Vol. 1 No. 01 (2022): PROBILITAS, pp 1-7
e-ISSN: XXXX-XXXX
DOI: https://doi.org/10.54482/PROBILITAS/

BIOINFORMATION STUDY OF NONI (MORINDA CITRIFOLIA) AS ANTITUSSIVE AGENT AGAINST SARS-COV-2

Zeeshan Ali[a], Mega Salamatul Masruroh[b], Viola Dwicha Asda[c]

[a]Magister Programme of Engineering, Postgraduate, Bahaudin Zakariya University, Pakistan
[b]Department of Chemistry, Faculty of Mathematics and Natural Sciences (FMIPA), Padang State University, 25171 Indonesia
[c]Magister Programme of Educational Chemistry, Postgraduate, Padang State University, 25171 Indonesia

*Coresponding email: megasalamatul636@gmail.com

ABSTRACT

Sars-Cov-2 which was first identified at the end of 2019 due to Corona Virus infection is still a worldwide pandemic because there is no specific drug that can fight this virus. Several problems, such as the performance of the vaccine that functions to relieve symptoms of Sars-Cov-2 virus infection, have sparked a new view of alternative medicine through natural ingredients as an alternative treatment for this viral infection. The chemical compound Zingiber officinale has potential as an antitussive, but its specific performance is unknown. So in this study, we will predict the molecular mechanism of chemical compounds from Zingiber officinale as a candidate for antitussive Sars-Cov-2, through an in silico approach. The samples of chemical compounds in this study were obtained from the database, then molecular docking simulations were carried out, protein-ligand interaction analysis, and 3D molecular visualization. The results showed that the drug candidate compoundsThe 1,8-cineole compound contained in Zingiber officinale is predicted as a candidate for antitussive drugs, because it has the lowest binding energy. It is recommended that the computational simulation results in this study can be used as a reference for conducting drug design through in vitro and in vivo tests.

Keywords: Antitussive Agent; Noni;. Sars-Cov-2.

1. INTRODUCTION

Since the end of 2019 until now the world has been hit by the Covid-19 pandemic which has had a major impact on changes in human behavior that requires humans to be able to coexist with this virus, said the World Health Organization, common signs of infection with this corona virus include respiratory symptoms, fever, coughing, shortness of breath and difficulty breathing [1] [2].

Some of the symptoms of COVID in the form of coughing can be treated with active antitussive compounds which are a heterogeneous group of compounds that inhibit cough by inhibiting the release of histamine [3][4]. Antitussive compounds can be found in herbal medicines obtained through the use of various plants available in the environment such as red ginger. Antitussive activity of noni copoletin, okoanoic acid, potassium, ascorbic acid, terpenoids, alkaloids, anthraquinones (such as damnacanthal, morindone, rubiadin, and rubiadin-1-methyl ether, anthraquinone glycosides), b-sitosterol, carotene, vitamin A, flavone glycosides, linoleic acid, Alizarin, amino acids, acubin, L-asperuloside, caproicasam, caprylic acid, ursolic acid, rutin, and presumably proxeronine. isolated from this plant, and reported to have antitussive properties [5] [6].

In this computational chemistry course, we conducted an experiment related to docking ligands derived from several active compounds found in the medicinal plant noni [7], namely Ascorbic acid [8][9][10], Beta- carotene and Rutin by shooting them at a nail from the Sars-Cov-2 virus, to see the presence or absence of bonds formed from the reaction between the ligands and spikes and the amount of bond energy obtained, in this case the type of spike that will be fired with the three ligands is used. One of the active compounds in noni with the results of the operation of several supporting applications such as Avogadro, PyMol, Pyrx and DSV (Discovery Studio Visualizer). So in this study, we will predict the potential molecular mechanism of chemical compounds from Morinda citrifolia as a candidate for Covid-19 antitussives.

2. LITERATURE REVIEW

2.1 Noni (Morinda Citrifolia)

Noni is a herbaceous plant that grows bent at a tree height of 3-10 m, has many branches with rectangular branches. The location of the leaves opposite each other in a cross, stemmed with broad oval leaf shape resembling an ellipse or oval with a leaf length of 20-45 cm and a leaf width of 7-25 cm, thick and looks shiny[11]. The leaf edge is flat, the tip is tapered, with a narrow leaf base, pinnate leaf bone with dark green leaf color [12][13].

