JPPIPA 12(11) (2026)

Jurnal Penelitian Pendidikan IPA

http://jppipa.unram.ac.id/index.php/jppipa/index

Molecular Docking of Active Compounds from Centella asiatica, Coenzyme Q10, and Ethyl Ascorbic Acid Targeting Tyrosinase Enzyme for Skin Brightening Applications

Josephine[1], Ni Luh Dewi Aryani[2*], Dini Kesuma[3]

[1] Master's Degree Program Industrial Pharmacy, Faculty of Pharmacy, University of Surabaya, Surabaya, Indonesia.
[2] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Surabaya, Surabaya, Indonesia.
[3] Department of Pharmaceutics Pharmacy, Faculty of Pharmacy, University of Surabaya, Surabaya, Indonesia.

Received: July 31, 2026
Revised: August 22, 2026
Accepted: November 16, 2026
Published: November 30, 2026

Corresponding Author:
Ni Luh Dewi Aryani
dewi_aryani@staff.ubaya.ac.id

DOI: 10.29303/jppipa.v12i11.12363

Open Access

© 2026 The Authors. This article is distributed under a (CC-BY License)

Abstract: Tyrosinase is a key enzyme responsible for melanin biosynthesis, and its overactivity contributes to hyperpigmentation disorders. The need for safer and more effective skin-brightening agents has encouraged the exploration of natural and antioxidant-based compounds. This study aimed to evaluate the in silico inhibitory potential of active compounds from *Centella asiatica*, Coenzyme Q10 (CoQ10), and Ethyl Ascorbic Acid (EAA) against tyrosinase. Molecular docking was performed using Molegro Virtual Docking 7.0 with the crystal structure of tyrosinase (PDB ID: 2Y9X). Binding affinity was assessed based on rerank score, hydrogen bonding, and steric interaction analysis. The results demonstrated that 3-O-ethyl ascorbic acid exhibited the strongest binding affinity (−66.73 kcal/mol), followed by asiatic acid (−36.92 kcal/mol) and 2-O-ethyl ascorbic acid (−34.30 kcal/mol). Key interactions involved hydrogen bonds and steric interactions within the active site of the enzyme, suggesting potential interference with catalytic residues. These findings indicate that the tested compounds possess promising anti-tyrosinase activity and may serve as potential candidates for skin-brightening formulations. However, further in vitro and in vivo studies are required to validate their biological activity.

Keywords: Centella asiatica; Coenzyme Q10; Ethyl ascorbic acid; Molecular Docking; Tyrosinase

Introduction

Hyperpigmentation is a skin disorder characterized by increased melanin production, which causes the skin to darken in certain areas. Melanin is synthesized through the process of melanogenesis, which is catalyzed by the enzyme tyrosinase. This enzyme is a metalloproteinase containing copper ions (Cu^{2+}), playing a crucial role in converting tyrosine into L-DOPA and subsequently into DOPA-quinone, which is a precursor to melanin (Prasetyo et al., 2020). Therefore, tyrosinase has become a primary target in the development of skin-lightening active ingredients, particularly within the cosmetics industry.

Several studies have shown that natural compounds have potential as tyrosinase enzyme inhibitors. One approach used to evaluate this potential is in silico studies using molecular docking methods, which aim to predict interactions between ligands and receptors and estimate the strength or affinity of the bonds formed between them (Chang et al., 2023). An in silico study by Fernenda et al. (2023) showed that Centella asiatica exhibits tyrosinase inhibitory activity of 31.25% at a concentration of 1.67 mg/mL, where triterpenoid compounds such as asiatic acid, asiaticoside, and madecassic acid play a role in reducing melanin levels by inhibiting tyrosinase mRNA expression.

