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Molecular Docking in red spinach plants (Amaranthus tricolor L.) as an inhibitory agent for genetic anemia

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ABSTRACT

This study aims to evaluate the potential of active compounds from the Red Spinach plant (Amaranthus tricolor L.) as an inhibitor agent for the genetic disease anemia through a molecular docking approach. The method used involved analyzing the 3D structures of four active compounds Phenol, Lutein, Quercetin, and Zeaxanthin in these plants, which were downloaded from PubChem and processed using the Swiss software Target Prediction, Super Prediction, PyMol, and PyRx. The interaction between the compound and the biological target, in this case, Erythropoietin, is evaluated to determine binding energy, binding affinity, and stability. The results showed that Phenol and Quercetin had a significant interaction with the lowest binding energy of -4.8 kcal/mol and -8.1 kcal/mol respectively, as well as the lowest RMSD value (0 Å), indicating good interaction stability with the protein target. The 3D molecular structure of these two compounds also indicates the presence of hydrogen bonds and effective interactions with amino acids, as well as low toxicity and favorable affinity energies. Based on these results, Phenol and Quercetin were identified as potential candidates in the development of drugs to treat anemia genetic diseases, thanks to their favorable interaction properties and molecular structural characteristics. This research underlines the importance of the molecular docking approach in identifying bioactive compounds that can be further developed as therapies for the genetic disease anemia.

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INTRODUCTION

A genetic disease is a sign of an abnormality in a gene or chromosome, which is a characteristic factor in an organism. Genetic diseases can occur in one gene, more than one gene, and even chromosomes. Genetic diseases that are multifactorial can involve genetic factors and are influenced by external factors such as the environment and lifestyle(Ambarwati et al., 2023)(Khairani, Afrianti, et al., 2024)(Khairani, Anggraini, et al., 2024). A genetic disease is a medical condition caused by mutations in an individual's genes. These genes contain instructions

for the process of forming proteins that are important in body function. When a genetic mutation occurs, the resulting protein does not function properly or is not produced at all. Genetic diseases can be hereditary, that is, inherited from one or both parents, or occur randomly in response to certain environmental factors(Effendi & Rumah, 2020)(Rahmat, 2021).

According to Laksono (2011), several diseases caused by genetic disorders include, Dentigenesis imperfecta, Achondroplasia, Albino, deaf-mute, Hemophilia, red-green color blindness, Thalassemia, Diabetes mellitus, Leukemia, and Anemia. Meanwhile, those caused by chromosomal abnormalities are Down syndrome, Turner syndrome, and chromosome structure abnormalities such as Cri du chat syndrome, de Groucy syndrome (mosaic chromosomes)(Laksono et al., 2011)(Aminah & Yunitasari, 2022).

The expression of genetic diseases can vary with some individuals being healthy carriers without showing symptoms, while others experience severe symptoms. The environment also influences the expression of disease with various factors such as pollution or exposure to toxic chemicals that can worsen symptoms or accelerate disease progression(Irianti & Pramono, 2022)(Indarwati et al., 2024)(Basri, 2024). Diagnosis and treatment of genetic diseases involves genetic testing with treatment that can vary depending on the type and severity, including gene therapy, symptomatic treatment, or genetic therapy. By knowing the relationship between gene mutations that can cause genetic diseases, early prevention or appropriate treatment can be carried out(Amanullah, 2022)(Damanik et al., 2024).

Anemia is a disease that is a global health problem that can affect millions of people throughout the world. This condition is caused by various factors, including iron deficiency, vitamin B12 or folic acid deficiency, bone marrow disorders, and also certain chronic diseases(Al Ikhsan et al., 2023). According to Aulya (2022) anemia is a medical condition characterized by a low number of red blood cells or low hemoglobin levels in the blood. Management of anemia often involves therapy aimed at increasing red blood cell production or increasing the availability of substances needed to form the hemoglobin structure(Cakrawati et al., 2024)(Islami et al., 2024). (Aditomo, 2019)(Rohmania, 2019)(Zulqifni & Suandika, 2022) added that anemia is characterized by a low number of red blood cells or hemoglobin content in the body and causes a lack of oxygen carried by the blood to the body's tissues. This can result in symptoms such as fatigue, weakness, dizziness, and shortness of breath. Anemia can be caused by various factors, including deficiencies in iron, vitamin B12, folic acid, or genetic disorders in the formation of red blood cells(Nurbaya et al., 2019)(Pinasti et al., 2020). According to Muhayati (2019), the normal Hb levels found in men and women are different, where the Hb levels for men with anemia are less than 13.5 g/dl, while the Hb levels for women with anemia are less than 12 g/dl. etc. One plant that the public can trust because it contains several active compounds and can treat anemia is the red spinach plant(Sholihah, 2022).

