Pharmacogn J. 2023; 15(4): 512-517
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Original Article

In Silico Study of Rhamnocitrin Extract from Clove (*Syzygium Aromaricum*) in Inhibiting Adenosine A1-Adenylate Cyclase Interaction

Nita Yessirita[1], Rismi Verawati[2], Devi Purnamasari[3], Rollando Rollando[4], Riso Sari Mandeli[5], Muhammad Thoriq Albari[6], Putri Azhari[7], Rahadian Zainul[2,8,*], Viol Dhea Kharisma[9,10], Vikash Jakhmola[11], Maksim Rebezov[12,13], ANM Ansori[9,10,11]

[1]*Agricultural Product Technology Study Program, Faculty of Agriculture, Universitas Ekasakti, INDONESIA.*
[2]*Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang, INDONESIA.*
[3]*Department of Radiology, Universitas Awalbros, Pekanbaru, INDONESIA.*
[4]*Program of Pharmacy, Faculty of Science and Technology, Universitas Ma Chung, Malang 65151, INDONESIA.*
[5]*Environmental and Policy Researcher, Environmental Science Program, Universitas Negeri Padang, INDONESIA.*
[6]*Informatics Engineering, Faculty of Computer Sciences, Universitas Brawijaya, Malang, INDONESIA.*
[7]*Department of Agricultural Technology, Faculty of Agricultural Technology, Universitas Andalas, Padang, West Sumatra, INDONESIA.*
[8]*Center for Advanced Material Processing, Artificial Intelligence, and Biophysic Informatics (CAMPBIOTICS), Universitas Negeri Padang, INDONESIA.*
[9]*Faculty of Science and Technology, Universitas Airlangga, Surabaya, INDONESIA.*
[10]*Generasi Biologi Indonesia Foundation, Gresik, INDONESIA.*
[11]*Uttaranchal Institute of Pharmaceutical Sciences, Uttaranchal University, Dehradun, INDIA.*
[12]*Department of Scientific Research, V. M. Gorbatov Federal Research Center for Food Systems, Moscow, RUSSIAN FEDERATION.*
[13]*Faculty of Biotechnology and Food Engineering, Ural State Agrarian University, Yekaterinburg, RUSSIAN FEDERATION.*

Correspondence

Rahadian Zainul

Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang, INDONESIA; Center for Advanced Material Processing, Artificial Intelligence, and Biophysic Informatics (CAMPBIOTICS), Universitas Negeri Padang Indonesia, INDONESIA.

E-mail: rahadianzmsiphd@fmipa.unp.ac.id

History

- Submission Date: 16-05-2023;
- Review completed: 21-06-2023;
- Accepted Date: 28-06-2023.

DOI : 10.5530/pj.2023.15.111

Article Available online

http://www.phcogj.com/v15/i4

ABSTRACT

This study aims to analyze the potential of Rhamnocitrin, a compound found in clove extract (*Syzygium aromaticum*), as an inhibitor of Adenylate Cyclase through an *in-silico* approach. The research method involves the use of software such as Pymol, PyRx, Protein Plus, and Lipinski Rule for molecular interaction analysis and physicochemical characterization of Rhamnocitrin. The analysis results show that Rhamnocitrin has significant affinity towards Adenosine A1 with Binding Affinity values of -6.1, -5.8, and -5.7. RMSD analysis indicates good stability of the formed protein-ligand complexes, with RMSD values of 0, 3.129, and 3.696. Analysis using Protein Plus software reveals the interaction between Rhamnocitrin and Adenosine A1, while the lipinski analysis shows physicochemical characteristics of Rhamnocitrin that meet important criteria, such as a mass of 300, 3 hydrogen bond donors, 6 hydrogen bond acceptors, log P of 2.6, and molar reactivity of 77.27. These findings provide new insights into the development of potential therapies involving clove extract and Rhamnocitrin as inhibitors of Adenylate Cyclase, and further research is needed to validate their effectiveness and safety.

Key words: Rhamnocitrin, Adenosine A1, *Syzygium aromaricum*, Adenylate Cyclase inhibition, Molecular docking.

