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In Silico Study of Natural Bioactive Compounds as Potential Anti-Mpox Through Molecular Docking on D13 Protein

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ABSTRACT

Mpox is a zoonotic disease caused by Monkeypox virus (MPXV), with a surge in cases posing a major challenge due to the unavailability of specific antivirals. Indonesia's biodiversity offers great opportunities for the exploration of bioactive compounds from natural materials as therapeutic alternatives, especially by targeting the D13 protein, which is an essential structural protein in MPXV. This study aims to evaluate the interaction and affinity of molecular tethering of bioactive compounds to D13 protein and analyse the physicochemical, pharmacokinetic and toxicity profiles of the compounds. The research was conducted using molecular tethering method using Gnina software on Google Colab platform. Antiviral activity prediction was performed using PASS Online, followed by Lipinski's Rule of Five (RO5) evaluation and pharmacokinetic and toxicity analysis using SwissADME and pkCSM. The results showed that the tested bioactive compounds had good potential antiviral activity and fulfilled the RO5 criteria. Pharmacokinetic and toxicity analyses indicated good pharmacokinetic profiles but poor metabolic profiles, with predicted low toxicity levels, supporting the feasibility of these compounds to be further developed as therapeutic candidates. In addition, the bioactive compound showed the ability to interact with D13 protein with the best affinity tethering value of myricetin with a free binding energy (ΔG) value of -8.37 kcal/mol, making it a potential candidate as an antiviral for Mpox.

Keywords: Mpox; bioactive compounds; in silico; D13 protein; molecular docking

INTRODUCTION

Mpox, or monkey pox, is a zoonotic disease caused by monkeypox virus (MPXV), a member of the genus Orthopoxvirus in the family Poxviridae. The virus was first discovered in monkeys in a Danish laboratory in 1958 and was first reported to infect humans in the Democratic Republic of Congo in 1970 (Sun et al., 2024). Symptoms of mpox resemble smallpox, such as fever, skin rash, and enlarged lymph nodes. Most cases recover within 2-4 weeks, but some infections can progress to become severe enough to cause death (Korespondensi and Kuncoro, n.d.) Based on genomic analysis, MPXV is divided into two main clades, namely the Central African clade (Congo Basin) with a mortality rate of 10.6% and the West African clade with a mortality rate of 3.6% (Xiang & White, 2022).

Director-General of World Health Organization (WHO) designated mpox on July 23, 2022 as a Public Health Emergency of International Concern (PHEIC) due to the significant increase in global cases (WHO, 2024). As of July 2024, more than 103,048 cases have been reported in 121 countries, with a total of 229 deaths. In Indonesia, the Ministry of Health reported one positive confirmed case in August 2022 (Kemkes.go.id, 2022). This global spread poses a major

challenge, especially as there is no antiviral or vaccine specifically approved for MPXV infection.

Drugs such as tecovirimat that were originally developed for smallpox are used as interim therapy for Mpox, but their effectiveness against MPXV remains limited. In addition, significant genomic changes in MPXV of 2022 compared to previous strains further emphasize the need for the development of new, more specific therapies (Isidro et al., 2022). Therefore, research looking for drug candidates needs to be carried out by targeting one of the stages of the mpox virus life cycle as a potential antiviral that is more effective against MPXV. One of them is by targeting important proteins in the viral life cycle, such as the D13 protein, which plays a role in the formation of the viral membrane and its structural integrity (Kharwar et al., 2023).

Indonesia is known as one of the countries with the highest biodiversity in the world. Bioactive compounds from natural materials such as apigenin, myricetin, kaempferol, and quercetin have long been used in traditional medicine and proven to have antiviral activity. Their safety, effectiveness, and abundant availability make these compounds potential candidates for the development of nature-based antivirals.