Red spinach is a plant that has long been known as a rich source of nutrients, including bioactive compounds that can provide health benefits. Red spinach contains antioxidants such as beta-carotene, phenol, lutein, quercetin, and zeaxanthin which help protect body cells from damage caused by free radicals and other diseases. Free radicals can damage red blood cells and interfere with hemoglobin production, which can cause anemia(Wijayanti & Qomariyah, 2023). Anjarwati (2023) added that red spinach is the plant most often consumed by the public because red spinach contains anthocyanins which act as antioxidants and function to prevent the formation of free radicals and other symptoms of disease. In an effort to increase prevention of various diseases in red spinach plants, a molecular docking technique can be used by analyzing the compound content in red spinach plants and the biological targets that will be obtained(Ahsan et al., 2020)(Monica Sari et al., 2022). *Molecular docking*is a computational procedure that can be used to efficiently predict the chemical bonding of a macromolecule (receptor) with a small molecule (ligand). Molecular docking can identify a new compound using its structure through molecular docking simulations which can enable predictions of interactions between target proteins and

ligands at the molecular level and describe the relationship between structure and activity. The purpose of docking is to determine the conformation and binding free energy involved in the interaction between the receptor and the ligand(Frimayanti et al., 2021)(Sihaloho & Arfan, 2023). Molecular docking is very relevant in research and development as an inhibitor agent. According to Aziz (2022), inhibitor agents aim to disrupt or regulate certain biological pathways. This can be done by inhibiting enzyme activity, blocking receptors, or disrupting interactions between certain molecules in biological systems. Inhibitory agents often have specificity towards certain targets with the aim of being designed to bind to the target with high affinity, but not interact with other molecules in the biological system to avoid undesirable side effects (Aziz et al., 2022).

The aim of this research is to identify active compounds in the Red Spinach plant (Amaranthus tricolor L.) which have potential as inhibitory agents for the genetic disease anemia through molecular docking analysis. This research aims to reveal the interactions between these compounds and biological targets that play a role in regulating hemoglobin production. Apart from that, this research also aims to evaluate the molecular structure of these potential compounds, with the hope of developing drugs or supplements that are effective in treating the genetic disease anemia.

With the background mentioned previously, researchers are interested in carrying out research on "Molecular Docking in Red Spinach Plants (Amaranthus tricolor L.) as an Inhibitory Agent for the Genetic Disease of Anemia". This research is intended to explore the potential of compounds contained in red spinach plants which may have inhibitory properties against the genetic disease anemia. Using molecular docking techniques, this research will model the interactions between compounds in red spinach and biological targets involved in the regulation of hemoglobin production.

RESEARCH METHOD

This research was conducted at the Biology Laboratory of the North Sumatra State Islamic University, Medan from 25 to 29 July 2024. The equipment used included an Asus A450C computer with Intel Core i3 CPU specifications, 2GB memory and 500GB storage, as well as various software such as PubChem, PASS Online, and PyRx. The research material consists of the 3D structure of the active compound red spinach (Phenol, Lutein, Quercetin, Zeaxanthin) and the reference compound Erythropoietin, which were downloaded from PubChem and processed with Swiss Target Prediction and Super Prediction software to obtain target protein data.

The research procedure begins with searching and preparing the 3D structure of the active compound, which is downloaded in *sdf format from PubChem, and analyzed using PASS Online to determine biological activity. Next, target protein identification was carried out using Swiss Target Prediction and Super Prediction, followed by validation of the 3D protein structure via NCBI and Saves Webserver. Ligand and target protein structures were prepared with PyMol and PyRx, including optimization and water content removal for docking analysis. Molecular docking analysis was carried out with PyRx to evaluate ligand interactions with target proteins. After that, ADME and toxicity analyzes were carried out using SwissADME and Protox to assess the compound's potential as a drug, including absorption, distribution, metabolism and excretion as well as side effects. The research data were analyzed based on binding energy, binding affinity, RMSD, and docking visualization by complying with Lipinski's rules to evaluate the potential of compounds as therapeutic agents.

RESULTS AND DISCUSSIONS

Energy Value of Target Proteins

Phenol

The results of testing the binding energy value of the target protein in phenol compounds are as follows.