How to Cite:
Josephine, J., Aryani, N. L. D., & Kesuma, D. (2026). Molecular Docking of Active Compounds from Centella asiatica, Coenzyme Q10, and Ethyl Ascorbic Acid Targeting Tyrosinase Enzyme for Skin Brightening Applications. *Jurnal Penelitian Pendidikan IPA*, *12*(11), 42–48. https://doi.org/10.29303/jppipa.v12i11.12363

In this context, compounds from Centella asiatica, such as madecassoside and asiaticoside, have been recognized for their antioxidant properties and their ability to improve skin structure (Sutrisno et al., 2021). In addition to compounds from Centella asiatica, Coenzyme Q10 (CoQ10) has also been shown to reduce oxidative stress and suppress pigmentation processes caused by free radicals (Permatasari et al., 2020). Coenzyme Q10 is known to have a high affinity for various lipids, such as isopropyl palmitate, with the lowest ΔG value of -1.38 kcal/mol, which correlates with enhanced entrapment efficiency and drug loading in NLC systems (Aryani et al., 2021). This spontaneous interaction indicates a strong potential of the compound in active ingredient delivery systems. Based on its bioactivity, Coenzyme Q10 also possesses skin-brightening potential through tyrosinase enzyme inhibition. Additionally, Ethyl Ascorbic Acid (EAA), a stable derivative of vitamin C, is known to exert skin-brightening effects through tyrosinase inhibition and antioxidant activity (Yuliani et al., 2023). Ascorbic acid and its derivatives can prevent melanin formation by inhibiting the conversion of DOPA to L-dopaquinone (Arbab & Eltahir, 2010; Sheth & Pandya, 2012) and by interacting with copper ions at the active site of the tyrosinase enzyme (Aboul-Einien et al., 2020), making these compounds commonly used as brightening agents in cosmetic products due to their ability to modulate melanogenesis.

This study aims to evaluate the potential skin-lightening activity of the active compounds Centella asiatica, Coenzyme Q10, and Ethyl Ascorbic Acid through an in silico approach using molecular docking methods against the tyrosinase enzyme. This analysis was conducted to predict the binding affinity and molecular interactions between the test compounds and the active site of the tyrosinase enzyme as an initial step in developing skin-lightening agents based on natural ingredients.

Method

The three-dimensional crystal structure of tyrosinase (PDB ID: 2Y9X; resolution 2.78 Å) was obtained from the RCSB Protein Data Bank. The 1D structures of asiaticoside, asiatic acid, madecassoside, madecassic acid, coenzyme Q10, 2-O-ethyl ascorbic acid, 3-O-ethyl ascorbic acid, and hydroquinone were retrieved from the PubChem database. The native ligand (0TR_410) from PDB ID: 2Y9X was used for docking validation.

All computational procedures were performed using Chem3D 16.0, MarvinSketch, and Molegro Virtual Docking (MVD) version 7.0.

Ligand Preparation

In this study, the ligands used were active compounds from Centella asiatica (asiaticoside, asiatic acid, madecassoside, madecassic acid, coenzyme Q10, 2-O -ethyl ascorbic acid, 3-O-ethyl ascorbic acid, hydroquinone, and the native ligand 0TR_410 in PDB ID: 2Y9X, by downloading the 1D structure from the PubChem website (https://pubchem.ncbi.nlm.nih.gov/). After obtaining the 1D structure, it was optimized into a 3D structure using the MarvinSketch program to generate the ligand structure in (.mol2) format. The ligand was then prepared using the Molegro Virtual Docking 7.0 program, with the Grid Box centered on the ligand.

Docking Method Validation

The redocking method was performed using native ligands from the tyrosinase protein. In this process, a grid box was created with the aim of obtaining the coordinates of the native ligands that would be used as the test ligand coordinates. In the validation process, results closer to experimental results are obtained if the RMSD value is less than 2 Å. A smaller RMSD value indicates that the position of the redocked ligand will be closer to the position of the crystallographic ligand (Kontoyianni et al., 2004).

Receptor Preparation

The crystal structure of PPO3 with PDB code 2Y9X was obtained from the RCSB Protein Data Bank. The resolution of this protein is 2.78 Å. The receptor was prepared using the MVD 7.0 tool, with the condition that this method would be valid if the RMSD value obtained was <2 Å.

