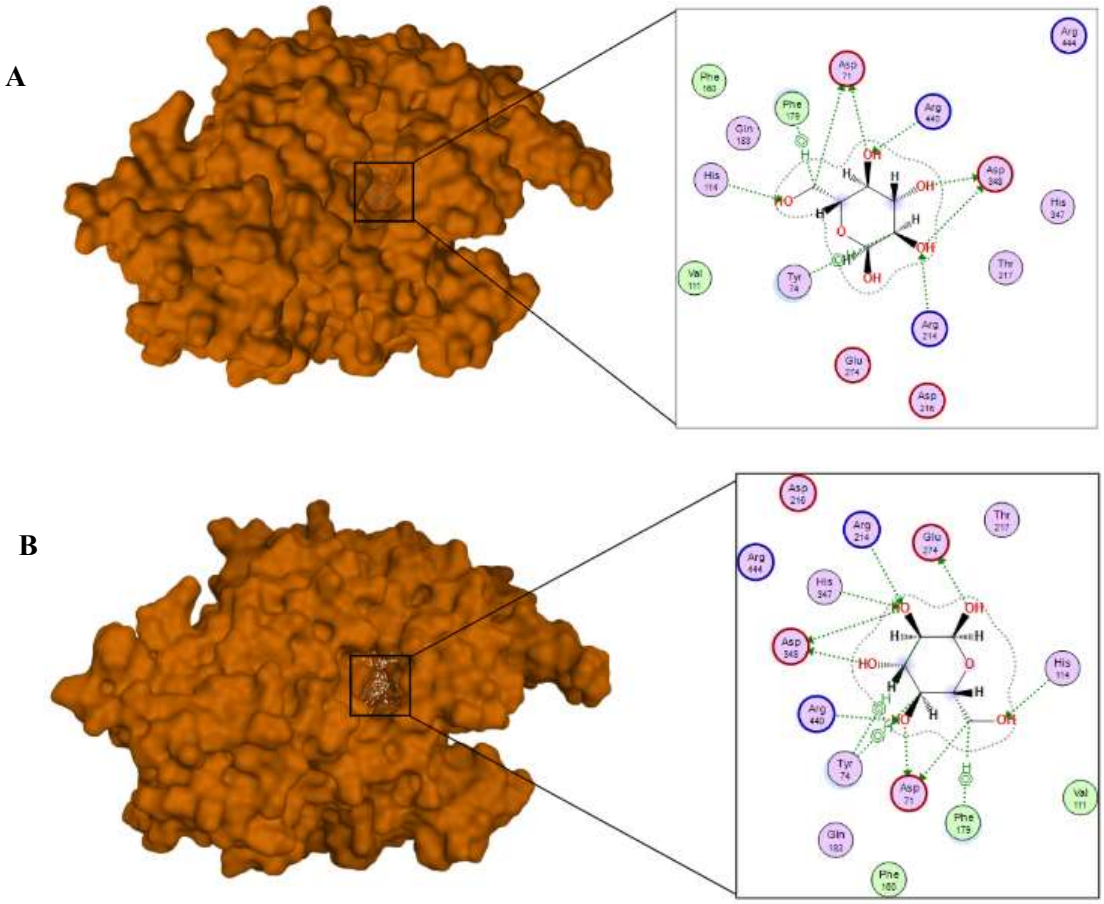

Figure 1. Visualization of molecular interactions of (A) galgravin, and (B) acarbose (reference) with the α-glucosidase enzyme (PDB ID: 7P07)

Conclusion

Based on the results of pharmacokinetic screening, Lipinski's Rule of Five analysis, and molecular docking simulation, active compounds from Jeringau (*A. calamus* L.) showed potential as α-glucosidase enzyme inhibitors. The main compound, galgravin, has a strong binding affinity with a docking score of -8.40 kcal/mol and an RMSD value < 2 Å, which indicates the stability of the interaction. All test compounds meet the criteria for pharmacokinetics and drug-likeness, so they have the potential to be developed as natural-based antidiabetic agents. These findings indicate that galgravin is a strong candidate as an α-glucosidase inhibitor. To strengthen the validity and potential for clinical development, further experimental tests are necessary, including in vitro, in vivo, molecular dynamics simulations, and experimental ADMET evaluations.