In silico-based studies have shown success in predicting the potential of bioactive compounds against various viruses, such as SARS-CoV-2, dengue virus, and HIV (Choudhury et al., 2021; Lim et al., 2021). Based on the similarity of structural proteins in the Orthopoxvirus family in MPXV and vaccinia virus(Lam et al., 2022). Therefore, this study used the structural protein of vaccinia virus D13 which is one of the selected as a molecular target in this study. This study aims to evaluate the potential of bioactive compounds from plants - specifically apigenin, myricetin, kaempferol, and quercetin in targeting the D13 MPXV protein using molecular docking techniques. With this approach, it is hoped that the research can make a significant contribution in the development of natural ingredient-based antivirals that are more effective, safe, and specific for MPXV infection.

METHODS

This study used the in-silico method with the Molecular Docking approach, which was conducted from August 2024 to November 2024 at the Pharmacology Department of Sam Ratulangi University.

The receptor preparation stages began with modeling the D13 protein structure using SwissMODEL and determining the receptor and ligand binding sites using AutoDock Tools. The binding area was determined based on the active stide identified in previous studies, which is includes residues Glu A:134, Asp A:137, Thr A:147, Ile A:148, Glu A:150, Ser B:285, Ser B:366, Ser B:385, His B:386, Ser B:387, and Asn B:389 (Gulati et al., 2023). Furthermore, the preparation of the test ligand began by downloading the three-dimensional structure of the ligand from PubChem. Prediction of biological activity of test compounds and comparator drugs was carried out using the PASS online web server to obtain probable activity (Pa) and probable inactivity (Pi) values as indicators of biological activity. Then, the prediction of physicochemical properties, pharmacokinetics, and toxicity was analyzed using SwissADME and pkCSM-pharmacokinetics starting with the download of the SMILES code from the

PubChem web server, then physicochemical analysis was carried out consisting of molecular weight parameters, lipophilicity, number of Hydrogen acceptors (H-acceptors), number of Hydrogen donors (H-donors), violation of Lipinski's Rule of 5. Furthermore, pharmacokinetic and toxicity parameters were adjusted according to the study.

Identification of the active site on the D13 protein was carried out using CASTp, which can identify cavities and pockets in the protein structure, and lists all atoms that play a role in protein formation. The next stage continued with the tethering of target receptor molecules and test ligands using Gnina software with a predetermined grid box size (McNutt et al., 2021). This process produces a free binding energy (ΔG) value between the test ligand and the target receptor, where the most negative ΔG value will be selected as the best result. The docking results are then analyzed and visualized using Discovery Studio Visualizer to observe 2D and 3D interactions between the ligand and the receptor, where 3D visualization is required to strengthen the analysis of the docking results. This analysis involves observing important amino acid residues as well as the type of interaction formed at the active site of the receptor. This study aims to evaluate the potential biological activity of test compounds against D13 protein based on binding energy values and interaction visualization.

RESULTS AND DISCUSSION

Bioinformatics research, especially through in silico approaches, has become an important method in modern drug design and discovery. In this study, an in-silico approach was applied to evaluate the activity of bioactive compounds from natural materials against D13 protein, which has potential as an anti-mpox target. By using molecular docking techniques, this study provides an in-depth insight into the interaction and binding affinity of the test compounds towards the active site of the D13 protein. This is important because the in-silico approach can reduce the need for intensive and expensive laboratory experiments, while accelerating the molecular screening process in a short time.

The bioactive compounds used in this study include apigenin, myricetin, kaempferol, and quercetin, which are known to have various pharmacological effects, including antiviral activity. Biological activity prediction results using PASS Online showed that all test compounds had Pa > Pi values (**Table 1**), indicating potential biological activity against anti-viruses (Filimonov et al., 2014).

Table 1. Pa and Pi based on PASS Online

Compound	Pa	Pi
Apigenin	0,209	0,089
Myricetin	0,334	0,026
Kaempferol	0,260	0,054
Quercetin	0,262	0,053
Rifampicin	0,294	0,062

Following the predicting of the biological activity, the physicochemical, pharmacokinetic and toxicity properties of the test compounds were analyzed using the pkCSM server (Pires et al., 2015). This evaluation aims to ensure that

the compound has suitable characteristics as a drug candidate. Based on Lipinski's law, an ideal compound for the oral route of administration must meet certain criteria, such as molecular weight < 500 g/mol, logP < 5, number of hydrogen bond donors < 5, and number of hydrogen bond acceptors < 10 (Chen et al., 2020). All bioactive compounds met these criteria, except myricetin which has six hydrogen bond donors (**Table 2**). However, Lipinski's rule allows a maximum of one parameter violation, so myricetin was still considered to meet the bioavailability criteria (Maharani et al., 2024).