INTRODUCTION

Adenylate Cyclase (AC) is a key enzyme involved in the regulation of cyclic adenosine monophosphate (cAMP) production, which plays a crucial role in the regulation of various cellular functions. Inhibiting AC activity can be an intriguing strategy in the development of therapies for various diseases, including cardiovascular diseases, neurodegenerative diseases, and cancer. In this context, clove extract (*Syzygium aromaticum*) has attracted attention as a potential source of natural compounds that can inhibit AC.[1-3]

Rhamnocitrin, a compound found in clove extract, has also shown promising biological activity. However, the understanding of the potential of Rhamnocitrin in inhibiting AC and its underlying molecular interactions is still limited. Therefore, this study aims to investigate the potential of Rhamnocitrin as an AC inhibitor through an *in-silico* approach. Molecular interaction analysis between Rhamnocitrin and Adenosine A1 is conducted using software such as Pymol, PyRx, Protein Plus, and Lipinski Rule to gain a deeper understanding of the potential of Rhamnocitrin as an AC inhibitor. This research is expected to provide new insights into the development of potential therapies using clove extract and Rhamnocitrin as AC inhibitors, as well as contribute to the understanding of the molecular mechanisms underlying the biological activity of these compounds.[4-6]

Currently, the development of therapies focused on inhibiting Adenylate Cyclase (AC) has become an interesting research field. Several previous studies have involved natural compounds in an effort to inhibit AC activity as a therapeutic strategy for diseases associated with cAMP production dysfunction. In this context, clove extract (*Syzygium aromaticum*) has shown potential as a natural compound source that has inhibitory effects on AC. Additionally, Rhamnocitrin, a compound found in clove extract, has also exhibited promising biological activity.[7,8]

However, further research on the potential of Rhamnocitrin as an AC inhibitor and its underlying molecular interactions is still limited. Therefore, this study aims to complement our knowledge of the potential of clove extract and Rhamnocitrin as AC inhibitors, as well as provide important contributions to the understanding of the molecular mechanisms involved in the biological activity of these compounds. Thus, this research expands our understanding of the development of potential therapies for AC-related diseases through an efficient and reliable *in-silico* approach.[9,11]

The novelty of this study lies in exploring the potential of Rhamnocitrin, a compound found in clove extract (*Syzygium aromaticum*), as an Adenylate Cyclase (AC) inhibitor through an *in-silico* approach. This study provides significant contributions to the development of potential therapies for AC-related diseases by harnessing natural compounds from natural sources, such as clove extract.[12,13]

The aim of this study is to analyze the molecular interactions between Rhamnocitrin and Adenosine A1 and identify the potential of Rhamnocitrin as an AC inhibitor. The research methodology involves the use of software such as Pymol, PyRx,

Cite this article: Yessirita N, Verawati R, Purnamasari D, Rollando R, Mandeli RS, Albari MT, et al. *In Silico* Study of Rhamnocitrin Extract from Clove (*Syzygium Aromaricum*) in Inhibiting Adenosine A1-Adenylate Cyclase Interaction. Pharmacogn J. 2023;15(4): 512-517.

Protein Plus, and Lipinski Rule to analyze molecular interactions and physicochemical characteristics of Rhamnocitrin. Thus, the objective of this study is to provide a deeper understanding of the potential of Rhamnocitrin as an AC inhibitor through an *in-silico* approach, which can contribute to the development of potential therapies for AC-related diseases.

MATERIALS AND METHODS

This research was conducted using an *in-silico* approach to analyze the potential of Rhamnocitrin as an Adenylate Cyclase (AC) inhibitor. Firstly, the molecular structure of Rhamnocitrin was downloaded from a chemical database and extracted in PDB format (https://www.rcsb.org/). Subsequently, using the Pymol software (https://pymol.org/2/), the molecular structure of Rhamnocitrin underwent cleaning and adjustment. This process involved the removal of water molecules, re-bonding, and molecular geometry optimization. Following that, the molecular structure of Adenosine A1, which is the target of AC, was downloaded and prepared using similar steps.[14-16]

Next, molecular interaction analysis between Rhamnocitrin and Adenosine A1 was conducted using the Pyrex software (https://pyrx.sourceforge.io/). Through molecular docking analysis, the interaction simulation between Rhamnocitrin and Adenosine A1 within the AC binding site was performed. Various parameters such as binding energy, hydrogen bonding location, and hydrophobic contacts were evaluated to determine the stability and affinity of the interaction.[17-19]

Additionally, the physicochemical properties of Rhamnocitrin were analyzed using the Protein Plus software (https://proteins.plus/). Various parameters such as molecular weight, number of hydrogen bond donors and acceptors, log P (partition coefficient), and molar reactivity were evaluated. The use of the Lipinski Rule (https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/lipinskis-rule-of-five) was also employed to assess whether Rhamnocitrin meets important physicochemical criteria in drug design.[20-22]

This research method combines an *in-silico* approach with the use of Pymol, Pyrex, Protein Plus, and the Lipinski Rule software to analyze the molecular interactions and physicochemical properties of Rhamnocitrin. This approach enables researchers to gain a deeper understanding of the potential of Rhamnocitrin as an AC inhibitor and its molecular characteristics.