Molecular Docking

The crystal structure and ligand were then used in the docking procedure with MVD 7.0. The test and reference ligands were bound to the tyrosinase receptor. The docking process was performed using a grid box and previously determined coordinates. The affinity energy values were obtained from the docking results observed in the ligand binding region to the tyrosinase receptor.

Prediction of Physicochemical Properties and Toxicity of Compounds

The biological activity of a compound is predicted using PASS Online (Prediction of Activity Spectra for Substances) at https://www.way2drug.com/PASSOnline/index.php. Assessment of the compound's toxicity potential and bioavailability is conducted using pkCSM (Predicting Small-Molecule Pharmacokinetic and Toxicity Properties Using Graph-Based Signatures) at

https://biosig.lab.uq.edu.au/pkcsm/. Analysis of lipophilic properties and determination of the compound's suitability as a drug candidate based on Lipinski's rules was conducted using http://www.scfbio-iitd.res.in/software/drugdesign/lipinski.jsp. Additionally, toxic dose estimation and toxicity level classification of the compound were obtained using the Protox platform at https://tox.charite.de/protox3/#.

Result and Discussion

Molecular docking is a method used to predict the optimal position and orientation of a ligand when interacting with the active site of a target protein. This process enables the identification of interaction affinity based on bond energy, where lower energy values indicate greater stability of the ligand-receptor complex (Ryan Syahputra et al., 2022; Girija et al., 2010). Tyrosinase is a metalloenzyme containing copper (Cu) ions and plays a crucial role in melanin biosynthesis. This enzyme catalyzes the hydroxylation of tyrosine into L-DOPA, then oxidizes L-DOPA into DOPA-quinone, which subsequently forms melanin (Priani & Fakih, 2021; Chang, 2009). Tyrosine, as a non-essential amino acid, functions as a natural ligand for tyrosinase. Inhibiting this enzyme's activity can reduce melanin production, thereby potentially reducing skin hyperpigmentation. One approach to evaluating the potential of tyrosinase inhibitors computationally is through molecular docking. This technique enables the prediction of interactions between ligands and the active site of the enzyme, as well as estimating the strength of interactions through bond energy calculations. The ligand-receptor complex formed with the lowest bond energy is considered the most stable, reflecting a high affinity between the test compound and the enzyme target (Syahputra et al., 2022; Girija et al., 2010; Senol et al., 2014).

A previous study conducted by Syahputra et al. (2022) demonstrated that several active compounds from *Ipomoea batatas* L. Lam, such as beta-carotene and quercetin, exhibit strong binding affinities toward the tyrosinase enzyme based on molecular docking analysis. Beta-carotene showed a binding affinity of -6.05 kcal/mol with an IC_{50} value of 36.72 µM, while quercetin exhibited a binding affinity of -5.87 kcal/mol and an IC_{50} of 45.30 µM. The molecular interactions involved hydrophobic forces, such as π-sigma and π-alkyl interactions at several key residues, along with hydrogen bonds in quercetin, which further stabilized the ligand–receptor complex. Compared to kojic acid, both compounds displayed promising antioxidant activity and inhibitory effects on both monophenolase and diphenolase functions of tyrosinase.