Table 1. Results of Adenylate cyclase target protein binding energy values

Ligand	Binding Affinity	RMSD/ub (Å)	RMSD/lb (Å)
1ZC_1	-4.8	0	0
1ZC_2	-4.5	2,605	1,873
1ZC_3	-4.3	3,172	2.18
1ZC_4	-4.2	10.34	9.13
1ZC_5	-4.1	14.1	13,269
1ZC_6	-4	4,207	3,105
1ZC_7	-4	3,978	3.28
1ZC_8	-4	25,565	24.59
1ZC_9	-3.9	12,626	12,189

Based on the results of testing the binding energy value of the target protein *Adenylate cyclase*on phenol compounds shows that the binding affinity value ranges from -4.8 to -3.9 kcal/mol. A negative value indicates that the interaction between the phenolic compound and the target protein is exothermic and stable. The value -4.8 kcal/mol indicates the strongest interaction, while -3.9 kcal/mol indicates a weaker interaction. At the point with a bond energy of -4.8 kcal/mol, the RMSD for both the upper and lower bounds is 0, which indicates that the ligand is in a stable position and there is no change in position. An increasing RMSD value indicates that the ligand position becomes more unstable. For example, at -4.2 kcal/mol, the RMSD reaches 10.34 Å for the upper bound and 9.13 Å for the lower bound, which indicates a significant change in the position of the ligand from its initial position. More negative binding energy values indicate more stable interactions, while increasing RMSD values indicate instability of the ligand position. Therefore, the phenol compound which has the lowest binding energy (-4.8 kcal/mol) and the lowest RMSD (0) Å is the best in terms of interaction stability with the protein target, namely 1ZC_Phenol1.

Lutein

The results of testing the binding energy value of the target protein in the lutein compound are as follows.

Table 1. Results of binding energy values for the target protein tyrosine-protein phosphatase non-receptor type 2

Ligand	Binding Affinity	RMSD/ub (Å)	RMSD/lb (Å)
7UAD_1	-8.2	0	0
7UAD_2	-8	19,642	2,739
7UAD_3	-7.8	2,089	1.19
7UAD_4	-7.7	39,246	34,882
7UAD_5	-7.6	18,692	1,806
7UAD_6	-7.4	18,742	1,802
7UAD_7	-7.3	2,628	1,522
7UAD_8	-7.3	2,699	1,643
7UAD_9	-7.2	18,808	1,716

Based on the results of testing the binding energy value of the target protein Tyrosine-protein phosphatase non-receptor type 2 in the lutein compound, it shows that the binding affinity value ranges from -8.2 to -7.2 kcal/mol. The highest binding energy value was -8.2 kcal/mol, which indicated that the interaction was the most stable between lutein and the target protein. The

binding energy values -8.0, -7.8, indicate that the interaction of the ligand with the protein becomes weaker. This can be seen in the bond energy of -7.2 kcal/mol which is the lowest value in the data. At the point with a bond energy of -8.2 kcal/mol, the RMSD for both upper and lower bounds is 0, which indicates that the ligand is in a stable position and there is no change in position. At a bond energy of -8.0 kcal/mol, the RMSD for the upper bound increases to 19.642 Å, which indicates a significant change in position from the initial position. The lower bound RMSD remains relatively low at 2.739 Å. At a binding energy value of -7.7 kcal/mol, the upper bound RMSD reaches 39.246 Å, which indicates greater instability of the ligand position. There is a negative relationship between bond energy and RMSD. As the binding energy decreases, the RMSD value often increases and indicates that the ligand is no longer tightly bound to the protein bond. This indicates that the interaction of the ligand with the protein is inaccurate due to the increased RMSD(Rena et al., 2022). For example, at a bond energy value of -7.6 kcal/mol, the upper bound RMSD remains high, namely 18.692 Å, while the lower bound remains more stable at 1.806 Å. The target protein that has the lowest binding energy (-8.2 kcal/mol) and the lowest RMSD (0) Å is the best in terms of interaction stability with the target protein.

Quercetin

The results of testing the binding energy value of the target protein in the quercetin compound are as follows.