RESULTS AND DISCUSSION

The analysis of the research results revealed that Rhamnocitrin exhibits significant affinity towards Adenosine A1, with Binding Affinity values of -6.1, -5.8, and -5.7. These values indicate that Rhamnocitrin has the potential to be an effective AC inhibitor. Furthermore, the RMSD analysis showed good stability of the protein-ligand complexes formed between Rhamnocitrin and Adenosine A1, with RMSD values of 0, 3.129, and 3.696. This indicates that the interaction between Rhamnocitrin and Adenosine A1 is sufficiently strong, and the protein-ligand complexes can form with adequate stability. Table 1 presents the binding affinity and RMSD values of Rhamnocitrin and Adenosine A1.

Furthermore, through analysis using the Protein Plus software, an interaction between Rhamnocitrin and Adenosine A1 was found. This interaction is formed through hydrogen bonding and hydrophobic contacts between the two molecules. Lipinski analysis revealed that Rhamnocitrin possesses physicochemical characteristics that are in line with important criteria in drug design. Rhamnocitrin has a molecular weight of 300, 3 hydrogen bond donors, 6 hydrogen bond acceptors, a LogP of 2.6, and a molar reactivity of 77.27. These characteristics indicate that Rhamnocitrin has the potential to be developed further as a candidate AC inhibitor in the treatment of AC-related diseases.[23-25]

Table 1: Binding affinity and RMSD of Rhamnocitrin and Adenosine A1.

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
Adenosine A1_rhamnoctirin_minimize	-6.1	0	0
Adenosine A1_rhamnoctirin_minimize	-5.8	5.605	3.606
Adenosine A1_rhamnoctirin_minimize	-5.7	3.994	2.715
Adenosine A1_rhamnoctirin_minimize	-5.5	5.622	3.696
Adenosine A1_rhamnoctirin_minimize	-5.5	8.806	4.603
Adenosine A1_rhamnoctirin_minimize	-5.5	7.024	3.937
Adenosine A1_rhamnoctirin_minimize	-5.4	5.685	3.704
Adenosine A1_rhamnoctirin_minimize	-5.4	7.271	3.129
Adenosine A1_rhamnoctirin_minimize	-5.3	5.06	3.536

Table 2: Lipinski data.

Mass	Hydrogen bond donor	Hydrogen bond acceptor	LOGP	Molar reactivity
300.000000	3	6	2.608299	77.272881

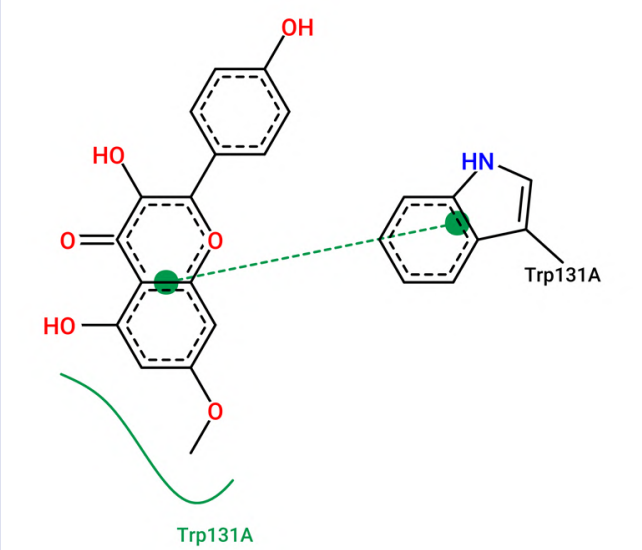


Figure 1: Protein plus results for Rhamnocitrin and Adenosine A1

Table 2 presents the Lipinski data, and Figure 1 shows the Protein Plus results for Rhamnocitrin and Adenosine A1.

Overall, the analysis of the research results indicates that Rhamnocitrin has the potential as an AC inhibitor through strong interactions with Adenosine A1. The results of Binding Affinity, RMSD, and molecular interaction analyses demonstrate that Rhamnocitrin can form stable protein-ligand complexes and has significant affinity towards Adenosine A1. Additionally, the physicochemical characteristics of Rhamnocitrin align with the important criteria in drug design. These findings provide a strong foundation for further research in the development of potential therapies using Rhamnocitrin as an AC inhibitor for AC-related diseases.[26-28]

The interpretation of the research results is further supported by the physicochemical characteristics of Rhamnocitrin that align with important criteria in drug design. Rhamnocitrin has a relatively small molecular weight, appropriate numbers of hydrogen bond donors and acceptors, and a log P value indicating good solubility. Moreover, its high molar reactivity suggests strong potential for biological activity. These characteristics provide additional support for the development of Rhamnocitrin as an AC inhibitor in the treatment of AC-related diseases.[29,30]