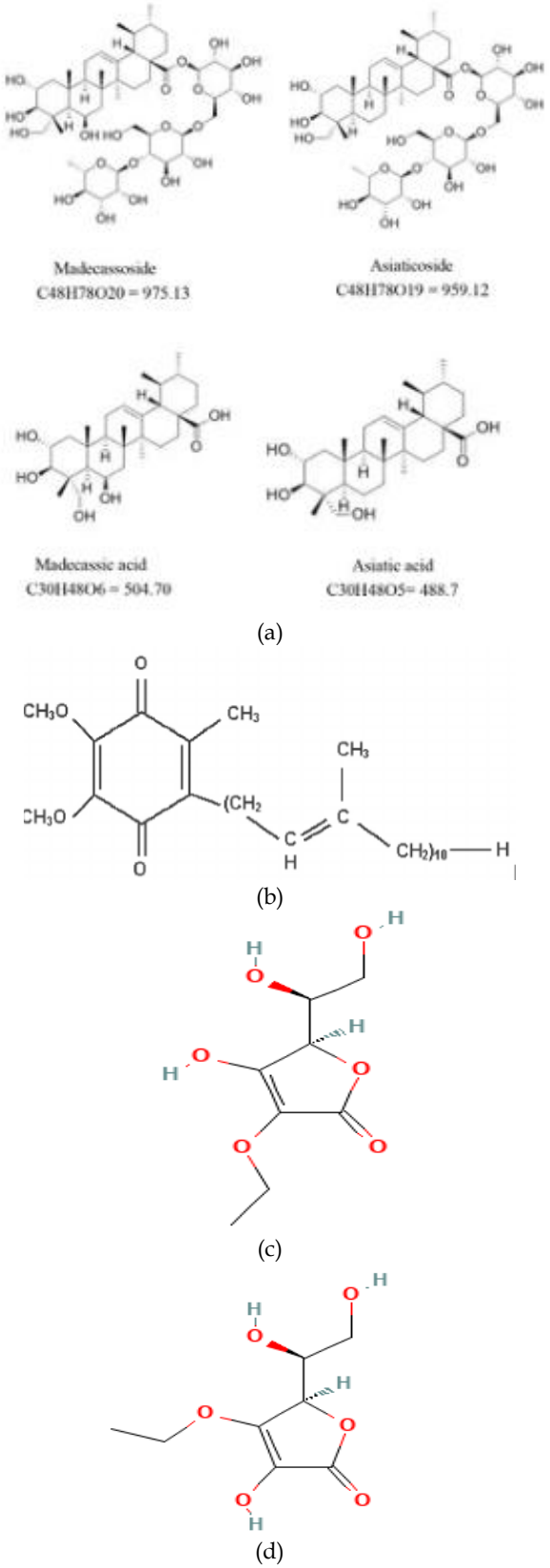


Figure 1. Active compounds of Centella asiatica (a); Coenzyme Q10 (b); Ethyl Ascorbic Acid (c, d)

Meanwhile, Ethyl Ascorbic Acid (EAA), a stable derivative of vitamin C, has also been shown to act as a skin-brightening agent through mechanisms involving tyrosinase inhibition and antioxidant activity. By assessing the binding affinities and molecular interactions of these compounds with the active site of the tyrosinase enzyme, this study aims to provide an initial understanding of their potential mechanisms of action as natural depigmenting agents for cosmetic applications. These findings further support the use of *in silico* approaches as a preliminary method for screening natural skin-brightening agents. In line with this, the present study aims to evaluate the potential skin-brightening activity of active compounds from *Centella asiatica*, Coenzyme Q10, and Ethyl Ascorbic Acid through molecular docking with the tyrosinase enzyme. By analyzing their binding affinities and molecular interactions with the enzyme's active site, this research is expected to provide a preliminary insight into the mechanism of action of these three compounds as natural depigmenting agents for cosmetic applications.

Prediction of Physicochemical Properties and Toxicity of Compounds

Predicting the physicochemical properties and toxicity of compounds is an important step in the initial screening of active compounds before further experimental testing. In this study, active compounds from Centella asiatica, Coenzyme Q10, and Ethyl Ascorbic Acid (EAA) were evaluated using an in silico approach through various online platforms. One of these approaches is the analysis of compliance with Lipinski's Rule of Five, which is used to assess the suitability of compounds as oral drug candidates based on parameters such as logP, molecular weight, number of hydrogen bond donors and acceptors, and number of rotatable bonds (Lipinski et al., 2001). Compounds that meet Lipinski's criteria generally exhibit good membrane permeability and bioavailability. Additionally, toxicity predictions were conducted using platforms such as pkCSM (Pires et al., 2015) and Protox (Banerjee et al., 2018) to assess the potential toxic effects and lethal dose (LD50) classification of each compound. These prediction results provide an initial overview of the safety and pharmacokinetic suitability of the active compounds in Centella asiatica, Coenzyme Q10, and EAA, supporting their potential use as safe skin-lightening agents in cosmetic formulations.