Table 3. Results of Epidermal growth factor receptor (EGFR) target protein binding energy values

Ligand	Binding Affinity	RMSD/ub (Å)	RMSD/lb (Å)
erBb1_1	-8.1	0	0
erBb1_2	-8	3,023	2,022
erBb1_3	-7.8	7,155	1,993
erBb1_4	-7.8	6,928	1,911
erBb1_5	-7.5	6,018	3,316
erBb1_6	-7.5	4,293	2,005
erBb1_7	-6.9	8,857	3,691
erBb1_8	-6.8	8,973	4,204
erBb1_9	-6.6	28.38	25,309

Based on the results of testing the binding energy value of the Epidermal growth factor receptor (EGFR) target protein in the quercetin compound, it shows that the binding value that has the potential to act as an inhibitor for the target protein erBB1 based on binding affinity analysis is (-8.1 kcal/mol). The binding affinity values for several ligands, including quercetin, provide an idea of the strength of the bond between the ligand and the protein. For example, erBb1_1 has the lowest binding affinity value (-8.1 kcal/mol), which indicates that the target protein binds very strongly. If quercetin shows a binding affinity value that is close to or more negative than -8.1 kcal/mol, this indicates that quercetin has the ability to bind well to the erBB1 protein which has the potential to inhibit the activity of this protein. If quercetin has a binding value close to or more negative than -8.1 kcal/mol, then quercetin can be considered a strong binder for erBB1. erBb1_1: RMSD/ub 0 Å and RMSD/lb 0 Å are stable bonds, erBb1_2: RMSD/ub 3.023 Å, RMSD/lb 2.022 Å, erBb1_3: RMSD/ub 7.155 Å, RMSD/lb 1.993 Å, erBb1_9: RMSD/ ub 28.38 Å, RMSD/lb 25.309 Å is the most unstable bond. From the RMSD data, it can be concluded that ligands with lower RMSD/lb show better binding stability. On the other hand, a high RMSD/lb value indicates that the ligand may not bind well to the target protein.

Zeaxanthin

The results of testing the binding energy value of the target protein in the zeaxanthin compound are as follows.

Table 4. Results of target protein binding energy values Protein-tyrosine phosphatase 1B (PTPN1)

Ligand	Binding Affinity	RMSD/ub (Å)	RMSD/lb (Å)
PTPN1_1	-8	0	0
PTPN1_2	-7	18,875	1,819
PTPN1_3	-7	12,804	10,039
PTPN1_4	-6.9	37,141	30,287
PTPN1_5	-6.8	18,843	13.4
PTPN1_6	-6.8	20,804	15,591
PTPN1_7	-6.8	31.8	27,111
PTPN1_8	-6.6	51,507	47,004
PTPN1_9	-6.6	51,696	47,234

Based on the results of testing the binding energy value of the target protein Protein-tyrosine phosphatase 1B (PTPN1) in the zeaxanthin compound, it shows that the ligand binds to the PTPN1 target protein. Binding affinity values are measured in calories per mole (kcal/mol), where lower values indicate stronger bonds. From the results of existing data testing, PTPN1_1 shows the best binding affinity with a value of -8 kcal/mol, which means this compound binds very strongly to PTPN1. Meanwhile, PTPN1_2 to PTPN1_9 have lower affinity values (-6.6 to -7 kcal/mol), which indicates that the bond is less strong than PTPN1_1. Higher RMSD values indicate greater structural changes when bound to the ligand. PTPN1_4 with RMSD/ub values of 37.141 Å and RMSD/lb 30.287 Å, this shows that the protein structure undergoes significant changes when it binds to the ligand. PTPN1_1 showed lower and stable RMSD/ub and RMSD/lb upon binding. Based on the data that has been tested, if zeaxanthin has a binding affinity that is close to or equivalent to PTPN1_1, then this compound can be considered a good candidate for binding to PTPN1 and is likely to have significant biological potential.

Drug Feasibility Test Based on Lipinski (rule of five)

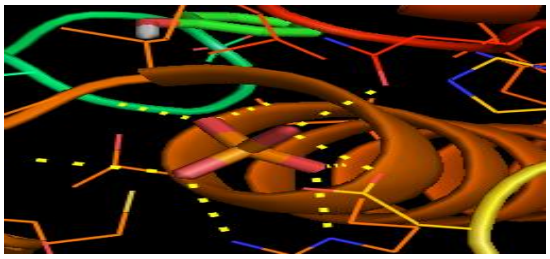
Table 5. Results of drug feasibility test analysis based on Lipinski's rule (rule of five)

Compound	Molecular weight <500 (g/mol)	H-bond acceptors <10	H-bond donors <5	LogP < 5	Molar Refractivity
Phenol	94.11 g/mol	1	1	1.24	28.46
Lutein	568.87 g/mol	2	2	7.15	186.76
Quercetin	302.24 g/mol	7	5	1.63	78.03
Zeaxanthin	568.87 g/mol	2	2	7.23	186.76
Erythropoietin	267.24 g/mol	7	2	1.93	61.73