Author's Contribution

Rani Sakila Nasution: designed the research, collected bioactive compound data, and conducted molecular docking analysis. Indang Dewata: design methodology and literature review related to pharmacoinformatics. Nofri Yuhelman: coordinated in silico simulation and data processing. Neny Sandrawati: played a role in interpreting the results. Arif Juliari Kusnanda: formulated the research idea, structured the article, and conducted final revisions.

Acknowledgement

The authors would like to express their sincere gratitude to the Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang, for the support and access to computational resources provided during this study.

Reference

[1] S. Octariani, D. Mayasari, and A. M. Ramadhan, "Penambahan molekuler senyawa metabolit sekunder bawang dayak (Eleutherine bulbosa) sebagai penghambat dipeptidil peptidase IV (DPP-4)," *Proceeding Mulawarman Pharm. Conf.*, no. April, pp. 146–153, 2021, [Online]. Available: http://prosiding.farmasi.unmul.ac.id/index.php/mpc/article/view/416/399

[2] IDF, "Type 2 diabetes in adults: management," *Natl. Inst. Heal. Care Excell.*, pp. 1–59, 2022, [Online]. Available: www.nice.org.uk/guidance/ng28

[3] R. Arif *et al.*, "Molecular Docking and Simulation Studies of Antidiabetic Agents Devised from Hypoglycemic Polypeptide-P of Momordica charantia," *Biomed Res. Int.*, vol. 2021, 2021, doi: 10.1155/2021/5561129.

[4] A. Mohammed and N. Tajuddeen, "Antidiabetic compounds from medicinal plants traditionally used for the treatment of diabetes in Africa: A review

update (2015–2020)," *South African J. Bot.*, vol. 146, pp. 585–602, 2022, doi: 10.1016/j.sajb.2021.11.018.

[5] K. G. P. Wasana, A. P. Attanayake, K. A. P. W. Jayatilaka, and T. P. Weerarathna, "Antidiabetic Activity of Widely Used Medicinal Plants in the Sri Lankan Traditional Healthcare System: New Insight to Medicinal Flora in Sri Lanka," *Evidence-based Complement. Altern. Med.*, vol. 2021, 2021, doi: 10.1155/2021/6644004.

[6] J. J. Gout-Zwart, L. A. de Jong, L. Saptenno, and M. J. Postma, "Budget Impact Analysis of Metformin Sustained Release for the Treatment of Type 2 Diabetes in The Netherlands," *PharmacoEconomics - Open*, vol. 4, no. 2, pp. 321–330, 2020, doi: 10.1007/s41669-019-00179-6.

[7] D. Jini, S. Sharmila, A. Anitha, M. Pandian, and R. M. H. Rajapaksha, "In vitro and in silico studies of silver nanoparticles (AgNPs) from Allium sativum against diabetes," *Sci. Rep.*, vol. 12, no. 1, pp. 1–13, 2022, doi: 10.1038/s41598-022-24818-x.

[8] P. Ansari, M. P. Hannon-Fletcher, P. R. Flatt, and Y. H. A. Abdel-Wahab, "Effects of 22 traditional anti-diabetic medicinal plants on DPP-IV enzyme activity and glucose homeostasis in high-fat fed obese diabetic rats," *Biosci. Rep.*, vol. 41, no. 1, pp. 1–15, 2021, doi: 10.1042/BSR20203824.

[9] F. A. Hawa and R. Ruswanto, "Molecular Docking Senyawa Sinamaldehida Kayu Manis Sebagai Penghambat Enzim DPP IV Untuk Terapi Diabetes Mellitus Tipe 2 Molecular Docking Cinnamaldehyde from Cinnamon as DPP IV Inhibitor for Treatment of Type 2 Diabetes Mellitus," *Pros. Semin. Nas. dan Penelit. Kesehat.*, pp. 178–188, 2021.

[10] T. I. Adelusi *et al.*, "GCMS fingerprints and phenolic extracts of Allium sativum inhibit key enzymes associated with type 2 diabetes," *J. Taibah Univ. Med. Sci.*, vol. 18, no. 2, pp. 337–347, 2023, doi: 10.1016/j.jtumed.2022.09.011.