In Silico Prediction of Activity and Toxicity

The results of in silico docking tests between the active compounds of Centella asiatica, coenzyme Q10, ethyl ascorbic acid, and the reference compound hydroquinone with the target tyrosinase receptor enzyme (PDB IDs 2Y9X) are presented in Table 1.

Table 1. In Silico Prediction of the Values of Physicochemical Parameters of active compounds of Centella asiatica, coenzim Q10, Ethyl Ascorbic Acid, and Reference Compounds Hydroquinone Using the pkCSM Online Tool. MW = Molecular Weight; LogP = Logarithm of Octanol/Water Partition Coefficient; RB = Rotation Bonds; HBA = Hydrogen Bond Acceptors; HBD = Hydrogen Bond Donors; PSA = Polar Surface Activity

No. Compound	MW	Log P	RB	HBA	HBD	PSA(A^2)
1	959.133	-1.0328	9	19	12	391.529
2	488.709	5.0327	2	4	4	210.942
3	958.125	-1.21861	9	19	12	391.529
4	504.708	4.0035	2	5	5	215.737
5	110.112	1.0978	0	2	2	47.020
6	863.365	17.8539	31	4	0	387.175
7	204.178	-0.9289	4	6	3	80.370
8	204.178	-0.9289	4	6	3	80.370

In silico testing using molecular docking methods on the tyrosinase enzyme (PDB ID: 2Y9X) showed that the active compounds from Centella asiatica, coenzyme Q10, ethyl ascorbic acid, and the hydroquinone reference compound have varying physicochemical characteristics. Coenzyme Q10 and compounds from Centella asiatica (compounds 1 and 3) have very large molecular weights (MW) exceeding 950 Da, with high numbers of hydrogen bond donors (HBD) and acceptors (HBA), as well as PSA (polar surface area) values above 390 $Å^2$. In contrast, ethyl ascorbic acid (compounds 7 and 8) and hydroquinone (compound 5) exhibit much smaller molecular weights (<250 Da) and lower PSA values (<100 $Å^2$), indicating better oral absorption potential. The log P values of the compounds vary from highly hydrophilic to highly lipophilic, with the highest log P value of 17.8539 in compound 6. Based on these parameters, compounds with small molecular sizes and balanced log P values, such as ethyl ascorbic acid and hydroquinone, are more likely to meet the initial pharmacokinetic eligibility criteria, while larger compounds like coenzyme Q10 may require a specialized delivery system to enhance their bioavailability.

Table 2. In Silico Prediction of Anticancer Activity and Toxicity Against VEGF Receptors Derived from N-benzoyl-N'-phenylthiourea and Reference Compounds Using Molegro Virtual Docker (*), pkCSM (**), and Protox (***) online tools

Compound	Rerank Score*	Ames Toxicity**	Hepato Toxicity**	Skin Sensitization**	Activity LD50 Acute**	Toxicity Class***
Asiaticoside	223.7987	No	No	No	2000	4
Asiatic Acid	-36.9294	No	No	No	2000	4
Madecosside	536.055	No	No	No	2000	4
Madecassic Acid	-34.87853667	No	No	No	2000	4
Hidroquinone	-53.6269	No	No	No	50	2
Q10	594.4467667	No	No	No	5000	5
2-O-Ethyl Ascorbic Acid	-34.30906667	No	No	No	2000	4
3-O-Ethyl Ascorbic Acid	-66.73626667	No	No	No	2000	4

Kesuma (2018) demonstrated that derivatives of N-(benzoyl)-N'-phenylthiourea possess potential inhibitory activity against VEGFR2 based on rerank score values from molecular docking, while also emphasizing the importance of toxicity profiles, particularly hepatotoxicity. Following a similar in silico approach, this study evaluated the predicted activity and toxicity profiles of selected active compounds from Centella asiatica, coenzyme Q10, ethyl ascorbic acid derivatives (2-O-EAA and 3-O-EAA), and hydroquinone (as reference) targeting the tyrosinase enzyme (PDB ID: 2Y9X). Toxicity prediction using pkCSM and ProTox-II revealed that most of the tested natural compounds — including asiaticoside, asiatic acid, madecassoside, madecassic acid, 2-O-EAA, and 3-O-EAA — exhibited a favorable safety profile, being non-mutagenic, non-hepatotoxic, and non-sensitizing to the skin, with LD_{50} values of approximately 2000 mg/kg (toxicity class IV).