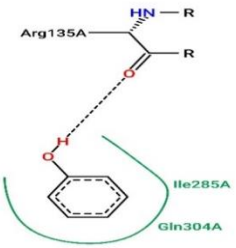
*Lipinski*is an experimental and computational method for estimating solubility, membrane permeability, and efficacy in the setting of drug design development. Lipinski (Rule of five) or Lipinski's rule of five which is also known as Pfizer's rule of five for short (RO5) is a rule of thumb for evaluating drug likeness and determining whether a chemical compound with certain pharmacological or biological activity has the chemical properties and physical properties that will make it be an active drug in humans. By looking at the pharmacological activity of each type of drug compound, drug suitability testing is carried out in accordance with Lipinski's rules(Riyaldi et al., 2022). Based on the drug suitability test results in the table, Lipinski (rule of five) values were obtained for three compounds that complied with the rules and no violations were found. The phenol compound has a molecular weight of 94.11 g/mol, 1 H-bond acceptor and 1 H-bond donor, a LogP value of 1.24 with a molar refractivity of 28.46. The quercetin compound has a molecular weight of 302.24 g/mol, 7 H-bond acceptors and 5 H-bond donors, a LogP value of 1.63 with a molar refractivity of 78.03. The drug compound erythropoietin has a molecular weight of 267.24 g/mol, 7 H-bond acceptors and 2 H-bond donors, a LogP value of 1.93 with a molar refractivity of 61.73. This shows that these three compounds have values that are in accordance with the test

results that have been carried out and no violations were found (0 violations), thus allowing these three compounds to bind and produce perfect values and bonds.(Kusmiati, 2012).

Visualization of Molecular Docking Results
3D Structure Visualization between Ligands and Phenol compounds



(A)



(B)

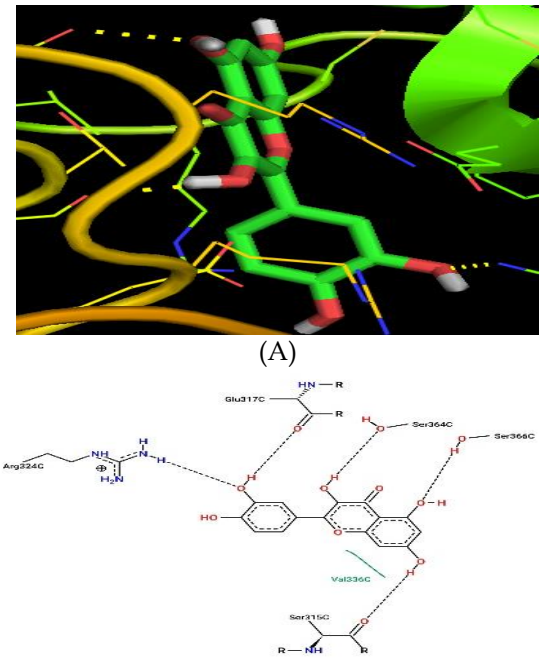
Figure 1. (A) Visualization of the 3D molecular docking structure of phenol compounds that bind to the Adenylate cyclase protein, (B) Visualization of the 2D structure of hydrogen bonds and hydrophobic bonds that bind to the Adenylate cyclase protein

Visualization of 3D structure docking results was carried out using PyMOL software using scoring data for each ligand and protein that had been prepared, while visualization of 3D and 2D structure bonding interactions used protein plus software. The 3D structure visualization results show that the first parameter seen from the docking results is the affinity energy (ΔG) that occurs. Affinity energy shows how strong the bond between the protein and the ligand is. Good affinity energy will show an increasingly negative (low) ΔG value. A low affinity value indicates that the compound requires little energy during the binding process, so it can be said that low affinity energy proves that the compound has greater potential to interact and form strong bonds with the target protein. The inhibition constant (ki) value shows the concentration required for the ligand to inhibit the target protein. A good inhibition constant is a ki value that is getting smaller. The stability of the ligand-receptor interaction is directly proportional to the binding potential of the compound, so it can be said that a target protein binding can predict the inhibitory ability of a compound to inhibit a disease on the protein it binds to. The value of the affinity energy for Adenylate cyclase protein in red spinach plants ranges from -4.8 to -3.9 kcal/mol, while the free binding energy (ΔG) of the validation ligand is -4.1 kcal/mol.

