BIOMA
p-ISSN: 0126-3552
e-ISSN: 2580-9032

DOI:10.xxxxx/Biomaxx(x).x Research article

Title no more than 20 words, short title no more than 6 words, and *Species name* italicised, followed by species author name

Corresponding Author's Full Name[1]*, and Author's Full Name[2, 3]
[1]*Insert affiliation information including email, phone and fax here*
[2]*Insert affiliation information including email, phone and fax here fot author from different affiliation*
*Corresponding author: your@emailaddress.xxx

ABSTRAK

Tuliskan abstrak dalam Bahasa Indonesia dan Bahasa Inggris, dengan panjang maksimal 200 kata. Gunakan Times New Roman, 10 pt, spasi tunggal, dalam satu paragraf berkesinambungan. Awali dengan kata ABSTRAK dalam huruf tebal, rata tengah, diikuti teks yang dipisahkan dengan satu spasi. Abstrak harus (1) menyampaikan pentingnya dan tujuan penelitian, (2) menjelaskan secara singkat metode yang digunakan, (3) merangkum temuan atau hasil utama, (4) menyajikan kesimpulan dengan jelas, (5) menekankan kebaruan, kontribusi, atau implikasi penelitian, dan (6) ditulis secara mandiri sehingga pembaca dapat memahami inti penelitian tanpa harus membaca keseluruhan naskah. Aturan penulisan: (1) jangan gunakan simbol, karakter khusus, atau ekspresi matematika dalam judul maupun abstrak, (2) abstrak harus ringkas, informatif, dan ditulis dengan gaya akademik yang netral, serta (3) hindari penggunaan sitasi atau referensi dalam abstrak.

Kata kunci: Cantumkan 5–8 kata kunci segera setelah abstrak. Kata kunci ditulis dengan huruf kecil, dipisahkan dengan koma, dan diurutkan secara alfabetis. Pilih istilah yang mencerminkan konsep inti, metode, atau ruang lingkup penelitian untuk memudahkan pengindeksan dan pencarian.

ABSTRACT

Write the abstract in Indonesian and English, with a maximum of 200 words. Use Times New Roman, 10 pt, single spacing, in one continuous paragraph. Begin with the word ABSTRACT in bold, centred, followed by the text separated by a single space. The abstract should (1) state the importance and purpose of the research, (2) briefly describe the methods used, (3) summarize the main findings or results, (4) present the conclusions clearly, (5) highlight the novelty, contribution, or implications of the study, and (6) ensure that it is self-contained, allowing readers to grasp the essence of the paper without referring to the full text. Formatting rules: (1) do not use symbols, special characters, or mathematical expressions in the title or abstract, (2) keep the abstract concise, informative, and written in a neutral, academic tone, and (3) avoid citations or references in the abstract.

Keywords: Provide 5—8 keywords immediately after the abstract. Keywords should be sorted alphabetically, written in lowercase, and separated by commas. Choose terms that reflect the core concepts, methods, or scope of the study to aid indexing and searchability.

INTRODUCTION

Except for the Bahasa Indonesia version of the abstract, the entire manuscript must be written in British English. Use Times New Roman font, size 12, with 1.15-line spacing. The introduction should provide the background of the study, supported by recent scientific evidence relevant to the manuscript title. References should preferably be drawn from accredited journals indexed in Sinta or Scopus and formatted according to the APA 7th edition guidelines. Authors are encouraged to cite and reference from the past issues of BIOMA.

Clearly state the research problem and objectives, ensuring the problem formulation logically leads to the study's purpose. Highlight the significance and

benefits of the research to strengthen its rationale. Optionally, provide a brief overview of the research gap and how this study contributes to filling it.

METHODOLOGY

The methodology should be written clearly and concisely to ensure the research can be replicated by other scholars. It includes descriptions of the study site, sampling, experimental design, procedures, and data analysis techniques.

Studies sites and sampling

This section describes the location, time, and sampling techniques used in the research. Figures or maps may be added to illustrate specific sites and methods.

Experimental design

Put this section when your research is experimental. Explain the type of experiment conducted, including tools, materials, and their specifications. If animals are used, ensure compliance with animal welfare guidelines (e.g., Helsinki Declaration at https://wma.net).

Research procedures

Detail the step-by-step process of the research. Flowcharts or diagrams may be included to enhance clarity.

Data analysis

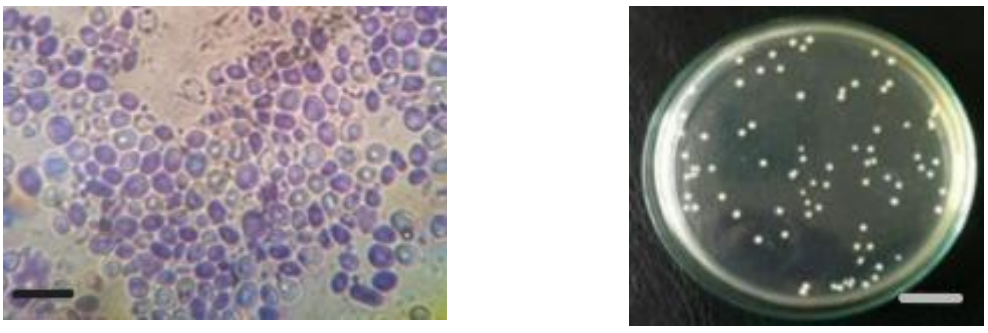
Describe the techniques used to process and analyse data, including statistical methods, formulas, or software. Cite relevant literature where appropriate.