Table 2. Physicochemical properties results based on Lipinski's Rule of Five

Compound	***Lipinski's Rule of Five***					
	Molecular Weight (g/mol)	Log P	H-Bond donor	H-Bond acceptor	Lipinski's Violations	Drug Likeness
	<500	<5	<5	<10	<2	
Apigenin	270,24	2,57	3	5	0	yes
Myricetin	318,24	1,69	6	8	1	yes
Kaempferol	286,23	2,28	4	6	0	yes
Quercetin	302,23	1,98	5	7	0	yes

The absorption parameters (**Table 3**), including water solubility, colorectal adenocarcinoma) Caco-2 permeability, and human intestinal absorption (HIA). All parameters showed good results, with compounds having suitable solubility and permeability for optimal absorption.

Table 3. Absorption prediction of bioactive compounds and comparators

Compound	**Absorption**		
	Water Solubility (log mol/L)	Caco-2 permeability (log Papp)	HIA (%)
Apigenin	-3,329	1,007	93,25
Myricetin	-2,951	1,007	65,93
Kaempferol	-3,04	0,032	74,29
Quercetin	-2,925	-0,229	77,207
Rifampicin	-2,947	-0,369	55.567

The distribution parameters such as volume of distribution at steady state (VDss), blood-brain barrier (BBB) permeability, and central nervous system (CNS) permeability were also assessed (**Table 4**). Results showed that none of the compounds meet the > 0,3 theshold, indicating poor BBB permeability for all. Myricetin (-1,492) and quercetin (1,098) are less likely to cross the BBB compared to Apigenin (-0,734) and kaempferol (0,939). Rifampicin shows the lowest BBB permeability (-2,543), indicating it is unlikely to penetrate the brain. Apigenin (0,734) and kaempferol (-0,939) fall well within the acceptable range for CNS permeability. Myricetin (-1.492) and Quercetin (-1.098) also exhibit acceptable CNS permeability, although slightly less favorable compared to Apigenin and Kaempferol. Rifampicin (-4.642) fails to meet the threshold, indicating it is highly unlikely to affect CNS functions.

Table 4. Distribution prediction of bioactive compounds and comparators

Compound	Distribution		
	VDss (log L/kg)	BBB permeability (log BB)	CNS permeability (log PS)
	>0,45	> 0,3	>-2
Apigenin	0,822	-0,734	-0,734
Myricetin	1,317	-1,492	-1,492
Kaempferol	1,274	-0,939	-0,939
Quercetin	1,559	-1,098	-1,098
Rifampicin	1,179	-2,543	-4,642

The metabolism of the compounds was also analyzed by looking at the interaction of the compounds with cytochrome P450 enzymes. Results showed that myricetin, kaempferol, and quercetin were not inhibitors of CYP1A2 or CYP2C19, but apigenin showed activity as an inhibitor against both enzymes (**Table 5**).

Table 5. Metabolism prediction of bioactive compounds and comparators

Compound	Metabolism			
	CYP1A2 *inhibitor*	CYP2C19 *inhibitor*	CYP2D6 *substrate*	CYP3A4 *substrate*
Apigenin	yes	yes	no	no
Myricetin	yes	no	no	no
Kaempferol	yes	no	no	no
Quercetin	yes	no	no	no
Rifampicin	no	no	no	no

The excretion parameters (**Table 6**), such as total clearance and renal organic cation transporter 2 (OCT2) substrate, showed that all four compounds had good excretory disposition and were independent of the OCT2 transporter.