Compound ligands and receptors interact with the smallest energy so that the molecules are in a stable state (Rena, 2022). In the 2D structure visualization results, it can be seen that the ligand binds a hydrogen bond and a hydrophobic bond. Phenol compounds, which have a basic structure in the form of a benzene ring with one hydroxyl group (-OH), are known for their ability to interact with various ligands through hydrogen bonds and hydrophobic interactions. When phenol interacts with a non-polar ligand, there will be changes in the water molecules surrounding the ligand and can cause an increase in complex stability through hydrophobic interactions. Positive hydrophobic energy values indicate that this interaction can be affinity beneficial, as it

reduces the entropy of the system by minimizing interactions with water. In phenol compounds the hydroxyl group can act as a hydrogen bond donor which interacts with the hydrogen bond acceptor in the ligand. This interaction not only increases the stability of the complex formed but also contributes to the binding affinity between the phenol and the ligand. The high hydrogen bond energy indicates a strong and specific interaction to increase the potential of phenol as a ligand in biological systems. Based on the RMSD value, it shows that phenol compounds have the lowest binding energy (-4.8 kcal/mol) and the lowest RMSD (0) Å, so this can be said to be good in terms of interaction stability with protein targets. This can be confirmed that phenol compounds can be used as conformations or candidates for a drug as an inhibitor in the genetic disease anemia.

3D Structure Visualization between Ligand and Quercetin compound



(A)

(B)

Figure 2. (A) Visualization of the 3D molecular docking structure of the quercetin compoundbinds to the Epidermal growth factor receptor (EGFR) protein, (B) Visualization of the 2D structure of hydrogen bonds and hydrophobic bonds that bind to the Epidermal growth factor receptor (EGFR) protein

Visualization of 3D structure docking results was carried out using PyMOL software using scoring data for each ligand and protein that had been prepared, while visualization of 3D and 2D structure bond interactions used protein plus software. The results of the visualization of the 3D structure of the quercetin compound show that the target protein Epidermal growth factor receptor (EGFR) in the quercetin compound shows a potential binding as an inhibitor for the target protein erBB1 based on binding affinity analysis, namely (-8.1 kcal/mol). The binding affinity value for the quercetin compound provides an idea of the strength of the bond between the ligand and the protein. The properties of the compounds used in the anchoring process will be assessed first using Lipinski's rule (Rule of five). The aim is to determine the active pharmacological activity of the compound that will be used as a ligand. In accordance with Lipinski's rules, where the molecular weight of quercetin compounds (<500 g/mol), LogP (<5), H-bond donor (<5) and H-bond acceptor (<10), so that no violations were found.

The results in the 3D structure image show molecular docking binding by the quercetin compound to the target protein Epidermal growth factor receptor (EGFR) with a binding affinity

value of -8.1 kcal/mol, while the results of molecular docking of the quercetin compound to the target protein Epidermal growth factor receptor (EGFR) obtained binding affinity is -7.6. A lower binding affinity value indicates better interaction stability between the ligand and receptor. The RMSD value is the main parameter in validating molecular docking bonds. The RMSD value also shows the comparison of the conformation of the natural ligand with the docking results, where this value will later show how strong the protein bonds are. The natural ligand of the quercetin compound with the target protein Epidermal growth factor receptor (EGFR) was able to demonstrate its binding by producing values that can be said to be valid and capable of being used for docking test ligands because the RMSD value = 0.8 Å.

Based on the docking visualization results between the Epidermal growth factor receptor (EGFR) receptor and the quercetin compound in the red spinach plant (Amaranthus tricolor L.), it shows that various bonds are formed, including several amino acid residues, namely hydrophobic bonds which are visible in the visualization results which indicate the presence of activity. hydrophobic. Hydrophobic bonds are non-polar molecules that do not dissolve in water and these bonds are very important in the process of uniting the non-polar region of the ligand molecule with the non-polar region of the target receptor (Hariz, 2019). Apart from that, there is a binding interaction between the compound and the active site of the target protein, which is characterized by the formation of energy in the form of conventional hydrogen bonds. Hydrogen and hydrophobic bonds cause changes in biological activity and provide certain pharmacological effects, or in other words, these compounds can react as drugs when they bind to marker receptors for anemia. The ability of quercetin compounds to bind to ligands through hydrophobic energy mechanisms and hydrogen bonds plays a key role in their biological activity. These interactions can influence various biological processes, including the regulation of inflammation, antioxidant activity, and the ability of quercetin to bind protein targets. Analysis of these hydrophobic and hydrogen energy affinity values is important for understanding the therapeutic potential of quercetin and for designing new compounds in the development of more effective drugs.