RESULTS AND DISCUSSION

This section presents the data obtained from the research and interprets them in relation to existing theories and previous studies. Results should be displayed clearly, using tables, figures, or diagrams where appropriate to enhance understanding.

Research findings are presented in a structured manner, supported by visual aids such as tables, charts, or graphs. Environmental or contextual data may also be included to strengthen the interpretation.

The data should be analysed descriptively or statistically, depending on the research design. Results must be interpreted in depth, supported by relevant theories and literature, to highlight patterns, relationships, or significant outcomes.



(a) (b)

FIGURE 1. Figures must be numbered consecutively (e.g., **FIGURE 1**) with the caption in bold. Captions should be placed below the figure and written concisely. If a figure has multiple parts, label each part as (a), (b), (c), etc. Every picture/illustration must be with a scale bar, which is explained, for

DOI:10.xxxxx/Biomaxx(x).x

example: “scale bar = 2 mm”. Figures should be high quality and, where necessary, accompanied by explanatory notes.

TABLE 1. Tables must be numbered consecutively (e.g., **TABLE 1**) with the caption in bold, centered above the table. Tables should include top and bottom rules, with an additional rule separating the column headings from the body of the table. Keep tables clear, concise, and self-explanatory.

Column Header Goes Here	Column Header Goes Here	Column Header Goes Here
Row name here	x	x
Row name here	x	x
Row name here	x	x

Conclusions

The conclusion should be presented in a separate paragraph at the end of the Discussion, without a separate subtitle. It must summarize the main findings, highlight their implications, and clearly state how the research contributes to the field.

Author contributions

List each author’s specific role in the research process, ensuring all contributors are named individually. For example: F.B., E.L., A.B.: project conception; F.B., E.L.: methodology; F.B.: data analysis; F.B.: original manuscript draft; E.L., A.B., F.B.: manuscript review and editing

Acknowledgments

Acknowledgments should be directed to individuals or institutions that made significant contributions to the research (e.g., data providers, materials, facilities, or technical support), but not to members of the author team. Funding sources must also be acknowledged here.

Conflicts of interest statement

All manuscripts must include a conflict-of-interest statement. Authors should disclose any financial, personal, or professional relationships that could influence the research. If no conflicts exist, state: “There are no conflicts to declare.”

Ethical compliance

As a requirement of publication, authors must confirm compliance with all legal and ethical obligations related to the protection of human and animal research subjects, where applicable. Ethical approval from the relevant institutional review board or ethics committee should be stated when studies involve humans or animals.

If the research *does not* involve human or animal subjects, authors should provide a brief statement clarifying this. For example: “The process of collecting plant growth data/molluscs population was conducted using non-invasive observation methods and did not involve human or animal subjects.” If the research *involves* animals, authors must declare adherence to recognized animal welfare guidelines (e.g., Helsinki Declaration, institutional animal care protocols). For example: “Experiments involving mice were conducted in accordance with institutional animal care and use guidelines, ensuring compliance with ethical standards.” If the research *involves* humans, authors must confirm that informed consent was obtained and that the study was approved by an ethics committee. For example: “All human participants provided informed consent, and the study protocol was approved by the University NNN Research Ethics Committee no. yyyy/yy year 20xx.”

DOI:10.xxxxx/Biomaxx(x).x

REFERENCES-INSTRUCTIONS

References must follow APA 7th edition style. (1) Arrange entries alphabetically by the surname of the first author. (2) Use a hanging indent format, where the first line is flush left and subsequent lines are indented. (3) Include complete details for each source: author(s), year of publication, title, journal or book, volume(issue), page range, and DOI or URL if available. (4) For books, provide publisher information; for book chapters, include editors, book title (italicized), page range, and publisher. (5) Journal names should be written in full, not abbreviated. (6) Ensure consistency between in-text citations and the reference list. Authors are encouraged to cite and reference one or two articles from earlier issues of **BIOMA** to strengthen the contextual relevance of their manuscript.

REFERENCES-EXAMPLES

Adyn, M. F., Sibarani, M. C., Utoyo, L., Surya, R. A., & Sedayu, A. (2022). Role of siamang (*Symphalangus syndactylus*) as seed dispersal agent in a Sumatran lowland tropical forest. *Biodiversitas Journal of Biological Diversity*, *23*(4), 2101–2110. https://doi.org/10.13057/biodiv/d230445

Backer, C. A., & Posthumus, O. (1939). *Varenflora voor Java*. Uitgave van 'S Lands Plantentuin.

