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Anchoring Analysis and Simulation of Molecular Dynamics of Dayak Onion Plant Compounds (Eleutherine bulbosa (Mill.) URB.) As an Antibacterial Candidate for Methicillin Resistant Staphylococcus aureus

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A B S T R A C T

MRSA infection that is growing and limited treatment is evidence that the handling and treatment of the disease is still inadequate so that appropriate drugs are needed as antibacterial against MRSA, the development of natural products, one of which is the dayak onion plant (Eleutherine bulbosa) which has the potential as antibacterial can be done with computational methods, one of which is molecular tethering, molecular dynamics and ADMET prediction. This study aims to predict the ability of natural compounds from dayak onions as antibacterial MRSA. Tethering and molecular dynamics are performed using AutoDock 4.2 and Yasara Dynamic software. The results showed that compounds with the greatest antibacterial potential were eleucanainones with binding energy of -11.91kcal / mol. The results of molecular tethering are then continued with molecular dynamics simulations. The results of molecular dynamics simulations show that the compound has a Root Mean Square Deviation (RMSD) value that is close to the native ligand. Conclusion: Dayak onion compounds (Eleutherine bulbosa) have potential as antibacterial MRSA

INTRODUCTION

Antibiotic resistance is a problem in the world of health because it has a bad influence on human health. Antibiotic resistance can cause various diseases caused by resistant bacteria that cannot be treated because the bacteria that cause the disease already have immunity to drugs or antibiotics so that the bacteria are no longer sensitive to antibiotics. One of the resistances that occurs in bacteria is the resistance of Staphylococcus aureus bacteria to penicillin and methicillin or commonly known as MRSA (Methicillin resistant Staphylococcus aureus) (Asri & Rasyid, 2017). A number of active compounds from natural ingredients have shown potential antibacterial activity, one of which is the Dayak onion plant (Eleutherine bulbosa). Drug development efforts can be carried out using molecular modeling or in silico testing, one of which is molecular docking, dynamics simulation and pharmacokinetic prediction. (Kesuma et al., 2018) therefore this research aims to anchor and simulate the molecular dynamics of Dayak onion compounds as antibacterial candidates for MRSA.

LITERATURE REVIEW

MRSA is the abbreviation for Methicillin-Resistant Staphylococcus aureus. This is a type of Staphylococcus aureus bacteria that has developed resistance to several types of antibiotics, including methicillin and other antibiotics related to the beta-lactam group. (Mlynarczyk-bonikowska et al., 2022) . In 2011, there were almost 460,000 patients in inpatient wards diagnosed as having been exposed to MRSA. According to data collected by the US Agency for Healthcare Research and Quality, in the United States, approximately 60% of Staphylococcus infections in intensive care units are caused by MRSA, and the percentage continues to increase, data shows that nearly 23,000 people have experienced deaths caused by MRSA while in Indonesia, the figure The incidence of bacterial infectious diseases at the advanced inpatient service level as of December 2014 reached 148,703 cases. In addition, it was found that 30% to 80% of antibiotic use was not based on indications for use. This is not only a threat to the relevant environment but also to the wider community (Ministry of Health of the Republic of Indonesia 2015).

One of the main factors in MRSA's resistance to beta-lactam antibiotics, including methicillin and oxacillin, is SCCmec (Staphylococcal Cassette Chromosome mec) which is a mobile genetic element found in MRSA. SCCmec is. SCCmec contains the mecA gene or other variants, which encode a modified penicillin-binding protein (PBP), namely PBP2a or PBP2'. PBP2a has low affinity for beta-lactam antibiotics, causing resistance to peptidoglycan synthesis inhibitors such as methicillin and oxacillin. In addition to the mecA gene, SCCmec also contains other genes related to mobile elements, cell wall modification, and regulation. SCCmec has a complex structure and variations in size and genetic composition, which influence the resistance level and epidemiological profile of MRSA. (Shore & Coleman, 2013)

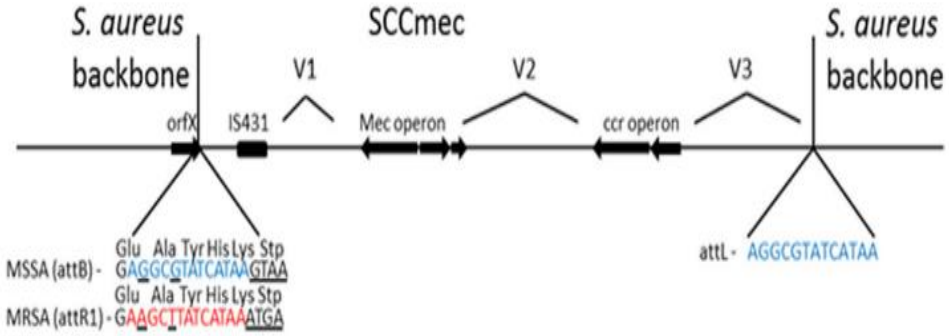


Figure 1. Activation of Beta Lactamase Enzyme by SCC Protein (Boundy *et al* ., 2013)