[11] I. M. W. A. Putra, N. Fakhrudin, A. Nurrochmad, and S. Wahyuono, "Antidiabetic activity of Coccinia grandis (L.) Voigt: Bioactive constituents, mechanisms of action, and synergistic effects," *J. Appl. Pharm. Sci.*, vol. 12, no. 1, pp. 041–054, 2022, doi: 10.7324/JAPS.2021.120103.

[12] M. Przeor, "Some Common Medicinal Plants with Antidiabetic Activity, Known and Available in Europe (A Mini-Review)," *Pharmaceuticals*, vol. 15, no. 1, 2022, doi: 10.3390/ph15010065.

[13] F. Frengki *et al.*, "SKRINING POTENSI SENYAWA AKTIF RIMPANG JERINGAU (Acorus calamus, L) SEBAGAI INHIBITOR TERHADAP RESEPTOR α-GLUCOSIDASE MANUSIA SECARA IN SILICO," *J. Ilm. Mhs. Vet. Fak. Kedokt. Hewan Univ. Syiah Kuala*, vol. 6, no. 4, p. 243, 2022, [Online]. Available: www.rscb.org

[14] N. Krishnan, P. K. Singh, M. Sakthivelu, P. Velusamy, S. C. B. Gopinath, and P. Raman, "Influence of thermal treatment on extraction and characteristics of phytochemicals from rhizome of Acorus calamus L," *Biomass Convers. Biorefinery*, no. May, 2022, doi: 10.1007/s13399-022-03415-y.

[15] S. Amalia, L. S. Hasibuan, N. A. Arianti, A. G. Fasya, D. C. Dewi, and D. K. Kadarani, "Sweet flag (Acorus calamus L.) rhizomes chromatography column isolates potential as rich antioxidant compounds," *Indones. J. Fundam. Appl. Chem.*, vol. 9, no. 2, pp. 66–73, 2024, doi: 10.24845/ijfac.v9.i2.66.

[16] I. M. Sugata, I. K. Darmo Suputra, P. Emy Suryanti, M. G. Juniartha, and I. G. A. A. Kartika, "Profil Fitokimia dan Aktivitas Antibakteri dari Massoia aromatic Becc., Acorus calamus L., dan Allium sativum L. terhadap Bakteri Penyebab Rinosinusitis," *J. Ilm. Medicam.*, vol. 9, no. 2, pp. 106–114, 2023, doi: 10.36733/medicamento.v9i2.5961.

[17] Z. Hao *et al.*, "Chemical constituents from Acorus calamus with potent anti-diabetic and hepatoprotective activities," *Fitoterapia*, vol. 169, no. September, pp. 1–5, 2023, doi: 10.1016/j.fitote.2023.105591.

[18] Z. Y. Hao *et al.*, "Alkaloids from the rhizomes of Acorus calamus and their PPARα, PPARγ, and glucokinase-activating activities," *Phytochem. Lett.*, vol. 45, no. May, pp. 37–43, 2021, doi: 10.1016/j.phytol.2021.07.009.

[19] R. Kashyap, S. Patel, and C. Dewangan, "Acorus Calamus : An Ancient Remedy with Modern Medicinal Applications," vol. 2, no. 2, pp. 140–148, 2025.

[20] A. D. Sarie and M. R. Utami, "Bioactivity Analysis of Chalcone-Derived Compounds Based on In-Silico Molecular Docking Study," *J. Pijar MIPA*, vol. 20, no. 2, pp. 251–259, 2025.

[21] M. I. Sugiharto, Y. R. Bintari, and D. S. Damayanti, "Mekanisme Senyawa Aktif Daun Sirsak (Annona muricata Linn.) Sebagai Anti Diabetes : Studi In Silico," *J. Kedokt. Komunitas*, vol. 9, no. 2, pp. 1–13, 2021.

[22] S. Syafrizayanti, A. Putri, M. Salim, and A. J. Kusnanda, "Simulasi Inhibisi Aktivitas Enzim α-Amilase dan α-Glukosidase oleh Senyawa Bioaktif Mikroalga Spirulina platensis," *ALCHEMY J. Penelit. Kim.*, vol. 19, no. 2, p. 223, 2023, doi: 10.20961/alchemy.19.2.73120.223-233.