Hakamashe, H. P., Arumsari, D. R., Komariah, E., Febriyani, H., Febrianty, I., Destiyana, N., Aulia, R., Sukmawati, W., Noer, M. I., & Sedayu, A. (2022). Vegetasi taman urban sebagai penyedia pakan bagi beberapa trophic guild burung herbivora: Studi Taman Lapangan Banteng, Jakarta Pusat. *Bioma*, *18*(2), 70–82. https://doi.org/10.21009/Bioma18(2).4

Isfaeni, H., Rusdi, R., Indriani, R. P., Mahardika, R. D., & Oetari, F. (2024). Gastropod community structure at Sepanjang beach, Yogyakarta. *AIP Conference Proceedings*, *2982*(1), 050009. https://doi.org/10.1063/5.0189738

Langemeyer, J., & Gómez-Baggethun, E. (2018). Urban biodiversity and ecosystem services. In A. Ossola & J. Niemelä (Eds.), *Urban biodiversity. From research to practice* (pp. 36–53). Routledge.

Raciborski, M. (1898). *Die Pteridophyten der Flora von Buitenzorg*. E.J. Brill.

Sedayu, A., Putri, N., Amiruddin, Mawardi, M., Noer, M. I., & Maulana, L. (2024). Fern species-area relationship in urban anthropogenic islands in Slawi, Tegal, Central Java. *Journal of Tropical Biodiversity and Biotechnology*, *9*(3), jtbb87781. https://doi.org/10.22146/jtbb.87781

DOI:10.xxxxx/Biomaxx(x).x

COVER LETTER

Dear **Bioma Editorial Team**

I hereby attach the article,

Manuscript title

xxxxxxx

Author name(s):

Author 1 Author 2 Author 3*

* denotes corresponding author i.e the person who contacts the editor for publishing purpose

Address:
(fill in the name of the institution, address, and email from the corresponding author)

Universitas Negeri Jakarta, Jl. R.Mangun Muka Raya No.11, RT.11/RW.14, Rawamangun, Kec. Pulo Gadung, Kota Jakarta Timur, Daerah Khusus Ibukota Jakarta 13220, mygmail@gmail.com

Mobile (Whatsapp) number:

08xxxxx

Novelty:
(State new findings you claim in your article compared to current knowledge)

Gynura divaricata potential as antieczema and antiinflammatory based on in silico study

Statement:

This article has never been published in another journal publication

Place and date:

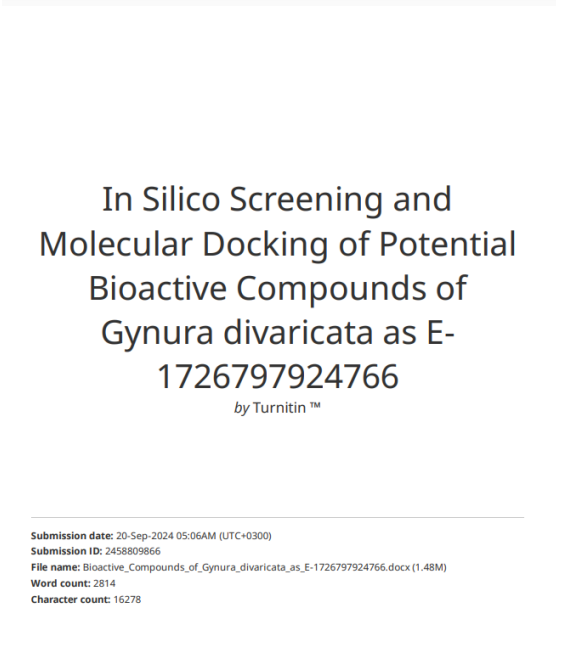
Jakarta, April 4, 2024

Best regards,
(enter your name)

Reza Dino

DOI:10.xxxxx/Biomaxx(x).x

TURNITIN CHECK RESULT
[as explained on https://journal.unj.ac.id/unj/index.php/bioma/plagiarismscreening]



In Silico Screening and Molecular Docking of Potential Bioactive Compounds of Gynura divaricata as E-1726797924766

by Turnitin ™

Submission date: 20-Sep-2024 05:06AM (UTC+0300)
Submission ID: 2458809866
File name: Bioactive_Compounds_of_Gynura_divaricata_as_E-1726797924766.docx (1.48M)
Word count: 2814
Character count: 16278

Jurnal Farmasi Dan Ilmu Kefarmasian Indonesia Vol..x No..x XXXXXX 202x: 1

In Silico Screening and Molecular Docking of Potential Bioactive Compounds of *Gynura divaricata* as Eczema Drug Candidates

Reza Dino Mahardika[1]*, Alika Firhandini[2], Sayid Ramadhan[2], Hazleini Misvayanty[2], Hanum Isfaeni[1], Rusdi[1]
[1]Department of Biology Education, Faculty of Mathematics and Natural Sciences, Universitas Negeri Jakarta, Jakarta, Indonesia
[2]Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Negeri Jakarta, Jakarta, Indonesia