CONCLUSION

Based on the results of research on molecular docking on red spinach (Amaranthus tricolor L.) as an inhibitor agent for the genetic disease anemia, it can be concluded that there are four active compounds in this plant which play an important role in the conformation of drug candidates, namely Phenol, Lutein, Quercetin, and Zeaxanthin. Molecular docking analysis shows that Phenol and Quercetin have the best interaction, with the lowest binding energy values of -4.8 kcal/mol and -8.1 kcal/mol respectively and the lowest RMSD value (0 Å), indicating optimal interaction stability with the target protein. In addition, the molecular structure characteristics in 3D form of Phenol and Quercetin indicate the presence of good hydrogen bonds and amino acid interactions with the reference drug Erythropoietin, as well as low toxicity and good affinity energy values. Therefore, these two compounds have the potential to be candidates for developing drugs for the genetic disease anemia.

References

Aditomo, M. H. R. (2019). *Gambaran Jumlah Trombosit dan Hematokrit Pada Pasien dengan Diagnosa Anemia di RSUD Bangil Pasuruan*. Universitas Muhammadiyah Surabaya.

Ahsan, F., Rahmawati, N. Y., & Alditia, F. N. (2020). *Lawan Virus Corona: Studi Nutrisi untuk Kekebalan Tubuh*. Airlangga University Press.

Al Ikhsan, M. F., Wardiati, W., & Aramico, B. (2023). Analisis Faktor Risiko Stres Kerja Pada Pekerja Pengolahan di Pabrik Kelapa Sawit Pt X Kabupaten Nagan Raya Tahun 2022. *Jurnal Kesehatan Tambusai*, *4*(1), 214–219.

Amanullah, A. S. R. (2022). Mengenal Anak Berkebutuhan Khusus: Tuna Grahita, Down Syndrom Dan Autisme. *ALMURTAJA: Jurnal Pendidikan Islam Anak Usia Dini*, *1*(1), 1–14.

Ambarwati, A., Pujiati, E., & Pramudaningsih, I. N. (2023). Peningkatan Pengetahuan Remaja Tentang Kelainan Genetik dan Cara Pencegahannya. *Jurnal Pengabdian Kesehatan*, *6*(4), 270–278.

Aminah, S., & Yunitasari, E. (2022). Faktor-Faktor yang Berhubungan dengan Asfiksia Neonatorum pada Bayi Baru Lahir di RSUD Kabupaten Pringsewu. *Journal of Current Health Sciences*, *2*(2), 73–80.

Basri, S. K. M. (2024). *PROTEKSI LINGKUNGAN DAN PRODUK BERSIH*. Rizmedia Pustaka Indonesia.

Cakrawati, R., Keb, M. T., Sumarni, S., Mid, B. M., & Sudiyono, S. E. (2024). *EKSTRAK BIJI LABU KUNING (CUCURBITA MOSCHATA): Sebagai Terapi Alternatif Pendamping Tablet Tambah Darah untuk Pencegahan dan Penanganan Anemia pada Remaja Putri*. PENERBIT KBM INDONESIA.

Damanik, A. S., Khairani, M., Nayla, N., Anggreniawira, P. A., & Afdan, R. K. (2024). Identifikasi Pengetahuan Siswa SMAS Teladan Medan Tentang Kelainan Genetik dan Cara Pencegahannya. *Maximal Journal: Jurnal Ilmiah Bidang Sosial, Ekonomi, Budaya Dan Pendidikan*, *1*(5), 306–312.

Effendi, Y., & Rumah, P. P. (2020). *Buku Ajar Genetika Dasar*. Penerbit Pustaka Rumah C1nta.

Frimayanti, N., Lukman, A., & Nathania, L. (2021). Studi molecular docking senyawa 1, 5-benzothiazepine sebagai inhibitor dengue DEN-2 NS2B/NS3 serine protease. *Chempublish Journal*, *6*(1), 54–62.

Indarwati, S. K. M., Agustina, N. W., Wahyuningsih, A., ST, S., Marasabessy, N. B., ST, S., Maryatun, S. K., Sri Handayani, S. K. M., Noviati Fuada, S. P., & Agustiningrum, R. (2024). *KESEHATAN MASYARAKAT*. CV Rey Media Grafika.

Irianti, T. T., & Pramono, S. (2022). *Penuaan Dan Pencegahannya: Proses Faali Biokimiawi dan Molekuler*. Ugm Press.