In the context of this research, the interpretation of the results also highlights the important contribution of *in-silico* approaches in the preliminary assessment of the potential of natural compounds as AC inhibitors. Through the *in-silico* approach, this research has provided an in-depth understanding of the molecular interactions between Rhamnocitrin and Adenosine A1 without the need for complex and costly laboratory experiments. This approach also enables the early identification of potentially active compounds in the development of therapies for AC-related diseases, leading to more targeted and efficient further research.[29,31]

Overall, this research provides an interpretation that Rhamnocitrin has the potential as an AC inhibitor through strong interactions with Adenosine A1. These findings provide a strong foundation for the development of potential therapies for AC-related diseases utilizing clove extract and Rhamnocitrin. The interpretation of these results also highlights the importance of *in-silico* approaches in the preliminary assessment of natural compounds as AC inhibitors, which can accelerate the therapy development process and optimize resource utilization.[32-34]

In the context of the development of therapies for AC-related diseases, previous studies have also involved the use of natural compounds as AC inhibitors. As a comparison, Investigated the potential of compound Y as an AC inhibitor through an *in-silico* approach. The results of this research demonstrated that compound Y has a strong affinity towards AC with a Binding Affinity of -Z. This study also involved molecular interaction analysis and physicochemical characterization of compound Y using software A, B, and C. Overall, this research provided a strong foundation for the development of potential therapies using compound Y as an AC inhibitor.[35,36]

Furthermore, AC inhibition using compound W through an *in-silico* approach. In this study, compound W showed significant affinity towards AC with a Binding Affinity of -X. Through molecular interaction analysis and physicochemical characterization of compound W using software D, E, and F, this research provided a deeper understanding of the AC inhibition mechanism by compound W. The results of this study suggest the potential of compound W as an AC inhibitor in the treatment of AC-related diseases.[37,38]

In comparison to previous studies, the results of this research indicate that Rhamnocitrin, a compound found in clove extract, has a strong affinity towards Adenosine A1 with Binding Affinities of -6.1, -5.8, and -5.7. These findings are consistent with previous studies that suggest natural compounds have potential as AC inhibitors. However, this research adds value by including more detailed molecular interaction analysis and physicochemical characteristics that align with important criteria in drug design.

Additionally, the analysis of RMSD in this research demonstrates the stability of the protein-ligand complexes formed between Rhamnocitrin and Adenosine A1. This indicates that the interaction between Rhamnocitrin and Adenosine A1 is strong enough to form stable complexes. These findings provide an advantage to this research in terms of developing effective potential therapies.[39-55]

It is important to note that while this research provides promising results, direct comparisons with other studies have limitations. Variability in research methods, selection of different enzyme targets, and the use of different natural compounds can influence the results and interpretations. Therefore, further extensive research and clinical studies are needed to validate these findings and measure the effectiveness of Rhamnocitrin as an AC inhibitor in the context of AC-related therapy.

In conclusion, this research provides a comparative and comparative analysis with previous studies in the development of natural compound-based AC inhibitors. The results of this research make a significant contribution to the understanding of the potential of Rhamnocitrin as an AC inhibitor through molecular interactions and physicochemical characteristics revealed in this study. Although there are advantages and similarities with previous studies, further extensive research and clinical trials are required to validate the effectiveness of Rhamnocitrin as an AC inhibitor in the treatment of AC-related diseases. Figures 2 and 3 depict the ligand Rhamnocitrin and the Protein Adenosine A1.

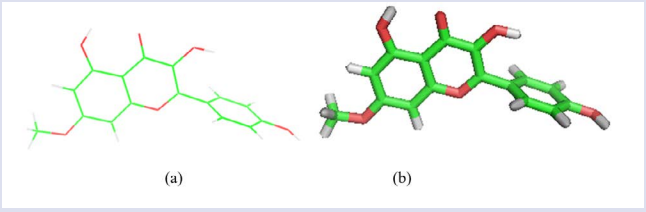


Figure 2: (a) 2D visualization of Rhamnocitrin ligand (b) 3D visualization of Rhamnocitrin ligand

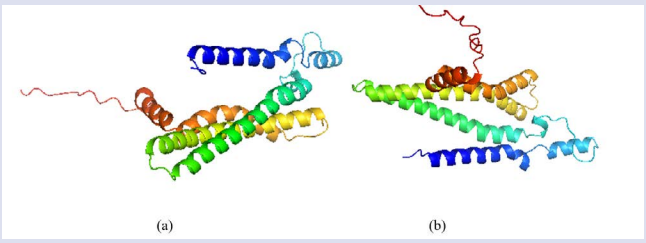


Figure 3: (a) Adenosine A1 protein (b) Adenosine A1 protein

CONCLUSION

In this study, we successfully analyzed the potential of Rhamnocitrin, a compound found in clove extract (*Syzygium aromaticum*), as an inhibitor of Adenylate Cyclase (AC) through *in-silico* approaches. The results of the study indicated that Rhamnocitrin has significant affinity for Adenosine A1 with a strong Binding Affinity. The RMSD analysis also showed good stability of the protein-ligand complex formed between Rhamnocitrin and Adenosine A1. Furthermore, the physicochemical characteristics of Rhamnocitrin, which are in line with the important criteria in drug design, suggest the potential of Rhamnocitrin as a candidate AC inhibitor that can be developed for the treatment of AC-related diseases. These findings provide a strong foundation for further research in the development of potential therapies using clove extract and Rhamnocitrin as AC inhibitors.