Taxonomy of noni fruit is as follows [14]

Kingdom : Plantae
Division : Spermatophyta
Subdivision : Angiosperms
Class : Dicotyledone
class boy : Sympetalae
Nation : Rubiales
Tribe : Rubiaceae
Genus : Morinda
Species : Citrifolia
Scientific name : Morinda citrifolia [15]

Noni fruit (Morinda citrifolia) contains a source of antioxidants consisting of a group of antioxidants consisting of xeronin, proxeronin, ascorbic acid, linoleic acid, -carotene, flavonoids and caprylit acid [16][17][18][19]. Endothelial dysfunction is an early stage of the atherosclerotic process. Antioxidants also function to inhibit the oxidation of LDL so that oxidized LDL is not formed [20].

Noni fruit also contains scopoletin. Scopoletin in noni fruit can increase the activity of endogenous antioxidants such as superoxide dismutase [21]. So that the noni fruit is not only a source of secondary antioxidants but can increase primary antioxidants in the body [22] [23] .The use of noni fruit and leaves as wound medicine and meat tenderizer is thought to be related to protease activity. The high potential of protease enzyme trade has encouraged the exploration of proteases from noni fruit and leaves [24] .

3. EXPERIMENTAL

In docking active compounds that act as ligands with spike proteins from viruses Sars_Cov_2, perform the following steps: and the last step we will see how the ligand interacts with the spike by circling the ligand with the spike then click the Non-Bond Interactions button select Within Selection and mark the entire Favorable column in the Interaction Type and we can see the bond that occurs between the ligand and the spike protein which is indicated by dotted line and we save the DS result data as the last step of the docking process of the ligand active compound with spike protein. The systematic diagram can be seen in (Figure 1).

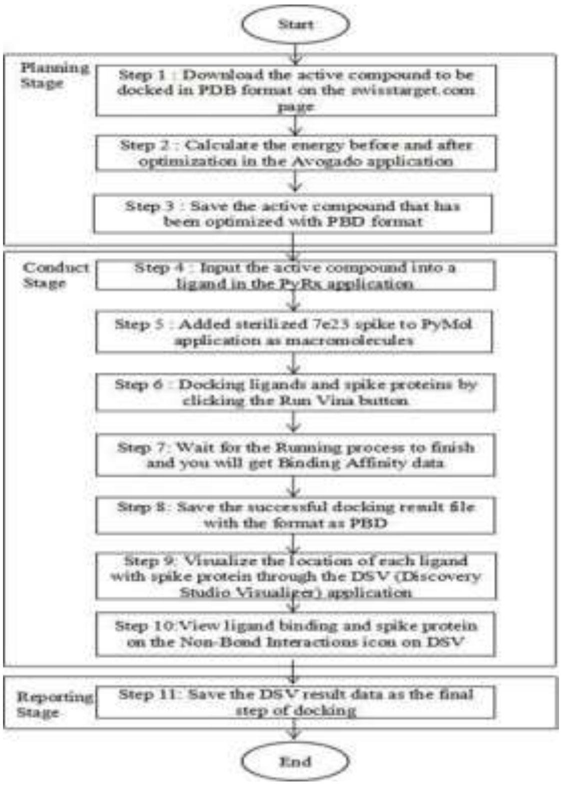

Figure 1. Docking Process

4. RESULTS AND DISCUSSION

4.1 Result

Ascorbic acid is the main active compound contained in noni (Morinda citrifolia) which ISOMERIC SMILE data has obtained at https://pubchem.ncbi.nlm.nih.gov/ then converted into protein databank (.pdb), before adding the active compound to ligands for docking with spikes, first calculate the energy of the active compound before and after optimization through the Avogadro application.

Mode of Action of Chemical Compounds from Zingiber officinale roce as Antivirus Agent Molecular docking is the process of binding ligands to target proteins and aims to determine the binding energy formed in stable molecular complexes Proteins were prepared using PyMol software to remove water molecules [25] [26]. This study used a blind docking method, because the functional side of the target protein is not yet known.