*Corresponding author: rezadino15@gmail.com

Abstract
Eczema is a skin disease that is characterised by damage to the skin barrier layer so that it is prone to allergies, inflammation and irritation. There needs to be treatment to overcome these problems, one of which utilises medicinal plants such as Gynura divaricata. Gynura divaricata *has long been known as a traditional medicinal plant, especially in treating skin wounds. Potential screening is needed to find out the specific potential of bioactive compounds in it. Screening of bioactive compounds of* Gynura divaricata *to be used as eczema drug candidates was carried out with an in silico approach by utilising open data in the database. The data were analysed for biological activity, ADME, skin absorption and molecular docking. The results showed that the bioactive compounds passed the analysis and could interact with the target protein, characterised by the formation of hydrophobic bonds and hydrogen bonds.*

Keywords: *Eczema*, Gynura divaricata, *In silico*, *Molecular docking*.

INTRODUCTION

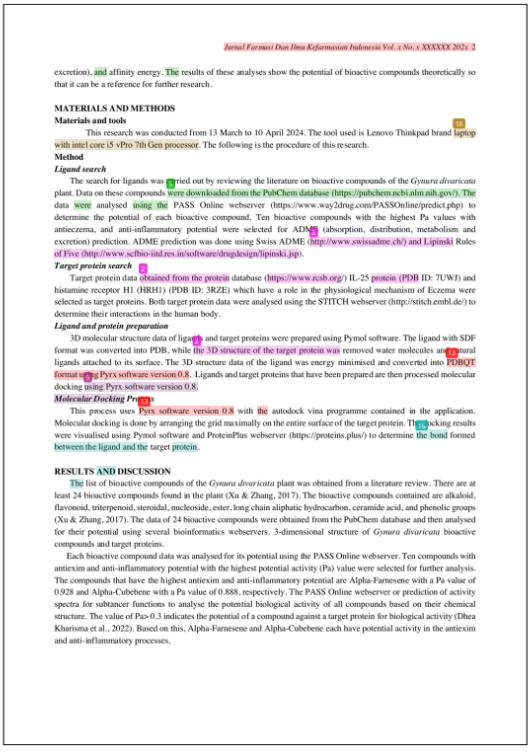
Eczema is a skin disease that makes the skin dry with a red or pink colour and becomes very easily irritated (Tsakok et al., 2019). Symptoms of eczema include itchy skin and a lighter colour in the area (Ramadhan, 2018). Eczema is common in body folds such as behind the knees, eyelids, and between the fingers (Lugović-Mihić et al., 2023). This condition is aggravated by extreme temperatures. Extreme heat can cause sweating which irritates the dry spots. There are three types of eczema: atopic eczema, contact dermatitis, and neurodermatitis. Atopic Eczema is the most common.

Atopic eczema affects about 25% of children and has a lifetime prevalence of 15-30% in children and 2-10% in adults in developed countries. One of the factors that cause atopic eczema is the decreased production of Filaggrin protein. The protein plays a role in forming hard and flat corneocytes as the structure of the outermost protective layer of the skin (Tsakok et al., 2019). A decrease in the amount of Filaggrin damages the skin barrier, making the skin more susceptible to irritation and inflammation (Tsakok et al., 2019). Filaggrin regulation is influenced by inhibitors such as interleukin (IL)-25. These inhibitors block Filaggrin gene expression (Hvid et al., 2011). IL-25 also works synergistically with IL-4 and IL-13 to increase Herpes Simplex Virus HSV-1 replication in vitro (Hvid et al., 2011). Another protein that affects the impact of eczema is the histamine (H1) receptor which is involved in pathophysiological processes such as allergy and inflammation. Histamine receptor antagonists are highly effective attempts to relieve symptoms of allergic reactions (Shimamura et al., 2012). Inhibition of IL-25 and TSLP function is needed to treat eczema. Inhibition of the function of these two proteins can be done by bioactive compounds with antieczema and anti-inflammatory potential. These bioactive compounds can be obtained from various organisms, one of which is the *Gynura divaricata* plant.

Gynura divaricata is a plant that has been used in traditional medicine in China and Indonesia (Aaron et al., 2016; Kantawong et al., 2021). The leaves of this plant are commonly used in treating wounds and diseases of the human skin. *Gynura divaricata* leaves are believed to prevent inflammation and accelerate wound healing on the skin (Aaron et al., 2016). *Gynura divaricata* leaves contain more than 24 bioactive compounds that have potential as antimicrobial, anti-inflammatory, and antifungal (Xu & Zhang, 2017). These compounds also have potential in treating skin diseases, such as Eczema.