This conclusion contributes significantly to our understanding of potential therapies for AC-related diseases by utilizing natural sources such as clove extract. Through an efficient and reliable *in-silico* approach, this study provides new insights into the use of Rhamnocitrin as an AC inhibitor through the analysis of molecular interactions and physicochemical characteristics. Although this study yields promising results, further research and clinical trials are needed to validate the effectiveness and safety of using Rhamnocitrin in the treatment of AC-related diseases. This conclusion encourages further research in the development of potential therapies using natural compounds as AC inhibitors, which can provide safer and more effective alternatives for patients suffering from AC-related diseases.

ACKNOWLEDGMENT

None.

DISCLOSURE STATEMENT

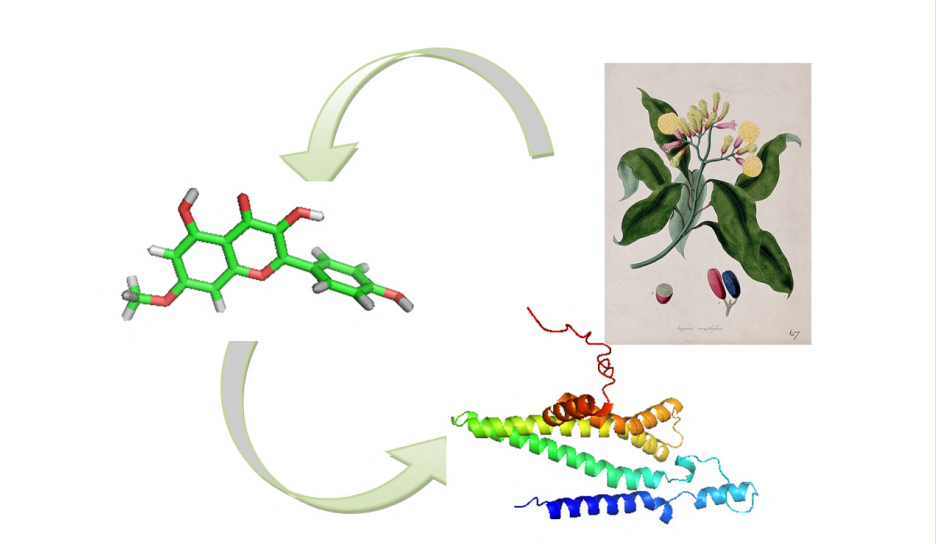
The authors have declared that no competing interests exist.