Molecular docking is a computational research method that aims to estimate the interaction and affinity of ligands for macromolecules (usually proteins) [27] [28]. A ligand and protein molecule are predicted by placing techniques in a certain area (active site) so as to give optimal results. Generate interaction poses and scores that determine whether or not an interaction pose is good (docking score). ChemPLP value is calculated based on Gibbs free energy where the smaller (more negative) the positive control compound can be said to have a good binding affinity, indicating that the compound easily binds to the receptor. Based on the results of the compound docking test and the positive control of the Glycogen Synthase Kinase 3 beta (1h8f) compound, the following data were obtained:

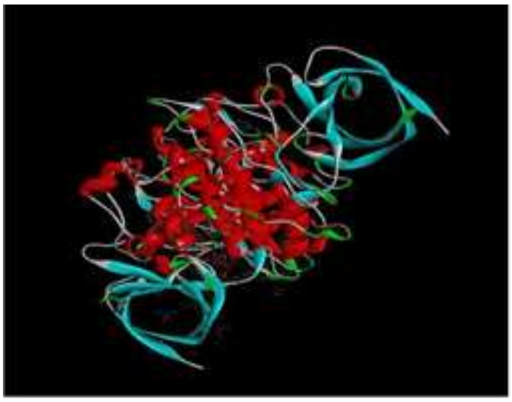

Figure 2. Glycogen Synthase Kinase 3 beta, Ascorbic acid compound docked with Cu_2O_3_396

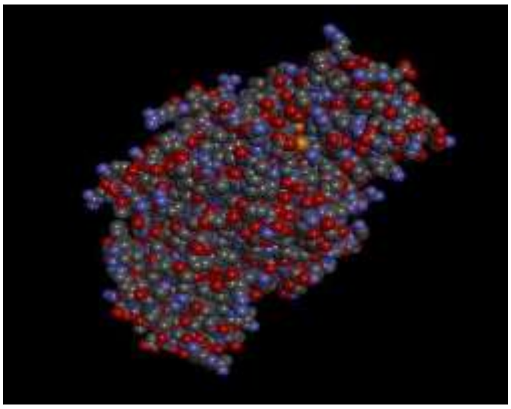

Figure 3. Glycogen Synthase Kinase 3 beta, Ascorbic acid compound docked

```
Ligand, Binding Affinity, rmsd/ub, rmsd/lb
1h8f_Cu2O3_396,-10.1.0.0,0.0
1h8f_Cu2O3_396,-10.0,33,269,27,262
1h8f_Cu2O3_396,-9.3,32.109,26.067
1h8f_Cu2O3_396,-9.3,10.402,2.292
1h8f_Cu2O3_396,-9.1,10.4,2.446
1h8f_Cu2O3_396,-8,4,32,326,26,677
1h8f_Cu2O3_396,-8.4,7.99,3.837
1h8f_Cu2O3_396,-8.3,9.239,3.584
1h8f_Cu2O3_396,-8.3,29.906,24.539
```

Ligands that have the lowest binding energy are able to affect the biological activity of a target protein. The lowest binding energy values allow the formation of molecular complexes under constant temperature and pressure [29] [30] .

5. CONCLUSION

There is Glycogen Synthase Kinase 3 beta, an ascorbic acid compound in limes which is an active compound that binds fat which is used as an anti-obesity agent. In the docking test process, the active compound was able to bind to the Cu-O ligand.

REFERENCES

[1] S. S. T. Asral and R. Zainul, “Pengembangan Konten Pembelajaran E-Learning untuk Materi Larutan Elektrolit dan Non Elektrolit Menggunakan Aplikasi Moodle,” *Entalpi Pendidik. Kim.*, vol. 1, no. 1, 2020, doi: 10.24036/epk.v1i1.92.

[2] V. D. Kharisma *et al.*, “Herbal combination from Moringa oleifera Lam. and Curcuma longa L. as SARS-CoV-2 antiviral via dual inhibitor pathway: A viroinformatics approach,” *J. Pharm. Pharmacogn. Res.*, vol. 10, no. 1, pp. 138–146, 2022.

[3] A. D. Husna and R. Zainul, “Analisis Molekular dan Karakteristik Hidrogen Sianida (HCN),” 2019, doi: 10.31227/osf.io/7xej9.

[4] A. Firdaus and R. Zainul, “SESIUM KLORIDA (CsCl) : TRANSPORT ION DALAM LARUTAN,” 2018, doi: 10.31227/osf.io/rj6gy.