[23] K. Ernits, C. Kjeldsen, K. Persson, E. Grigor, T. Alamäe, and T. Visnapuu, "Structural insight into a yeast maltase—The BaAG2 from blastobotrys adeninivorans with transglycosylating activity," *J. Fungi*, vol. 7, no. 10, 2021, doi: 10.3390/jof7100816.

[24] W. P. Salim, Y. O. Hutahaean, and F. A. Sitohang, "Molecular Docking and Pharmacoinformatics Study of Curcumin and Arturmeron Compounds in Turmeric Plants (Curcuma Longa Linn.) as Antihypertensive," *J. Sains dan Kesehat.*, vol. 3, no. 1, pp. 242–247, 2024.

[25] R. Mardianingrum, K. R. Bachtiar, S. Susanti, A. N. Aas Nuraisah, and R. Ruswanto, "Studi In Silico Senyawa 1,4-Naphthalenedione-2-Ethyl-3-Hydroxy sebagai Antiinflamasi dan Antikanker Payudara," *ALCHEMY J. Penelit. Kim.*, vol. 17, no. 1, p. 83, 2021, doi: 10.20961/alchemy.17.1.43979.83-95.

[26] Annisa Fitriyani Suryana, Hilda Aprilia, and Taufik

Muhammad Fakih, "Uji Aktivitas In Silico Senyawa Amritoside, Tinosporaside dan Turunannya sebagai Kanditat Senyawa," *Bandung Conf. Ser. Pharm.*, vol. 2, no. 2, pp. 1–10, 2022, doi: 10.29313/bcsp.v2i2.4369.

[27] H. S. Wu *et al.*, "Insulin sensitizing activity of ethyl acetate fraction of Acorus calamus L. in vitro and in vivo," *J. Ethnopharmacol.*, vol. 123, no. 2, pp. 288–292, 2009, doi: 10.1016/j.jep.2009.03.004.

[28] B. Lee, B. Sur, M. Yeom, I. Shim, H. Lee, and D. H. Hahm, "Alpha-asarone, a major component of Acorus gramineus, attenuates corticosterone-induced anxiety-like behaviours via modulating TrkB signaling process," *Korean J. Physiol. Pharmacol.*, vol. 18, no. 3, pp. 191–200, 2014, doi: 10.4196/kjpp.2014.18.3.191.

[29] V. Ivanović, M. Rančić, B. Arsić, and A. Pavlović, "Lipinski's rule of five, famous extensions and famous exceptions," *Chem. Naissensis*, vol. 3, no. 1, pp. 171–181, 2020, doi: 10.46793/chemn3.1.171i.

[30] C. A. Lipinski, "Lead- and drug-like compounds: The rule-of-five revolution," *Drug Discov. Today Technol.*, vol. 1, no. 4, pp. 337–341, 2004, doi: 10.1016/j.ddtec.2004.11.007.

[31] N. Yulia and L. Setiyabudi, "Skrining Fitokimia dan Uji Aktivitas Antibakteri Ekstrak Jeringau dan Brotowali terhadap Streptococcus pyogenes," *Pros. Semin. Nas. dan Disem. Penelit. Dosen*, vol. 1, no. 1, pp. 36–41, 2021.

[32] N. Frimayanti, A. Lukman, and L. Nathania, "Studi molecular docking senyawa 1,5-benzothiazepine sebagai inhibitor dengue DEN-2 NS2B/NS3 serine protease," *Chempublish J.*, vol. 6, no. 1, pp. 54–62, 2021, doi: 10.22437/chp.v6i1.12980.

[33] P.- Purwaniati, "Molecular Docking Study on COVID-19 Drug Activity of N-(2-phenylethyl)methanesulfonamide Derivatives as Main Protease Inhibitor," *ad-Dawaa' J. Pharm. Sci.*, vol. 3, no. 1, pp. 1–11, 2020, doi: 10.24252/djps.v3i1.13945.

[34] D. Ramírez and J. Caballero, "Is It Reliable to Take the Molecular Docking Top Scoring Position as the Best Solution without Considering Available Structural Data?," *Molecules*, vol. 23, no. 5, pp. 1–17, 2018, doi: 10.3390/molecules23051038.

[35] R. Arcinthya Rachmania, Supandi;, and O. Anggun Larasati, "Senyawa diterpenoid lakton herba sambiloto (," *Pharmacy*, vol. 12, no. 02, pp. 210–222, 2015.