Table 6. Excretion prediction of bioactive compounds and comparators

Compound	Excretion	
	Total Clearance (log ml/min/kg)	Renal OCT2 substrate
Apigenin	0,566	no
Myricetin	0,422	no
Kaempferol	0,477	no
Quercetin	0,407	no
Rifampicin	-0,653	no

All compounds, including the comparator Rifampicin, are non-mutagenic (negative for AMES toxicity). This suggests these compounds have no genotoxic risk, supporting their safety profiles for further exploration. Apigenin, myricetin, kaempferol, and quercetin are predicted to have no hERG I/II inhibition, indicating a low likelihood of cardiotoxicity. In contrast, Rifampicin is predicted to inhibit hERG channels, suggesting a potential cardiotoxic risk that warrants further evaluation. Lethal dose 50 (LD50) values that fell into the “acutely harmless” category according to WHO classification (WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification, 2019 Edition, 2020). In addition, all compounds were also not hepatotoxic (**Table 7**).

Table 7. Toxicity prediction of bioactive compounds and comparators

Compound	Toxicity			
	AMES toxicity	hERG I&II *inhibitors*	LD50 (mol/kg)	Hepatotoxicity
Apigenin	no	no	2,45	no
Myricetin	no	no	2,49	no
Kaempferol	no	no	2,44	no
Quercetin	no	no	2,47	no
Rifampicin	no	yes	2,53	no

Through molecular tethering techniques, the strength of the compound's interaction with the active site of the D13 protein was analyzed based on the binding affinity score (ΔG) (**Table 8**). More negative the ΔG value, more stable the ligand-protein interaction, indicating a high biological potential of the compound (Muhammed & Aki-Yalcin, 2024). The results showed that the four bioactive compounds had ΔG values ranging from -8.37 kcal/mol to -6.98 kcal/mol against D13 protein. Based on the test results, it was found that four test ligands and one comparator drug produced negative values (<0) against the receptor (Meiyanto, 2012). These results are in accordance with the expected value, namely the lower the ΔG value, the more stable the ligand and receptor bond interaction (Tallei et al., 2024). The best value was obtained by myricetin with ΔG -8.37 kcal/mol, which was lower than that of the comparator drug, rifampicin. This indicates that myricetin has the potential to interact more stably with the target protein than the comparator.

Table 8. Free binding energy values

Compound	**Binding Affinity (ΔG) (kcal/mol)**
Apigenin	-6,98
Myricetin	-8,37
Kaempferol	-7,11
Quercetin	-7,39
Rifampicin	-8,00

Visualization of the tethering results also showed the presence of various types of interactions, including hydrogen bonds, hydrophobic interactions, and electrostatics, which strengthened the stability of the ligand-protein complex. Amino acid residues in the active site of the D13 protein involved in the interaction include His B:386 for apigenin and Ser B:366 for rifampicin. The hydrogen bonds formed contribute to the stability of the interaction, while hydrophobic and electrostatic interactions help to increase the conformational stability of the ligand. The presence of van der Waals interactions also supports the positional alignment of the ligand and receptor, which is important in ensuring bond stability.

Table 9. 2D visualization of interactions between test ligands and comparator ligands

Ligand	Hydrogen Bond		Hydrophobic Interactions	Interaksi Electrostatic
	AA	Distance (Å)		
Apigenin	Lys B:281	2,95	His B:383, Ser B:385, Ile B:388, Asn B:389, Glu A:134, Asp B:285, Ser A:133	His B:386, Ile B:284
	Ile B:384	2,78		
	His B:386	3,22		
	Lys B:436	2,88		
Myricetin	Tyr A: 276	2,43;2,99	Lys A:127, Ser A:132, Glu A:134, Asp B:285, His B:386, Ile B:388, Asn B:389, Ile B:284, Lys B:281	Glu B:280
	Glu B:280	2,53; 3,89		
	Lys B:436	3,36		
	Ser A:133	3,67		
Kaempferol	Ser A:133	3,33	Glu A:134, Glu B:280, Lys B:281, Ile B:284, Asp B:285 His B:386, Ser B:387, Ile B:388, Asn B:389	-
Quercetin	Ser A:133	2,07;2,22	Ser A:132, Glu A:134, Asp B:279, Asn B:435, Asn B:471, Lys B:434, Lys B:436	Lys A:127, Glu B:280
	Tyr A:276	4,13		
Rifampicin	Ile A:140	1,84	Ser B:387, Ser B:386, B:385, Lys B:364, Phe B:365, Leu A:142, Thr A:147, Gly A:141, Ile A:140, Asn B:389, Asp A:146, Ile B:390	Glu B:280, Glu A:134, Lys B:436
	Ser B:366	3,04:3,25		
	Thr B:37	3,36		