The general regulatory scheme of SCCmec is that attachment of SCCmec to the C terminus of orfX at the attB attachment site converts it to attR1. The five terminal amino acids and the stop codon do not change even if the DNA sequence is changed. Also shown is the region that specifies SCCmec: the mec contains the mecA operon, the gene responsible for lactam resistance, the cassette chromosome recombinase (ccr) operon that facilitates the insertion and excision of SCCmec and three hypervariable regions in between. The sequences of mec and ccroperon define SCCmec (Boundy et al ., 2013) .

Even though synthetic drugs have high efficacy in treating MRSA disease, it is important to develop drugs from natural ingredients that have the potential to be an alternative treatment for MRSA (Kumar, 2021). Therefore, the use of compounds from natural ingredients is an option for MRSA disease therapy with low side effects. Based on in vitro research (Masumi et al. , 2022) it shows that the active compounds contained in Dayak onions are capable of inhibiting MRSA disease, however, there has been no research that shows the active compounds contained in Dayak onions are capable of inhibiting the SSCMec protein. Therefore, this research aims to predict the potential of active compounds contained in red betel leaves as anti-alzheimer candidates through the SSCMec inhibition mechanism using a combination of two methods, namely in silico molecular docking.

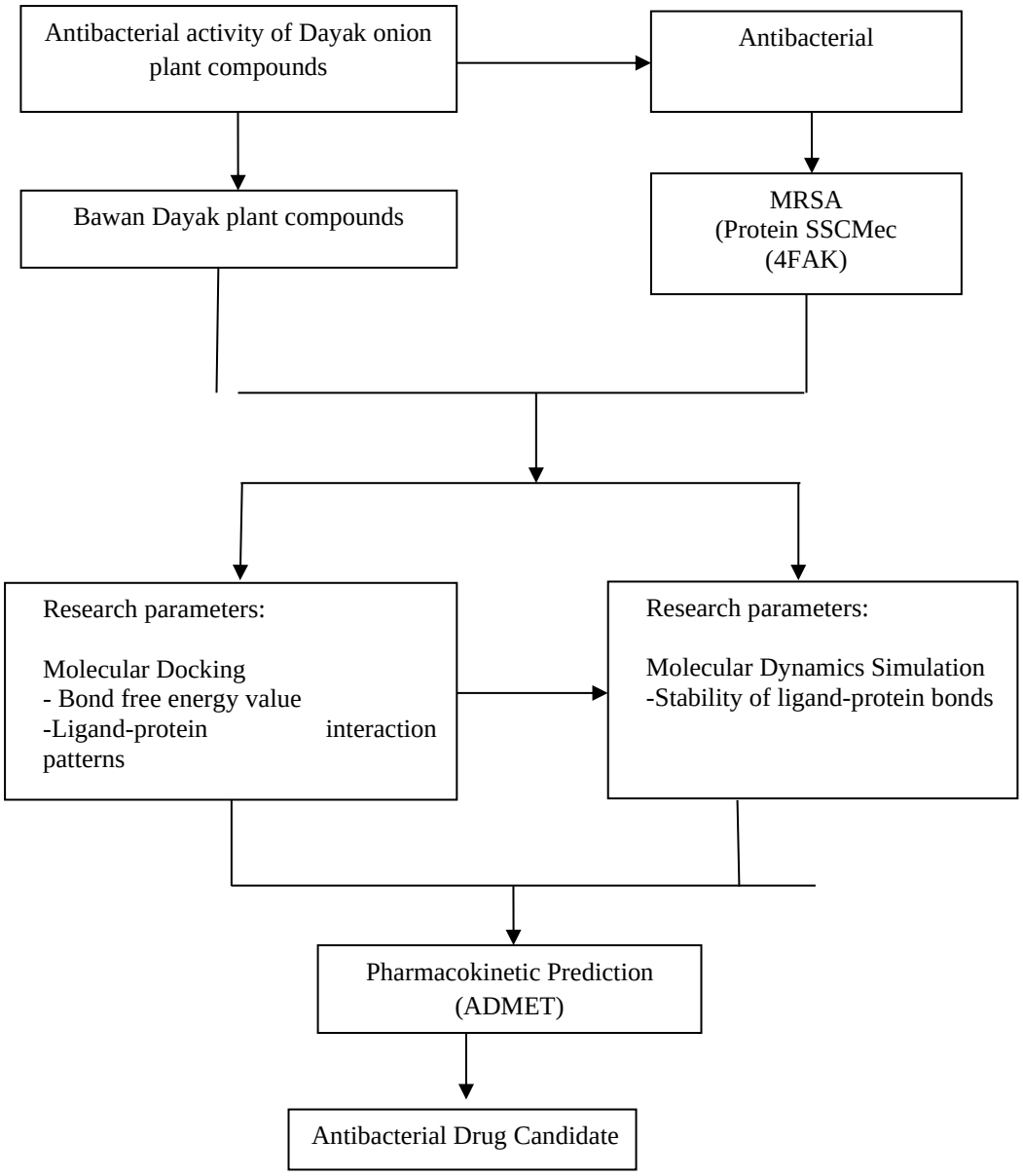
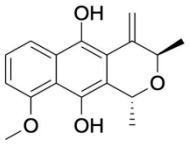
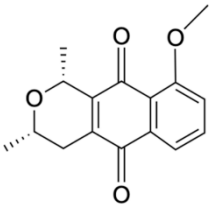
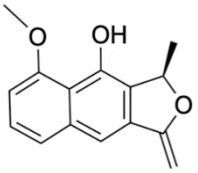
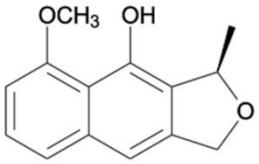