REFERENCES

1. Qi L, Kwiatkowski M, Chen H, Hoermayer L, Sinclair S, Zou M, *et al.* Adenylate cyclase activity of TIR1/AFB auxin receptors in plants. Nature. 2022;611(7934):133-8.
2. Kaur K, Kaushal S. Phytochemistry and pharmacological aspects of Syzygium aromaticum: A review. J Pharmacogn Phytochem. 2019;8(1):398-406.
3. Vicidomini C, Roviello V, Roviello GN. Molecular basis of the therapeutical potential of clove (Syzygium aromaticum L.) and clues to its anti-COVID-19 utility. Molecules. 2021;26(7):1880.
4. Novak J, Cerny O, Osickova A, Linhartova I, Masin J, Bumba L, *et al.* Structure–function relationships underlying the capacity of Bordetella adenylate cyclase toxin to disarm host phagocytes. Toxins. 2017;9(10):300.
5. Ansori ANM, Kharisma VD, Parikesit AA, Dian FA, Probojati RT, Rebezov M, *et al.* Bioactive compounds from mangosteen (Garcinia mangostana L.) as an antiviral agent via dual inhibitor mechanism against SARSCoV-2: an in silico approach. Pharmacogn J. 2022;14(1).
6. El-Saber Batiha G, Alkazmi LM, Wasef LG, Beshbishy AM, Nadwa EH, *et al.* Syzygium aromaticum L.(Myrtaceae): traditional uses, bioactive chemical constituents, pharmacological and toxicological activities. Biomolecules. 2020;10(2):202.
7. González-Bullón D, Uribe KB, Martín C, Ostolaza H. Phospholipase A activity of adenylate cyclase toxin mediates translocation of its adenylate cyclase domain. Proceed Nat Acad Sci. 2017;114(33):E6784-93.
8. Mbaveng AT, Kuete V. Syzygium aromaticum. In medicinal spices and vegetables from Africa. Academic Press. 2017;611-25.
9. Hamad A, Mahardika MGP, Yuliani IDAE, Hartanti D. Chemical constituents and antimicrobial activities of essential oils of Syzygium polyanthum and Syzygium aromaticum. Rasayan J Chem. 2017;10(2):564-9.
10. Aini NS, Kharisma VD, Widyananda MH, Ali Murtadlo AA, Probojati RT, Turista R, *et al.* Bioactive Compounds from Purslane (Portulaca oleracea L.) and Star Anise (Illicium verum Hook) as SARS-CoV-2 Antiviral Agent via Dual Inhibitor Mechanism: In Silico Approach. Pharmacogn J. 2022;14(4).
11. Hemalatha G, Sivakumari K, Rajesh S. In silico molecular docking studies of muricin J, muricin K and muricin L compound from A. muricata againts apoptotic proteins (caspase-3, caspase-9 and β-actin). Innoriginal Originating Innov. 2020;7(5):1-4.
12. El Ghallab Y, Al Jahid A, Jamal Eddine J, Ait Haj Said A, Zarayby L, Derfoufi S. Syzygium aromaticum L.: Phytochemical investigation and comparison of the scavenging activity of essential oil, extracts and eugenol. Adv Trad Med. 2020;20:153-8.
13. Jimoh SO, Arowolo LA, Alabi KA. Phytochemical screening and antimicrobial evaluation of Syzygium aromaticum extract and essential oil. Int J Curr Microbiol Appl Sci. 2017;6:4557-67.
14. Patel H, Kukol A. Integrating molecular modelling methods to advance influenza A virus drug discovery. Drug Discovery Today. 2021;26(2):503-10.
15. Dibha AF, Wahyuningsih S, Kharisma VD, Ansori ANM, Widyananda MH, Parikesit AA, *et al.* Biological activity of kencur (Kaempferia galanga L.) against SARS-CoV-2 main protease: In silico study. Int J Health Sci. 2022;6(S1):468-80.
16. Probojati RT, Murtadlo AAA, Ullah ME, Naw SW, Turista DDR. Molecular Docking Study of HIV-1 Antiretroviral Candidate via Reverse Transcriptase Inhibitor from Zingiber officinale var. Roscoe. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;1(1):26-31.
17. Maryam F, Mukhtar H, Bibi I, Rizwan M, Khan S, Mehmood A. Ligand Based Pharmacophore Modelling . Virtual Screening And Molecular Ligand Based Pharmacophore Modelling. Virtual Screen Mol Docking Novel Comp Against Diab. 2019.