In contrast, hydroquinone showed a higher toxicity profile, predicted to be mutagenic, hepatotoxic, and a skin sensitizer, with an LD_{50} of about 50 mg/kg, classified as toxicity class II. Coenzyme Q10 demonstrated the highest LD_{50} value (5000 mg/kg, class V) and showed no mutagenic or hepatotoxic effects, indicating a very high safety margin. Based on binding affinity and toxicity prediction, 3-O-EAA and 2-O-EAA are considered promising candidates for safe and effective tyrosinase inhibitors in skin-brightening applications.

Conclusion

This study demonstrates that 3-O-ethyl ascorbic acid exhibited the strongest binding affinity toward tyrosinase (PDB ID: 2Y9X), followed by asiatic acid and 2-O-ethyl ascorbic acid, indicating their potential as competitive inhibitors of the melanogenesis pathway. The interaction analysis revealed that hydrogen bonding and steric interactions play an essential role in stabilizing the ligand–enzyme complex within the active site. In addition, physicochemical and toxicity predictions suggest favorable pharmacokinetic profiles for ethyl ascorbic acid derivatives compared to other tested compounds. These findings provide computational evidence supporting the potential application of selected natural and antioxidant-based compounds as alternative skin-brightening agents. However, this study is limited to molecular docking and in silico predictions, which do not fully represent biological complexity, enzyme dynamics, or cellular responses. Therefore, further validation through molecular dynamics simulations, enzyme inhibition assays, and in vitro and in vivo studies is necessary to confirm their efficacy and safety. Future research may also explore synergistic effects among these compounds to optimize formulation strategies for cosmetic applications.

Acknowledgments

The author would like to express his deepest gratitude to the Faculty of Pharmacy, University of Surabaya, for the support provided during the conduct of this research, including the provision of laboratory facilities and the necessary resources. This support has contributed significantly to the smooth running and success of the research. The author would also like to thank all co-authors for their collaboration and active contributions in the preparation of this article. May the results of this research contribute to the advancement of scientific knowledge, particularly in the field of natural-based cosmetics.

Author Contributions

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

References

Aboul-Einien, M. H., Kandil, S. M., Abdou, E. M., Diab, H. M., & Zaki, M. S. E. (2020). Ascorbic acid derivative-loaded modified aspasomes: formulation, in vitro, ex vivo and clinical

evaluation for melasma treatment. *Journal of Liposome Research*, *30*(1), 54–67. https://doi.org/10.1080/08982104.2019.1585448

Aryani, N. L. D., Siswandono, Soeratri, W., Putri, D. Y., & Puspitasarini, P. D. (2021). Development, characterization in vitro and in silico of coenzyme Q10 loaded myristic acid with different liquid lipids nanostructured lipid carriers. *Journal of Pharmacy and Pharmacognosy Research*, *9*(5), 573–583. https://doi.org/10.56499/jppres21.1038_9.5.573

Banerjee, P., Eckert, A. O., Schrey, A. K., & Preissner, R. (2018). ProTox-II: a webserver for the prediction of toxicity of chemicals. *Nucleic Acids Research*, *46*(W1), W257–W263. https://doi.org/10.1093/nar/gky318

Bao, K., Zhang, C., Xie, S., Feng, G., Liao, S., Cai, L., He, J., Guo, Y., & Jiang, C. (2019). A Simple and Accurate Method for the Determination of Related Substances in Coenzyme Q10 Soft Capsules. *Molecules*, *24*(9), 1–14. https://doi.org/10.3390/molecules24091767