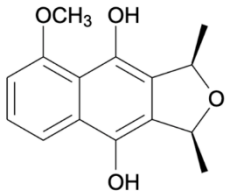
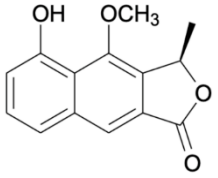
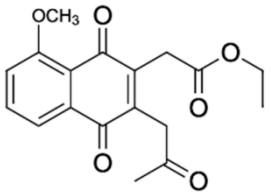
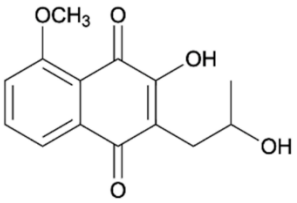
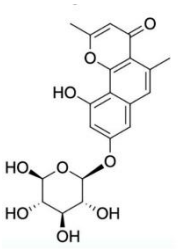
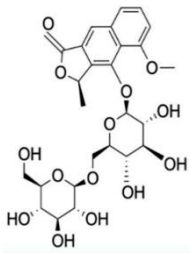
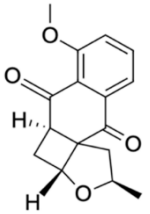
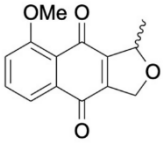
Figure 2. Conceptual Framework

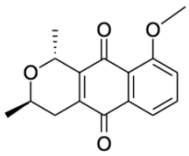
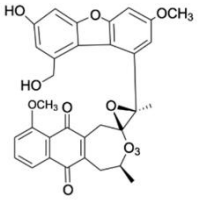
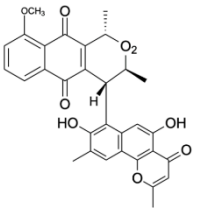
METHODOLOGY

The tools needed for the research are Asus VivoBook S13 Version: DirectX 12. which is equipped with software such as Discovery Studio 2016, AutoDockTools, VegaZZ and Yasara Dinamik. The materials needed for the research are the three-dimensional structure of the receptor, namely the MRSA target protein sourced from PDB with the code: 4 factors, namely ribosomal RNA large subunit methyltransferase, namely the protein containing the gene that codes for resistance to lactam antibiotics, the three-dimensional structure of the comparison ligand, namely paracetamol (extension *.SDF), and the three-dimensional structure of the test ligand derived from the active compound contained in Dayak onions (Eleutherine bulbosa) according to Table 1 obtained from literature from the journal (Kamarudin, 2021). The experimental procedure used in this research starts from preparation of the ligand structure, preparation of the receptor structure, validation of the docking area (gridbox), virtual screening, pharmacokinetic and toxicity prediction, molecular docking, and ends with two-dimensional visualization of the molecular docking of the ligand against SSCMec (result analysis) . The following is a description of each experimental procedure