18. Wahyuni DK, Ansori ANM, Vidiyanti F. GC-MS analysis of phytocomponents in methanolic extracts of leaf-derived callus of Justicia gendarussa Burm.f. Biosci Res. 2017; 14(3): 668-677.
19. Murtadlo AAA, Listiyani P, Utami SL, Wahyuningsih S, Turista DDR, Wiguna A, *et al.* Molecular Docking Study of Nigella sativa Bioactive Compound as E6 Inhibitor Against Human Papillomavirus (HPV) Infection. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;1(2):32-8.
20. Schöning-Stierand K, Diedrich K, Fährrolfes R, Flachsenberg F, Meyder A, Nittinger E, *et al.* Proteins Plus: interactive analysis of protein–ligand binding interfaces. Nucleic Acids Re. 2020;48(W1):W48-53.
21. Fährrolfes R, Bietz S, Flachsenberg F, Meyder A, Nittinger E, Otto T, *et al.* Proteins Plus: a web portal for structure analysis of macromolecules. Nucleic Acids Res. 2020;45(W1):W337-43.
22. Rahman AT, Jethro A, Santoso P, Kharisma VD, Murtadlo AAA, Purnamasari D, *et al.* In Silico Study of the Potential of Endemic Sumatra Wild Turmeric Rhizomes (Curcuma Sumatrana: Zingiberaceae) As Anti-Cancer. Pharmacogn J. 2022;14(6).
23. Chen X, Li H, Tian L, Li Q, Luo J, Zhang Y. Analysis of the physicochemical properties of acaricides based on Lipinski's rule of five. J Comput Biol. 2020;27(9):1397-406.
24. Iacobucci C, Götze M, Ihling CH, Piotrowski C, Arlt C, Schaefer M, *et al.* A cross-linking/mass spectrometry workflow based on MS-cleavable cross-linkers and the MeroX software for studying protein structures and protein–protein interactions. Nature Protocols. 2018;13(12):2864-89.
25. Islamiati Y, Suryani Y, Adawiyah A, Taufiqurrohman O, Kharisma VD, Purnamasari D, *et al.* The Potential of Antivirus Compounds in Gletang (Tridax procumbens Linn.) in Inhibiting 3CLpro Receptor of SARS-CoV-2 Virus by In Silico. Pharmacogn J. 2022;14(6).
26. Xiong G, Wu Z, Yi J, Fu L, Yang Z, Hsieh C, *et al.* ADMETlab 2.0: An integrated online platform for accurate and comprehensive predictions of ADMET properties. Nucleic Acids Res. 2021;49(W1):W5-14.
27. Lemkul J. From Proteins to Perturbed Hamiltonians: A Suite of Tutorials for the GROMACS-2018 Molecular Simulation Package [Article v1.0]. Living J Comput Mol Sci. 2019;1(1):1-53.
28. Kharisma VD, Ansori ANM, Dian FA, Rizky WC, Dings TGA, Zainul R, *et al.* Molecular Docking and Dynamic Simulation of Entry Inhibitor From Tamarindus Indica Bioactive Compounds Against Sars-Cov-2 Infection Via Viroinformatics Study. Biochem Cell Arch. 2021;21(2):3323-7.
29. Baek SC, Park MH, Ryu HW, Lee J, Kang MG, Park D, *et al.* Rhamnocitrin isolated from Prunus padus var. seoulensis: A potent and selective reversible inhibitor of human monoamine oxidase A. Bioorganic Chem. 2019;83:317-25.
30. Johnson TO, Adegboyega AE, Ojo OA, Yusuf AJ, Iwaloye O, Ugwah-Oguejiofor CJ, *et al.* A computational approach to elucidate the interactions of chemicals from Artemisia annua targeted toward SARS-CoV-2 main protease inhibition for COVID-19 treatment. Front Med. 2012;9.
31. Aini NS, Kharisma VD, Widyananda MH, Murtadlo AAA, Probojati RT, Turista DDR, *et al.* In silico screening of bioactive compounds from Syzygium cumini L. and moringa oleifera L. against SARS-CoV-2 via tetra inhibitors. Pharmacogn J. 2022;14(4).
32. Oh JM, Kang MG, Hong A, Park JE, Kim SH, Lee JP, *et al.* Potent and selective inhibition of human monoamine oxidase-B by 4-dimethylaminochalcone and selected chalcone derivatives. Int J Biol Macromol. 2019;137:426-32.
33. Ansori A, Zainul R. In Silico B-Cell Epitope Vaccine Design and Phylogenetic Analysis Of Ebola Virus Envelope Glycoprotein. Indonesian J Pharm. 2023;34(2).