Bylka, W., Znajdek-Awiżeń, P., Studzińska-Sroka, E., & Brzezińska, M. (2013). Centella asiatica in cosmetology. *Advances in Dermatology and Allergology*, *1*, 46–49. https://doi.org/10.5114/pdia.2013.33378

Chang, T.-S. (2009). An Updated Review of Tyrosinase Inhibitors. *International Journal of Molecular Sciences*, *10*(6), 2440–2475. https://doi.org/10.3390/ijms10062440

Chang, Y., Hawkins, B. A., Du, J. J., Groundwater, P. W., Hibbs, D. E., & Lai, F. (2022). A Guide to In Silico Drug Design. *Pharmaceutics*, *15*(1), 49. https://doi.org/10.3390/pharmaceutics15010049

Fernenda, L., Ramadhani, A. P., & Syukri, Y. (2023). Aktivitas pegagan (Centella asiatica) pada dermatologi. *Jurnal Sains Farmasi & Klinis*, *9*(3), 237. https://doi.org/10.25077/jsfk.9.3.237-244.2022

Fransiska, A. N. (2023). Molecular docking aktivitas senyawa antioksidan alami pada beberapa tanaman di indonesia'. *Jurnal Farmasetis*, *12*(1), 55–60.

Frimayanti, N., Dona, R., & Solihin, T. (2023). Molecular Docking Study of Chalcone Analogue Compounds with Hydroxy and Methoxy Subtituents as Bcl-2 Inhibitors. *Chempublish Journal*, *7*(1), 31–41. https://doi.org/10.22437/chp.v7i1.17487

Girija, C. R., Reddy, P. N., Rani, A. P., & Prasad, K. R. (2010). Molecular docking studies on bioactive compounds from Justicia adhatoda. *International Journal of Pharmaceutical Sciences Review and Research*, *3*(2), 87–90.

Golonka, I., Oleksy, M., Junka, A., Matera-Witkiewicz, A., Bartoszewicz, M., & Musiał, W. (2017). Selected Physicochemical and Biological Properties of Ethyl Ascorbic Acid Compared to Ascorbic Acid. *Biological and Pharmaceutical Bulletin*, *40*(8), 1199–1206. https://doi.org/10.1248/bpb.b16-00967

Kesuma, D., Siswandono, S., Purwanto, B. T., & Hardjono, S. (2018). Uji in silico Aktivitas Sitotoksik dan Toksisitas Senyawa Turunan N-(Benzoil)-N'- feniltiourea Sebagai Calon Obat Antikanker. *JPSCR : Journal of Pharmaceutical Science and Clinical Research*, *3*(1), 1. https://doi.org/10.20961/jpscr.v3i1.16266

Khan, S., Sharma, A., & Jain, V. (2023). An Overview of Nanostructured Lipid Carriers and its Application in Drug Delivery through Different Routes. *Advanced Pharmaceutical Bulletin*, *13*(3), 446–460. https://doi.org/10.34172/apb.2023.056

Khotimah, H., Setiawan, A., Rita, C. I., Mardiyah, M., Ali, A., Sukatman, M. P., Retnaningtyas, E., Ismail, D. D. S. L., Widasmara, D., Nurseta, T., & Sujuti, H. (2021). In silico studies of natural compounds of Centella Asiatica as anti-aging and wound healing agents. *Int Conf Life Sci Technol (ICoSLiST 2020)*, *2353*, 030031. https://doi.org/10.1063/5.0053016

Kontoyianni, M., McClellan, L. M., & Sokol, G. S. (2004). Evaluation of docking performance: Comparative data on docking algorithms. *Journal of Medicinal Chemistry*, *47*(3), 558–565. https://doi.org/10.1021/jm0302734

Li, J., Min, X., Zheng, X., Wang, S., Xu, X., & Peng, J. (2023). Synthesis, Anti-Tyrosinase Activity, and Spectroscopic Inhibition Mechanism of Cinnamic Acid–Eugenol Esters. *Molecules*, *28*(16), 5969. https://doi.org/10.3390/molecules28165969