This potential can be tested theoretically with an in silico approach. The test uses a set of data stored in a database. The data can be analysed using a webserver and Bioinformatics software. Analyses that can be done with the in silico approach such as prediction of potential biological activity (PA), ADME (absorption, distribution, metabolism and

P-ISSN: 2406-9388
E-ISSN: 2580-8303



Jurnal Farmasi Dan Ilmu Kefarmasian Indonesia Vol..x No..x XXXXXX 202x: 2

excretion), and affinity energy. The results of these analyses show the potential of bioactive compounds theoretically so that it can be a reference for further research.

MATERIALS AND METHODS

Materials and tools

This research was conducted from 13 March to 10 April 2024. The tool used is Lenovo Thinkpad brand laptop with intel core i5 vPro 7th Gen processor. The following is the procedure of this research.

Method

Ligand search

The search for ligands was carried out by reviewing the literature on bioactive compounds of the *Gynura divaricata* plant. Data on these compounds were downloaded from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/). The data were analysed using the PASS Online webserver (https://www.way2drug.com/PASSOnline/predict.php) to determine the potential of each bioactive compound. Ten bioactive compounds with the highest Pa values with antieczema, and anti-inflammatory potential were selected for ADME (absorption, distribution, metabolism and excretion) prediction. ADME prediction was done using Swiss ADME (http://www.swissadme.ch/) and Lipinski Rules of Five (http://www.scfbio-iitd.res.in/software/drugdesign/lipinski.jsp).

Target protein search

Target protein data obtained from the protein database (https://www.rcsb.org/) IL-25 protein (PDB ID: 7UWJ) and histamine receptor H1 (HRH1) (PDB ID: 3RZE) which have a role in the physiological mechanism of Eczema were selected as target proteins. Both target protein data were analysed using the STITCH webserver (http://stitch.embl.de/) to determine their interactions in the human body.

Ligand and protein preparation

3D molecular structure data of ligands and target proteins were prepared using Pymol software. The ligand with SDF format was converted into PDB, while the 3D structure of the target protein was removed water molecules and natural ligands attached to its surface. The 3D structure data of the ligand was energy minimised and converted into PDBQT format using Pyrx software version 0.8. Ligands and target proteins that have been prepared are then processed molecular docking using Pyrx software version 0.8.

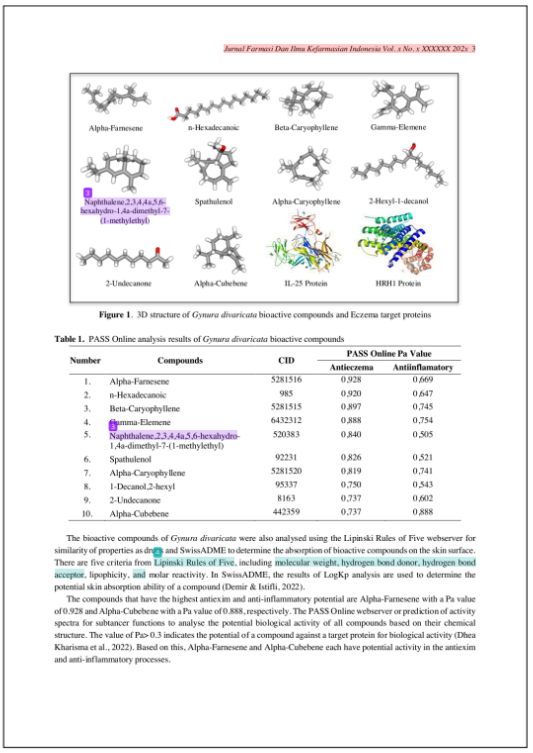
Molecular Docking Pro

This process uses Pyrx software version 0.8 with the autodock vina programme contained in the application. Molecular docking is done by arranging the grid maximally on the entire surface of the target protein. The docking results were visualised using Pymol software and ProteinPlus webserver (https://proteins.plus/) to determine the bond formed between the ligand and the target protein.

RESULTS AND DISCUSSION

The list of bioactive compounds of the *Gynura divaricata* plant was obtained from a literature review. There are at least 24 bioactive compounds found in the plant (Xu & Zhang, 2017). The bioactive compounds contained are alkaloid, flavonoid, triterpenoid, steroidal, nucleoside, ester, long chain aliphatic hydrocarbon, ceramide acid, and phenolic groups (Xu & Zhang, 2017). The data of 24 bioactive compounds were obtained from the PubChem database and then analysed for their potential using several bioinformatics webservers. 3-dimensional structure of *Gynura divaricata* bioactive compounds and target proteins.

Each bioactive compound data was analysed for its potential using the PASS Online webserver. Ten compounds with antiexim and anti-inflammatory potential with the highest potential activity (Pa) value were selected for further analysis. The compounds that have the highest antiexim and anti-inflammatory potential are Alpha-Farnesene with a Pa value of 0.928 and Alpha-Cubebene with a Pa value of 0.888, respectively. The PASS Online webserver or prediction of activity spectra for subtancer functions to analyse the potential biological activity of all compounds based on their chemical structure. The value of Pa> 0.3 indicates the potential of a compound against a target protein for biological activity (Dhea Kharisma et al., 2022). Based on this, Alpha-Farnesene and Alpha-Cubebene each have potential activity in the antiexim and anti-inflammatory processes.