The four bioactive compounds used almost all amino acid residues act on the active site of the D13 receptor. Visualization results show that rifampicin as a comparative drug binds to active site residues through hydrogen bonds such as Ile A:140 at a distance of 1.84, Ser B:366 at a distance of 3.04; 3.25 (**Table 9**). The interaction of rifampicin with the target receptor also involves hydrophobic interactions in the form of van der Waals bonds that occur with active site residues namely Ser B:387, Ser B:386, B:385, Lys B:364, Phe B:365, Leu A:142, Thr A:147, Gly A:141, Ile A:140, Asn B:389, Asp A:146, and Ile B:390. Van der Waals bonding can optimize other stronger interactions such as hydrogen bonding and electrostatic interactions by precisely aligning the position of the ligand and receptor (Gottschalk et al., 2016). Both van der Waals and hydrogen bonds play an important role and become equally important in determining the outcome of molecular tethering. Meanwhile, electrostatic interactions play a role in increasing conformational stability (Ratu et al., 2021). Hydrogen bonds formed between the test ligand and the same amino acid residue as in the natural ligand or comparator

ligand indicate a similar type of interaction (**Figure 1**), which reflects similarity in activity.

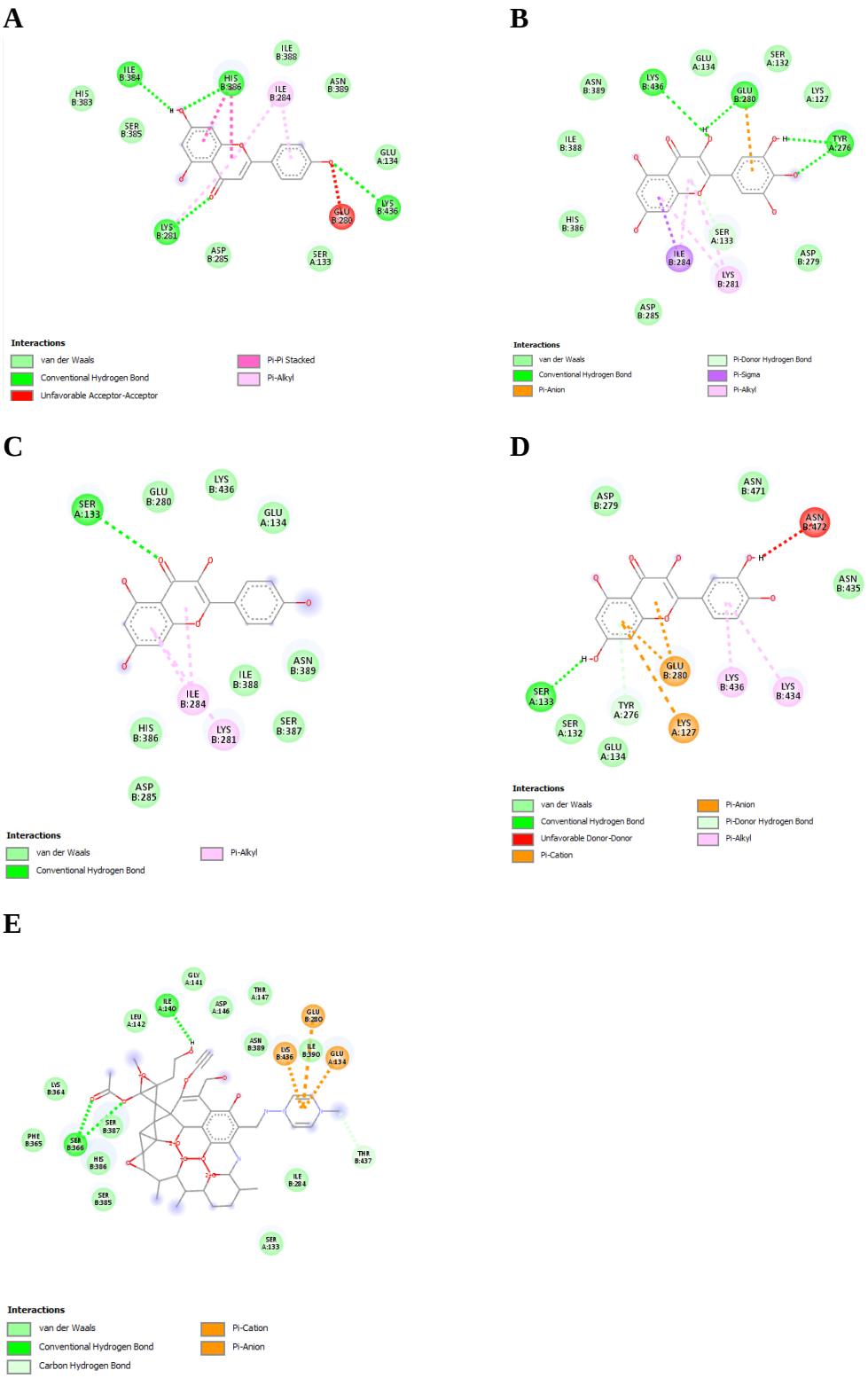

Figure 1. Visualization of tethering results with each ligand
Description: (A) *apigenin*, (B) *myricetin*, (C) *kaempferol*, (D) *quercetin*, (E) rifampicin

Thus, based on the test results of the physicochemical properties, it shows that the four compounds meet the criteria for ideal physicochemical properties based on Lipinski's rule of five. Meanwhile, the pharmacokinetic and toxicity profiles of the four test compounds show that the four compounds have good profiles.

COCLUSIONS