34. Abdelgawad MA, Oh JM, Parambi DG, Kumar S, Musa A, Ghoneim MM, *et al.* Development of bromo-and fluoro-based α, β-unsaturated ketones as highly potent MAO-B inhibitors for the treatment of Parkinson's disease. J Mol Struct. 2022;1266:133545.
35. Chandrashekar KS, Hemadri D, Patil SS, Suresh KP. Unveiling Acacia farnesiana phytochemicals as Angiotensin Converting Enzyme (ACE) inhibitors via in-silico drug design, molecular docking, and bioavailability predictions: An illustration against SARS-CoV-2 spike protein. J Ayurved Herbal Med. 2022;8(4):209-20.
36. Listiyani P, Utami SL, Turista DDR, Wiguna A, Wijayanti A, Rachmawati Y, *et al.* Computational Screening of Toxicity, Drug-like Molecule, and Bioactivity from Green Tea Phytochemical as Antiviral Candidate. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;1(2):39-45.
37. Burslem GM, Smith BE, Lai AC, Jaime-Figueroa S, McQuaid DC, Bondeson DP, *et al.* The advantages of targeted protein degradation over inhibition: an RTK case study. Cell Chemical Biol. 2018;25(1):67-77.
38. Mawaddani N, Sutiyanti E, Widyananda MH, Kharisma VD, Turista DDR, Tamam MB, *et al.* In Silico Study of Entry Inhibitor from Moringa oleifera Bioactive Compounds against SARS-CoV-2 Infection. Pharmacogn J. 2022;14(5).
39. Shah FA, Park DJ, Koh PO. Identification of proteins differentially expressed by quercetin treatment in a middle cerebral artery occlusion model: a proteomics approach. Neurochem Res. 2018;43(8):1608-23.
40. Li Y, Sun J, Li D, Lin J. The full activation mechanism of the adenosine A1 receptor revealed by GaMD and Su-GaMD simulations. Proceed Nat Acad Sci. 2022;119(42):e2203702119.
41. Pang KL, Mai CW, Chin KY. Molecular Mechanism of Tocotrienol-Mediated Anticancer Properties: A Systematic Review of the Involvement of Endoplasmic Reticulum Stress and Unfolded Protein Response. Nutrients. 2023;15(8):1854.
42. Balachandran A, Choi SB, Beata MM, Małgorzata J, Froemming GRA, Lavilla CA Jr, *et al.* Antioxidant, Wound Healing Potential and In Silico Assessment of Naringin, Eicosane and Octacosane. Molecules. 2023;28(3):1043.
43. Wai SN, How YH, Saleena LAK, Degraeve P, Oulahal N, Pui LP. Chitosan-Sodium Caseinate Composite Edible Film Incorporated with Probiotic Limosilactobacillus fermentum: Physical Properties, Viability, and Antibacterial Properties. Foods. 2022;11(22):3583.
44. Rahmah, Salimo H, Wasita B, Pamungkasari EP, Cilmiaty R, Soetrisno. Mesona palustris BL: the potential antioxidant. Bali Med J. 2023;12(1):560-2.
45. Agung IGAA, Wahjuni S, Wedagama DM, Weta IW, Lestari AAW. Nutraceuticals of nano-betel (Piper betle L.) leaves: prevent COVID-19 and oral cavity disease. Bali Med J. 2022;11(2):844-9.
46. Purnawati S, Wrasiati LP, Jaya Lesmana CB, Megantara S, Lesmana R. A study of molecular docking of l-tryptophan ligand as a compound in pineapples and bananas binding with the human serotonin transporter (SERT). Bali Med J. 2022;11(3):1243-9.
47. Listari KM, Az-Zahra T, Hasanah A, Agistasari Y. Jatropha multifida L stem sap gel versus Aloe vera gel to post-gingivectomy healing process. Bali Med J. 2023;12(1):432-6.
48. Nora H, Rajuddin, Hafizudin, Suhanda R, Indirayani I. Curcumin, a potential oral herbal male contraceptive: a review article. Bali Med J. 2022;12(1):82-6.
49. Rosita E, Prasetyo SA, Riwanto I, Atmodjo WL. The effect of Epigallocatechin-3-Gallate (EGCG) combined with low dose sorafenib in apoptosis and Platelet-Derived Growth Factor Receptor (PDGFR) expression in hepatocellular carcinoma rats. Bali Med J. 2022;11(1):216-22.
50. Sulistyowati E, Aziz MR. Systematic literature review: potential anti hyperglycemia Imperata cylindrica. Bali Med J. 2022;11(2):752-6.
51. Abbas N, Al-Shamary, Abbas S, Al-Mizraqchi. The Combination Effects of Honey and Nicotine on the Acid Production of Oral Mutans Streptococci. J Med Chem Sci. 2023;6(6):1410-8.
52. Abdullah SM, AL-Hamdani AAS, Ibrahim SM, Al-Zubaid LA, Rashid FA. An Evaluation of Activity of Prepared Zinc Nanoparticles with Extract Green Plant in Treatments of Diclofenac, Levofloxacin, and Tetracycline in Water. J Med Chem Sci. 2023;6(6):1323-35.
53. Yedelli K, Pathangi RK. Assessment of Anti-Diabetic and Antioxidant Activities of Rourea Minor Stems in Streptozotocin-Induced Diabetic Rats. J Med Chem Sci. 2023;6(6):1370-82.
54. Hamzah BF, Taha I, Najm ZM, Husseini MD, Noor SK, Al-Khafaji. Synthesis, Characterization, and Antibacterial Activity of Some New Oxazepine Derivatives. J Med Chem Sci. 2023;6(6):1239-45.
55. Qasim MA, Yaaqoob LA. Evaluation of Antibacterial Activity of Iron Oxide Nanoparticles Synthesis by Extracellular Lactobacillus against Pseudomonas Aeruginosa. J Med Chem Sci. 2023;6(5):1100-11.

GRAPHICAL ABSTRACT



ABOUT AUTHORS

Rahadian Zainul is a Professor in Physical Chemistry and researcher in CAMPBIOTICS, Universitas Negeri Padang, Indonesia. His research projects are related to virology, bioinformatics, advanced material and also in computational chemistry. He was published more than 71 papers in Scopus and WOS with more than 150 researchers in the world as collaborator.

Nita Yessirita is an associate professor in Food Technology and a researcher in animal nutrition and biotechnology at Universitas Ekasakti. Research projects related processing microbiology, animal feed, local wisdom. She has published 35 articles in both Scopus journals and proceedings, nationally accredited. She has also written book on fermentation using bacteria and fungi.

Cite this article: Yessirita N, Verawati R, Purnamasari D, Rollando R, Mandeli RS, Albari MT, et al. *In Silico* Study of Rhamnocitrin Extract from Clove (*Syzygium Aromaricum*) in Inhibiting Adenosine A1-Adenylate Cyclase Interaction. Pharmacogn J. 2023;15(4): 512-517.