Jurnal Farmasi Dan Ilmu Kefarmasian Indonesia Vol..x No..x XXXXXX 202x: 3

Figure 1. 3D structure of *Gynura divaricata* bioactive compounds and Eczema target proteins

Table 1. PASS Online analysis results of *Gynura divaricata* bioactive compounds

Number	Compounds	CID	PASS Online Pa Value	
			Antieczema	Antiinflamatory
1.	Alpha-Farnesene	5281516	0.928	0.669
2.	n-Hexadecanoic	985	0.920	0.647
3.	Beta-Caryophyllene	5281515	0.897	0.745
4.	Gamma-Elemene	6432312	0.888	0.754
5.	Naphthalene,2,3,4,4a,5,6-hexahydro-1,4a-dimethyl-7-(1-methylethyl)	520383	0.840	0.505
6.	Spathulenol	92231	0.826	0.521
7.	Alpha-Caryophyllene	5281520	0.819	0.741
8.	1-Decanol,2-hexyl	95337	0.750	0.543
9.	2-Undecanone	8163	0.737	0.602
10.	Alpha-Cubebene	442359	0.737	0.888

The bioactive compounds of *Gynura divaricata* were also analysed using the Lipinski Rules of Five webserver for similarity of properties as drugs and SwissADME to determine the absorption of bioactive compounds on the skin surface. There are five criteria from Lipinski Rules of Five, including molecular weight, hydrogen bond donor, hydrogen bond acceptor, lipophicity, and molar reactivity. In SwissADME, the results of LogKp analysis are used to determine the potential skin absorption ability of a compound (Demir & Istifli, 2022).

The compounds that have the highest antiexim and anti-inflammatory potential are Alpha-Farnesene with a Pa value of 0.928 and Alpha-Cubebene with a Pa value of 0.888, respectively. The PASS Online webserver or prediction of activity spectra for subtancer functions to analyse the potential biological activity of all compounds based on their chemical structure. The value of Pa> 0.3 indicates the potential of a compound against a target protein for biological activity (Dhea Kharisma et al., 2022). Based on this, Alpha-Farnesene and Alpha-Cubebene each have potential activity in the antiexim and anti-inflammatory processes.

DOI:10.xxxxx/Biomaxx(x).x

The bioactive compounds of *Gynura divaricata* were also analysed using the Lipinski Rules of Five webserver for similarity of properties as drug and SwissADME to determine the absorption of bioactive compounds on the skin surface. There are five criteria from Lipinski Rules of Five, including molecular weight, hydrogen bond donor, hydrogen bond acceptor, lipophicity, and molar reactivity. In SwissADME, the results of LogKp analysis are used to determine the potential skin absorption ability of a compound (Demir & Istifli, 2022).

Table 2. PASS Online analysis results of *Gynura divaricata* bioactive compounds

Number	Compound Name	Lipinski Rules of Five					SwissADME
		Molecule Weight (<500 g/mol)	HBD (<5)	HBA (<10)	LogP (<5)	Molar Refractivity (40<x<130)	Skin permeation (cm/s)
1.	Alpha-Farnesene	204.35	0	0	5,20	70,99	-3,20
2.	Beta-Caryophyllene	204.35	0	0	4,73	66,74	-4,44
3.	Gamma-Elemene	204.35	0	0	4,89	68,83	-3,75
4.	n-Hexadecanoic	256.42	1	2	5,55	174,67	-2,77
5.	Naphthalene,2,3,4a,5,6-hexahydro-1,4a-dimethyl-7-(1-methylethyl)	204.35	5	6	-0,05	77,15	-4,49
6.	Spathulenol	220.35	1	1	3,39	65,97	-5,44
7.	Alpha-Caryophyllene	204.35	0	0	5,04	68,90	-4,32
8.	1-Decanol,2-hexyl	242.44	0	2	6,09	115,85	-2,81
9.	2-Undecanone	170.29	0	1	4,21	62,38	-4,43
10.	Alpha-Cubebene	204.35	0	0	4,27	64,51	-4,37

The Lipinski Rules of Five analysis measures five criteria of important compound properties as drug candidates. It shows the high success or failure of drug similar [18] Molecular weight analysis is intended to determine the ability of bioactive compounds to penetrate cell membranes. Molecular weight not greater than 500 g/mol is unable to diffuse into the cell membrane (Lipinski, 2004). The ten bioactive compounds have a molecular weight of less than 500 g/mol so they are predicted to be able to diffuse into the cell membrane. HBA and HBD values are directly proportional to the energy required for absorption (Lipinski, 2004). Based on the analysis results, only the Naphthalene,2,3,4,4a,5,6-hexahydro-1,4a-dimethyl-7-(1-methylethyl) compound has an HBD value of 5 which exceeds the criterion limit, which is an HBD value of less than 5. The LogP value or partition coefficient is the equilibrium of bioactive compounds in polar and nonpolar solvents related to the ability of these compounds to enter target cells. The results of the analysis show that there are four bioactive compounds with LogP values of more than 5, indicating that the four compounds require more energy to enter the target cells. Molar refractivity shows the polarisability of a compound or the ability to form instantaneous dipoles of a molecule. There is one bioactive compound that does not fulfil this criterion, namely n-Hexadecanoic with a molar refractivity value of more than 130. Based on the Lipinski Rules of Five results, at least one bioactive compound fulfils two criteria. Ten bioactive compounds fulfilled more than two Lipinski Rules of Five criteria so they passed the analysis.