The test ligands apigenin, myricetin, kaempferol, and quercetin demonstrated binding affinity values to D13, with myricetin exhibiting the optimal interaction value, which is lower than the drug rifampicin. Myricetin exhibited interactions with the same key residues as the amino acid residues of rifampicin. The results of the analysis using the pKCSM program also show that the four active compounds have pharmacokinetic and toxicity profiles that meet the criteria, have low toxicity potential, and are thus suitable for further development as anti-mox candidates.

REFERENCES

Chen, X., Li, H., Tian, L., Li, Q., Luo, J., & Zhang, Y. (2020). Analysis of the Physicochemical Properties of Acaricides Based on Lipinski's Rule of Five. *Journal of Computational Biology*, *27*, 1397–1406.

Choudhury, A., Das, N. C., Patra, R., Bhattacharya, M., Ghosh, P., Patra, B. C., & Mukherjee, S. (2021). Exploring the Binding Efficacy of Ivermectin Against the Key Proteins of SARS-CoV-2 Pathogenesis: An *in silico* Approach. *Future Virology*, *16*, 277–291.

Filimonov, D. A., Lagunin, A. A., Gloriozova, T. A., Rudik, A. V., Druzhilovskii, D. S., Pogodin, P. V., & Poroikov, V. V. (2014). Prediction of the Biological Activity Spectra of Organic Compounds Using the Pass Online Web Resource. *Chemistry of Heterocyclic Compounds*, *50*, 444–457.

Gottschalk, H. C., Altnöder, J., Heger, M., & Suhm, M. A. (2016). Control over the Hydrogen-Bond Docking Site in Anisole by Ring Methylation. *Angewandte Chemie International Edition*, *55*, 1921–1924.

Gulati, P., Chadha, J., Harjai, K., & Singh, S. (2023). Targeting envelope proteins of poxviruses to repurpose phytochemicals against monkeypox: An in-silico investigation. *Frontiers in Microbiology*, *13*. https://doi.org/10.3389/fmicb.2022.1073419

Isidro, J., Borges, V., Pinto, M., Sobral, D., Santos, J. D., Nunes, A., … Gomes, J. P. (2022). Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. *Nature Medicine*, *28*, 1569–1572.