[5] R. Geng, R. Chang, Q. Zou, G. Shen, T. Jiao, and X. Yan, “Biomimetic Nanozymes Based on Coassembly of Amino Acid and Hemin for Catalytic Oxidation and Sensing of Biomolecules,” *Small*, vol. 17, no. 19, 2021, doi: 10.1002/smll.202008114.

[6] F. Yuliani and R. Zainul, “Analisis Termodinamika Molekul Magnesium Sulphate (MgSO4),” vol. 0, pp. 5–6, 2018, doi: 10.31227/osf.io/uxz4y.

[7] S. Khotijah, “Synthesis of silver nanoparticles used chemical reduction method by glucose as reducing agent Synthesis of silver nanoparticles used chemical reduction method by glucose as reducing agent,” 2019, doi: 10.1088/1742-6596/1317/1/012027.

[8] R. Yulis, R. Zainul, and M. Mawardi, “Effect of natrium sulphate concentration on indoor lights photovoltaic performance,” *J. Phys. Conf. Ser.*, vol. 1185, no. 1, 2019, doi: 10.1088/1742-6596/1185/1/012019.

[9] D. T. Rahmandhias and D. Rachmawati, “Pengaruh Asam Humat terhadap Produktivitas dan Serapan Nitrogen pada Tanaman Kangkung Darat (Ipomoea reptans Poir .) (The Effect of Humic Acid on Productivity and Nitrogen Uptake in Kangkong (Ipomoea reptans Poir .)),” vol. 25, no. April, pp. 316–322, 2020, doi: 10.18343/jipi.25.2.316.

[10] S. Mandar, D. Purnamsari, and R. Zainul, “Chataliytic activity of nano ZnO/Cu for degradation humic acid under ilumination outdoor light,” *J. Phys. Conf. Ser.*, vol. 1481, no. 1, 2020, doi: 10.1088/1742-6596/1481/1/012038.

[11] H.-J. Hwang, K.-O. Shin, and K.-S. Han*, “A Study on the Function and Role of Morinda citrifolia L. (Noni),” *Korean J. Food Nutr*, vol. 32, no. 4, pp. 275–283, 2019, [Online]. Available: https://doi.org/10.9799/ksfan.2019.32.4.275.

[12] Z. Wang, R. Dou, R. Yang, K. Cai, C. Li, and W. Li, “Changes in phenols, polysaccharides and volatile profiles of noni (Morinda citrifolia l.) juice during fermentation,” *Molecules*, vol. 26, no. 9, pp. 1–15, 2021, doi: 10.3390/molecules26092604.

[13] G. Rajivgandhi *et al.*, “Enhanced anti-cancer activity of chitosan loaded Morinda citrifolia essential oil against A549 human lung cancer cells,” *Int. J. Biol. Macromol.*, vol. 164, pp. 4010–4021, 2020, doi: 10.1016/j.ijbiomac.2020.08.169.

[14] L. Arya, R. K. Narayanan, A. Kak, C. D. Pandey, M. Verma, and V. Gupta, “ISSR marker based genetic diversity in Morinda spp. for its enhanced collection, conservation and utilization,” *Genet. Resour. Crop Evol.*, pp. 1–13, 2022, doi: 10.1007/s10722-021-01321-2.

[15] S. A. Saah and D. Adu-Poku, “Phytochemical, Proximate, and Vitamin C Content in Morinda citrifolia (Noni),” *J. Trop. Pharm. Chem.*, vol. 5, no. 3, pp. 182–187, 2021, doi: 10.25026/jtpc.v5i3.274.

[16] D. Njus, P. M. Kelley, Y. J. Tu, and H. B. Schlegel, “Ascorbic acid: The chemistry underlying its antioxidant properties,” *Free Radic. Biol. Med.*, vol. 159, no. 313, pp. 37–43, 2020, doi: 10.1016/j.freeradbiomed.2020.07.013.

[17] I. D. P. Kartika Pratiwi, I. K. Suter, P. A. S. Widpradnyadewi, and A. A. I. S. Wiadnyani,

"Perubahan Fisiko-Kimiawi dan Mikrobiologis Minuman Tradisional Bali (Loloh) selama Penyimpanan," *agriTECH*, vol. 39, no. 1, p. 70, 2019, doi: 10.22146/agritech.17261.