Prediction of skin permeation or permeability coefficient (Kp) aims to determine the ability of bioactive compounds to pass through the mammalian skin epidermis. The LogKp value of a compound is an important consideration in drug development with a transdermal mode of action (Abdullah et al., 2021). Bioactive compounds with LogKp values > -2.5 cm/hour are considered to have relatively low skin absorption abilities (Demir & Istifli, 2022). The SwissADME analysis results showed that the n-Hexadecanoic and 1-Decanol,2-hexyl compounds had the closest positive values. This indicates that these two compounds have the potential to penetrate the skin epidermis most easily. This ability can be applied in drugs that are applied to the skin surface.

The potential of the bioactive compounds from the leaves of god was further analysed by molecular docking method to determine the interaction that occurs with the target protein of eczema disease. In this study, target proteins were selected, namely interleukin-25 (IL-25) and human receptor histamine 1 (HRH1). Both proteins play a role in the mechanism of eczema physiology in the human body. The results of STITCH webserver analysis show that both target

proteins play a role in the inflammatory process that is a symptom of eczema. IL-25 induces NF-kappa-B activation and stimulates the production of proinflammatory chemokine IL-8 (Hvid et al., 2011). Proinflammatory cytokines favour the Th2-type immune response which is a common response to allergic reactions (Pandaleke & Pandaleke, 2014). On the other hand, HRH1 in peripheral tissues mediates smooth muscle contraction, increased capillary permeability due to terminal venule contraction, and catecholamine release from the adrenal medulla, as well as mediating neurotransmission in the central nervous system (Shimamura et al., 2012). Increased capillary permeability affects the allergic skin response.

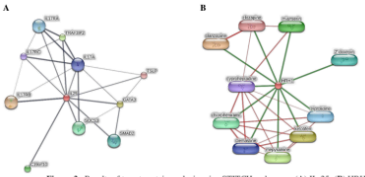


Figure 2. Results of target protein analysis using STITCH webserver. (**A**) IL-25; (**B**) HRH1

Inhibition of the function of these two target proteins is needed to inhibit the inflammatory and allergic processes that are part of eczema. One way to inhibit them is by tethering small bioactive compounds (ligands) to the surface or pockets of the two target proteins. The tethering can be simulated by molecular docking method (Demir & Istifli, 2022). The method tethers the ligand with different positions on the surface of the target protein. The following are the results of molecular docking analysis using Pyrx software version 0.8.

Table 3. Molecular docking results of *Gynura divaricata* bioactive compounds

Compounds	Binding Affinity	
	IL-25	HRH1
2-Hexyl-1-decanol	-5,1	-4,4
2-Undecanone	-4,7	-4,7
Alpha-Caryophyllene	-6,4	-6,2
Gamma-Elemene	-6	-6,3
Naphthalene	-7	-6,7
Spathulenol	-6,3	-6,3
Alpha-Cubebene	-6,5	-7,1
Alpha-Farnesene	-4,6	-4,8
Beta-Caryophyllene	-6,1	-6,3
n-Hexadecanoic	-5,4	-5,3
Wild Ligand of IL-25		
2-acetamido-2-deoxy-beta-D-glucopyranose (CID : NAG)	-6,2*	
Wild Ligand of HRH1		
(2R)-2,3-dihydroxypropyl (9Z)-octadec-9-enoate (CID : OLC)		-4,6*
(3Z)-3-(dibenzo[b,e]oxepin-11(6H)-ylidene)-N,N-dimethylpropan-1-amine (CID : D7V)		-6,8*
(3E)-3-(dibenzo[b,e]oxepin-11(6H)-ylidene)-N,N-dimethylpropan-1-amine (CID : 5EH)		-7,2*

The result of molecular docking shows the prediction of bond affinity energy required to tether the ligand to the target protein (Demir & Istifli, 2022). The results of the analysis on IL-25 showed that the ligand from god's leaf, Naphtalene, had the lowest affinity energy value than the others and was lower than the natural ligand with CID: OLC. In HRH1, Alpha-Cubebene became the ligand with the lowest affinity energy value and even lower than two natural ligands, CID : OLC and D7V. The smaller affinity energy indicates that the ligand will bind more easily to the target protein. Based on this, Naphtalene is predicted to bind more easily than the natural ligand of IL-25 and Alpha-Cubebene is predicted to bind more easily than the two natural ligands of HRH1. The tethering of the ligand with the target protein forms an interaction between the two. The interaction is in the form of the formation of hydrogen bonds between the ligand and the amino acid residues of the target protein.