Kemkes.go.id. (2022). *Kasus Monkeypox Pertama di Indonesia Terkonfirmasi*.

Kharwar, R., Bhatt, M., Patel, K., Patel, S., & Daxini, N. (2023). A computational approach to identify natural putative inhibitors to combat monkeypox. In *Nanotechnology and in Silico Tools: Natural Remedies and Drug Discovery* (pp. 285–308). Elsevier.

Korespondensi, A., & Kuncoro, C. S. (n.d.). *Monkeypox: Manifestasi dan Diagnosis*.

Lam, H. Y. I., Guan, J. S., & Mu, Y. (2022). In Silico Repurposed Drugs against Monkeypox Virus. *Molecules*, *27*. https://doi.org/10.3390/molecules27165277

Lim, S. Y. M., Chieng, J. Y., & Pan, Y. (2021). Recent insights on anti-dengue virus (DENV) medicinal plants: Review on *in vitro* , *in vivo* and *in silico* discoveries. *All Life*, *14*, 1–33.

Maharani, D. S., Redjeki, S. G., Emamia, E. S., Aulia, A. P., Nurviana, D., Aulifa, D. L., … Karim, B. K. (2024). *Identifikasi Senyawa Aktif Rimpang Kunyit (Curcuma longa L.) sebagai Kandidat Antikanker Melalui Studi In Silico terhadap Reseptor Lymphocyte-Specific Protein Tyrosine Kinase*. *12*.

McNutt, A. T., Francoeur, P., Aggarwal, R., Masuda, T., Meli, R., Ragoza, M., … Koes, D. R. (2021). GNINA 1.0: Molecular docking with deep learning. *Journal of Cheminformatics*, *13*, 43.

Meiyanto, E. (2012). Docking Kurkumin Dan Senyawa Analognya Pada Reseptor Progesteron: Studi Interaksinya Sebagai Selective Progesterone Receptor Modulators (SPRMs). *Pharmacon: Jurnal Farmasi Indonesia*, *13*, 55–60.

Muhammed, M. T., & Aki-Yalcin, E. (2024). Molecular Docking: Principles, Advances, and Its Applications in DrugDiscovery. *Letters in Drug Design & Discovery*, *21*, 480–495.

Pires, D. E. V., Blundell, T. L., & Ascher, D. B. (2015). pkCSM: Predicting small-molecule pharmacokinetic and toxicity properties using graph-based signatures. *Journal of Medicinal Chemistry*, *58*, 4066–4072.

Ratu, B. D. P. M., Bodhi, W., Budiarso, F., Kepel, B. J., Fatimawali, ., & Manampiring, A. (2021). Molecular Docking Senyawa Gingerol dan Zingiberol pada Tanaman Jahe sebagai Penanganan COVID-19. *Jurnal e-Biomedik*, *9*. https://doi.org/10.35790/ebm.v9i1.32361

Sun, Y., Nie, W., Tian, D., & Ye, Q. (2024). Human monkeypox virus: Epidemiologic review and research progress in diagnosis and treatment. *Journal of Clinical Virology*, *171*. https://doi.org/10.1016/j.jcv.2024.105662

Tallei, T. E., Fatimawali, Adam, A. A., Ekatanti, D., Celik, I., Fatriani, R., … Idroes, R. (2024). Molecular insights into the anti-inflammatory activity of fermented pineapple juice using multimodal computational studies. *Archiv Der Pharmazie*, *357*, 2300422.

WHO. (2024). *2022-24 Mpox Outbreak: Global Trends. Geneva: World Health Organization, 2024.*

WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification, 2019 Edition (2nd ed). (2020). Geneva: World Health Organization.

Xiang, Y., & White, A. (2022). Monkeypox virus emerges from the shadow of its more infamous cousin: Family biology matters. *Emerging Microbes and Infections*, *11*, 1768–1777.