Islami, S., Haq, R. A., Arianto, N. N., & Sabina, D. L. (2024). Teknik Penyuntingan Gen Clustered Regularly Interspaced Short Palindromic Repeats-Cas9 (CRISPR-Cas9) sebagai Terapi Penyakit Genetik Bawaan: Ulasan Literatur. *Medical Profession Journal of Lampung University*, *14*(2), 334–343.

Khairani, M., Afrianti, B., Rambe, D. R. K., Hafizhah, K. N., & Nahombang, S. Z. (2024). EFEKTIVITAS PEMBELAJARAN GENETIKA DALAM PENINGKATAN KESADARAN PENYAKIT GENETIK PADA SISWA KELAS 11 MAN 1 MEDAN. *JURNAL ILMIAH NUSANTARA*, *1*(4), 610–617.

Khairani, M., Anggraini, A. S., Aulia, A. R., Saragih, F. E., & Khairuddin, F. (2024). ANALISIS KELAINAN GENETIK. *JURNAL ILMIAH NUSANTARA*, *1*(4), 556–564.

Kusmiati. (2012). *Kemampuan Senyawa Lutein Dari Daun Bayam (Amaranthus sp) Untuk Menetralisir Oksidan T-BHP Dalam Sel Darah*. 691–697.

Laksono, S. P., Qomariyah, Q., & Purwaningsih, E. (2011). Persentase distribusi penyakit genetik dan penyakit yang dapat disebabkan oleh faktor genetik di RSUD Serang. *Majalah Kesehatan Pharmamedika*, *3*(2), 267–271.

Monica Sari, A., Dewi, B. S., RUSITA, R., & Harianto, S. P. (2022). *Upaya Konservasi Mangrove Berbasis Masyarakat (Kasus di Desa Purworejo, Kecamatan Pasir Sakti, Kabupaten Lampung Timur)*.

Nurbaya, S., Yusra, S., & Handayani, S. I. (2019). *Cerita Anemia*. Universitas Indonesia Publishing.

Pinasti, L., Nugraheni, Z., & Wiboworini, B. (2020). Potensi tempe sebagai pangan fungsional dalam meningkatkan kadar hemoglobin remaja penderita anemia. *AcTion: Aceh Nutrition Journal*, *5*(1), 19–26.

Rahmat, P. S. (2021). *Perkembangan peserta didik*. Bumi Aksara.

Rena, S. R., Nurhidayah, N., & Rustan, R. (2022). Analisis Molecular Docking Senyawa Garcinia Mangostana L Sebagai Kandidat Anti SARS-CoV-2. *Jurnal Fisika Unand*, *11*(1), 82–88. https://doi.org/10.25077/jfu.11.1.82-88.2022

Riyaldi, M. R., Fatiya, N. U., Dipadharma, R. H. F., Kusnadi, I. F., Hidayat, S., Suhandi, C., & Muchtaridi. (2022). Studi In-Silico Senyawa Pada Ekstrak Bawang Putih (Allium Sativum L.) Sebagai Inhibitor Neuraminidase Pada Influenza. *Farmaka*, *20*(3), 1–11.

Rohmania, M. (2019). *Pengaruh Pemberian Buah Juwet (Syzygium Cumini) terhadap Kadar Hemoglobin pada Mencit (Mus Musculus)*. Universitas Muhammadiyah Surabaya.

Sholihah, N. F. (2022). Review Artikel: Terapi Tanaman Herbal Untuk Peningkatan Kadar Hemoglobin. *Jurnal Ilmiah Wahana Pendidikan*, *8*(19), 312–320.

Sihaloho, M., & Arfan, A. (2023). Pencarian Inhibitor DYRK2 dari Database Bahan Alam Zinc15: Analisis Farmakofor, Simulasi Docking dan Dinamika Molekuler. *JSFK (Jurnal Sains Farmasi & Klinis)*, *10*(1), 100–113.

Wijayanti, A. R., & Qomariyah, N. (2023). Pengaruh Ekstrak Daun Mengkudu (Morinda Citrifolia L.) terhadap Kadar Hemoglobin dan Histopatologi Hepar Mencit Diabetes. *LenteraBio: Berkala Ilmiah Biologi*, *12*(1), 14–24.

Zulqifni, F., & Suandika, M. (2022). Pemberian Transfusi Darah sebagai Upaya Peningkatan Perfusi Jaringan pada Pasien Anemia. *Jurnal Inovasi Penelitian*, *3*(5), 6151–6156.