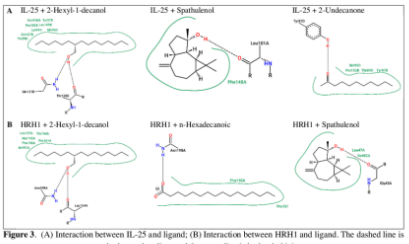


Figure 3. (A) Interaction between IL-25 and ligand; (B) Interaction between HRH1 and ligand. The dashed line is hydrogen bonding, and the green line is hydrophobicity

Visualisation results using ProteinPlus show that in each target protein there are three ligands that form specific chemistry. These bonds are hydrophobic and hydrogen. Hydrophobic bonds cause minimal interaction between water and nonpolar residues, while hydrogen bonds show the stability of ligands on proteins (Frimayanti et al., 2021). The more hydrophobic and hydrogen bonds formed, the greater the stability and interaction between the ligand and the target protein (Frimayanti et al., 2021). Based on the visualisation results, the bioactive compound 2-Hexyl-1-decanol bond has two hydrogen bonds on both target proteins while the other compound only forms one hydrogen bond.

CONCLUSION

Gynura divaricata has bioactive compounds that have potential as eczema drugs. Ten bioactive compounds from deity leaves in silico have potential as anti-eczema and anti-inflammatory, and pass the ADME test. These bioactive compounds are also predicted to be tethered and interact with IL-25 and HRH1 which are eczema target proteins. The interaction is in the form of the formation of hydrophobic bonds and hydrogen bonds.

ACKNOWLEDGMENT

Gynura divaricata potential as antieczema and antiinflammatory based on in silico study.

DOI:10.xxxxx/Biomaxx(x).x

Inhibiting Filaggrin Expression, and Acts Synergistically with TH2 Cytokines to Enhance HSV-1 Replication", Journal of Investigative Dermatology, 2013.
Publication

9 Lusi Suciati, Sri Rahayu Lestari, Betty Lukiati. "Molecular docking studies of geraniin, corilagin, and ellagic acid from rambutan (Nephelium lappaceum L.) peel extract against squalene synthase as potential anti hypercholesterolemia", AIP Publishing, 2020 — 1%
Publication

10 accounts.public.ce.basespace.illumina.com — <1%
Internet Source

11 epdf.tips — <1%
Internet Source

12 Maria Flynn, Kali Amelia Heale, Laleh Alisaraie. "Mechanism of Off-Target Interactions and Toxicity of Tamoxifen and Its Metabolites", Chemical Research in Toxicology, 2017 — <1%
Publication

13 S. Shashidhar Bharadwaj, Boja Poojary, S. Madan Kumar, K. Byrappa et al. "Design, synthesis and pharmacological studies of some new quinoline Schiff bases and 2,5-(disubstituted-[1,3,4])-oxadiazoles", New Journal of Chemistry, 2017 — <1%

22 Internet Source — <1%

23 Angela Mally, Carmen Graff, Olga Schmal, Sabrina Moro et al. "Functional and proliferative effects of repeated low-dose oral administration of furan in rat liver", Molecular Nutrition & Food Research, 2010 — <1%
Publication

24 Elok R. Firdiana, Elga Renjana, Linda W. Ningrum, Melisnawati H. Angio, Muhamad Nikmatullah, Syaiful Rizal. "In Silico Study of the Active Compounds of Lindera aggregata (Sims) Kosterm as Anti-coronavirus", Current Nutrition & Food Science, 2021 — <1%
Publication

Exclude quotes Off
Exclude bibliography Off
Exclude matches Off

Publication

14 McNally, V.A.. "Identification of a novel class of inhibitor of human and Escherichia coli thymidine phosphorylase by in silico screening", Bioorganic & Medicinal Chemistry Letters, 20031103 — <1%
Publication

15 Submitted to University of Wales Swansea — <1%
Student Paper

16 pdfs.semanticscholar.org — <1%
Internet Source

17 swissmodel.expasy.org — <1%
Internet Source

18 www.bestbuy.com — <1%
Internet Source

19 Waterhouse, R.N.. "Determination of lipophilicity and its use as a predictor of blood-brain barrier penetration of molecular imaging agents", Molecular Imaging and Biology, 200311/12 — <1%
Publication

20 assets.researchsquare.com — <1%
Internet Source

21 journals.innovareacademics.in — <1%
Internet Source

www.biowebdb.org

In Silico Screening and Molecular Docking of Potential Bioactive Compounds of Gynura divaricata as E-1726797924766

PAGE 1
PAGE 2
PAGE 3
PAGE 4
PAGE 5
PAGE 6

DOI:10.xxxxx/Biomaxx(x).x