[18] W. Ngwa *et al.*, "Potential of Flavonoid-Inspired Phytomedicines against COVID-19," pp. 1–10, 2020.

[19] M. Cap *et al.*, "Inactivation of Shiga toxin-producing Escherichia coli in fresh beef by electrolytically-generated hypochlorous acid, peroxyacetic acid, lactic acid and caprylic acid," *Meat Sci.*, vol. 157, p. 107886, 2019, doi: 10.1016/j.meatsci.2019.107886.

[20] V. J. van den Berg *et al.*, "Anti-oxidized LDL antibodies and coronary artery disease: A systematic review," *Antioxidants*, vol. 8, no. 10, pp. 1–17, 2019, doi: 10.3390/antiox8100484.

[21] S. Il Choi *et al.*, "Development and validation of an analytical method for deacetylasperulosidic acid, asperulosidic acid, scopolin, asperuloside and scopoletin in fermented morinda citrifolia l. (noni)," *Separations*, vol. 8, no. 6, 2021, doi: 10.3390/separations8060080.

[22] T. M. Wardiny, Sumiati, Y. Retnani, and A. Setiyono, "Production of Functional Kampong Chicken Meat with Low Cholesterol, High Antioxidant, and Unsaturated Fatty Acids Fed Noni (Morinda citrifolia) Leaf Shoot Meal," *Trop. Anim. Sci. J.*, vol. 43, no. 1, pp. 35–42, 2020, doi: 10.5398/tasj.2020.43.1.35.

[23] Rabima, L. Harlim, and Sogandi, "Bioactive compound analysis and antioxidant activity of endophytic bacterial extract from Noni fruits (Morinda citrifolia L.)," *IOP Conf. Ser. Earth Environ. Sci.*, vol. 475, no. 1, 2020, doi: 10.1088/1755-1315/475/1/012077.

[24] W. N. F. Wan Osman, N. A. Che Ahmad Tantowi, S. F. Lau, and S. Mohamed, "Epicatechin and scopoletin rich Morinda citrifolia (Noni) leaf extract supplementation, mitigated Osteoarthritis via anti-inflammatory, anti-oxidative, and anti-protease pathways," *J. Food Biochem.*, vol. 43, no. 3, 2019, doi: 10.1111/jfbc.12755.

[25] A. I. Jarmolinska, Q. Zhou, J. I. Sulkowska, and F. Morcos, "DCA-MOL: A PyMOL Plugin To Analyze Direct Evolutionary Couplings," *J. Chem. Inf. Model.*, vol. 59, no. 2, pp. 625–629, 2019, doi: 10.1021/acs.jcim.8b00690.

[26] B. Schiffrin, S. E. Radford, D. J. Brockwell, and A. N. Calabrese, "PyXlinkViewer: A flexible tool for visualization of protein chemical crosslinking data within the PyMOL molecular graphics system," *Protein Sci.*, vol. 29, no. 8, pp. 1851–1857, 2020, doi: 10.1002/pro.3902.

[27] L. Pinzi and G. Rastelli, "Molecular docking: Shifting paradigms in drug discovery," *Int. J. Mol. Sci.*, vol. 20, no. 18, 2019, doi: 10.3390/ijms20184331.

[28] S. Kumar *et al.*, "Discovery of New Hydroxyethylamine Analogs against 3CLproProtein Target of SARS-CoV-2: Molecular Docking, Molecular Dynamics Simulation, and Structure-Activity Relationship Studies," *J. Chem. Inf. Model.*, vol. 60, no. 12, pp. 5754–5770, 2020, doi: 10.1021/acs.jcim.0c00326.

[29] Z. Wu, M. Jiang, Z. Liu, A. Jamshaid, L. K. Ono, and Y. Qi, "Highly Efficient Perovskite Solar Cells Enabled by Multiple Ligand Passivation," *Adv. Energy Mater.*, vol. 10, no. 10, pp. 1–5, 2020, doi: 10.1002/aenm.201903696.

[30] H. Cheng *et al.*, "Ligand-Exchange-Induced Amorphization of Pd Nanomaterials for Highly Efficient Electrocatalytic Hydrogen Evolution Reaction," *Adv. Mater.*, vol. 32, no. 11, 2020, doi: 10.1002/adma.201902964.