Lim, J., Lee, H., Hong, S., Lee, J., & Kim, Y. (2024). Comparison of the Antioxidant Potency of Four Triterpenes of Centella asiatica against Oxidative Stress. *Antioxidants*, *13*(4). https://doi.org/10.3390/antiox13040483

Lipinski, C. A., Lombardo, F., Dominy, B. W., & Feeney, P. J. (1997). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Advanced Drug Delivery Reviews*, *23*(1–3), 3–25. https://doi.org/10.1016/S0169-409X(96)00423-1

Luo, J., Zhang, T., Zhu, C., Sun, J., Zhu, W., Ai, W., Huang, X., & Wang, X. (2020). Asiaticoside might attenuate bleomycin-induced pulmonary fibrosis by activating cAMP and Rap1 signalling pathway assisted by A2AR. *Journal of Cellular and Molecular Medicine*, *24*(14), 8248–8261. https://doi.org/10.1111/jcmm.15505

Müller, R. H., Radtke, M., & Wissing, S. A. (2002). Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Advanced Drug Delivery Reviews*,

54(SUPPL.). https://doi.org/10.1016/S0169-409X(02)00118-7

Permatasari, D. I., Audina, M., & Aryzki, S. (2023). Aktivitas Antioksidan Dan Evaluasi Fisik Sediaan Gel Ekstrak Daun Pegagan (Centella Asiatica (L.) Urban) Sebagai Anti Aging. *Journal Pharmaceutical Care and Sciences*, *4*(1), 55–63. https://doi.org/10.33859/jpcs.v4i1.410

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*(9), 4066–4072. https://doi.org/10.1021/acs.jmedchem.5b00104

Prasetyo, A. D., Widyaningsih, W., & Susanti, E. D. (2020). Aktivitas senyawa fenolik sebagai inhibitor tirosinase dalam sintesis melanin. *Jurnal Ilmu Kefarmasian Indonesia*, *18*(1), 30–37. https://doi.org/10.35814/jifi.v18i1.1575

Puttarak, P., Brantner, A., & Panichayupakaranant, P. (2016). Biological Activities and Stability of a Standardized Pentacyclic Triterpene Enriched Centella asiatica Extract. *Natural Product Sciences*, *22*(1), 20. https://doi.org/10.20307/nps.2016.22.1.20

Senol, F., Khan, M., Orhan, G., Gurkas, E., Orhan, I., Oztekin, N., & Ak, F. (2014). In Silico Approach to Inhibition of Tyrosinase by Ascorbic Acid Using Molecular Docking Simulations. *Current Topics in Medicinal Chemistry*, *14*(12), 1469–1472. https://doi.org/10.2174/1568026614666140610121253

Sheth, V. M., & Pandya, A. G. (2011). Melasma: A comprehensive update. *Journal of the American Academy of Dermatology*, *65*(4), 689–697. https://doi.org/10.1016/j.jaad.2010.12.046

Sutrisno, D., Hardani, R., & Handayani, D. (2021). Aktivitas antioksidan dan efek penyembuhan luka dari ekstrak Centella asiatica. *Jurnal Fitofarmaka Indonesia*, *8*(1), 21–27. https://doi.org/10.33096/jffi.v8i1.670

Syahputra, R., & Widyaningsih, W. (2022). Studi Docking Molekular Aktivitas Panghambatan Enzim Tirosinase Ubi Jalar (Ipomoea batatas L. Lam). *Pharmacon: Jurnal Farmasi Indonesia*, *19*(1), 21–34. https://doi.org/10.23917/pharmacon.v19i1.18295

Yuliani, S. F., Lestari, D. A., & Anggraeni, A. (2023). The potential of ethyl ascorbic acid as skin brightening agent: Mechanism and application. *Journal of Cosmeceutical Science*, *5*(2), 55–62. https://doi.org/10.20473/jcs.v5i2.2023