Table 1. List of Active Compounds in Dayak Leeks (Eleutherine bulbosa) (Kamarudin, 2021)

No	Compound	Phytochemicals	Chemical Structures
1	Hengocin	Naphthalene	
2	Eleutherin	Naphthoquinone	
3	Eleutherol	Naphthalene	
4	Elautherol A	Naphthoquinone	

5	Elautherol B	Naphthoquinone	
6	Elautherol C	Naphthoquinone	
7	Eleuthilones B	Naphthoquinone	
8	Eleuthilones C	Naphthoquinone	
9	Eleutherinoside A	Naphthalene	
10	Eleuthoside B	Naphthalene	
11	Elacanacin	Naphthoquinone	
12	Eleutherinone	Naphthoquinone	

13	Isoeleutherin	Naphthoquinone	
14	Eleucanainones A	Naphthoquinone	
15	Eleucanainones B	Naphthoquinone	

Ligand Structure Preparation (Modification)

Ligand structure preparation was carried out using the method referring to the Pratama report, 2015; Hasanah, 2017 with modifications. A total of 15 test ligands derived from the Dayak onion compound (Eleutherine bulbosa) and the comparison ligand, namely Paracetamol, were downloaded via the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) which is a three-dimensional structure. Next, the ligand structure is saved (extension *.PDB). The ligand structure was opened again using the VegaZZ program for preparation by adding hydrogen ions. Next, optimization of the ligand is carried out using the AutoDockTools program, then the number of bond torques is adjusted.

Receptor Structure Preparation (Modification)

Receptor Structure preparation was carried out using the method referring to the report by Fikrika et al., 2016 with modifications. The receptor used in this research is the SSCMec protein which has the downloaded PDB code 4FAK which is a three-dimensional structure . The receptor structure was obtained from the RCSB PDB database (https://www.rcsb.org/). The process carried out in receptor preparation is first, opening the Discovery Studio 2016 program for preparation by removing water, molecules, ligands attached to the receptor, and ions located on the receptor. The receptor in this study has one chain, namely chain A which is used in this study and then the natural ligand attached to the receptor is s-adenosylmethionine which is on the chain. The natural ligand used in the research is the natural ligand s-adenosylmethionine which is in chain A, then the other natural ligand is removed. The two structures are placed on the worksheet separately. For the receptor and natural ligand, the same ligand structures are prepared as in the previous stage. Next, optimization was carried out on both structures using the AutoDockTools program. First, for the receptor, hydrogen ions, non-hydrogen ions were added, and Gasteiger charge calculations were carried out.

Mooring Area Validation (gridbox) (Modification)

Validation of the Mooring Area (gridbox) was carried out using a method referring to the report by Anitha et al., 2013; Prime, 2018; Sari et al., 2020 with

modifications. At the validation stage of the mooring area (gridbox), the validation search process uses oriented docking techniques through the AutoDockTools program. The gridbox zone obtained is center Files required in molecular docking simulations.

Next, a split is carried out in the CMD program, by passing it back with the following command "C:\vina>vina_split.exe –input output.pdbqt ". This process is intended to quickly obtain natural ligand poses from validation results separately in output form. Meanwhile, apart from the output produced, there is also a log file which is a file containing a number of natural ligand binding free energies resulting from validation and RMSD. The ligand file is opened using the Discovery Studio 2016 program to see the RMSD results of the ligand which is similar to the original natural ligand pose. Validation results obtained. RMSD results are acceptable if they have an RMSD of ≤2.0 Å.

Molecular Docking (Modification)

Molecular docking was carried out using a method referring to the report by Rachmania et al., 2016; Jeniossa, 2018 with modifications. Test ligands, comparison ligands and natural ligands that have been previously prepared using the AutoDockTools program are then continued with the molecular docking process. Files required to perform molecular docking. The next stage is the molecular docking simulation in the CMD program using the same commands as in the docking area (gridbox) validation stage. Then, each test ligand used is the test ligand pose that has the lowest binding free energy value. Ligands and receptors are opened through the Discovery Studio 2016 program on separate worksheets. Copy the worksheet containing the ligand, then paste it onto the worksheet containing the receptor. Next, the ligand is pulled towards the receptor so that the ligand is integrated with the receptor.

Results Analysis (Modification)

Results analysis was carried out using a method referring to the report by Ibrohim et al., 2015 with modifications. The results of molecular docking using the AutoDockTools program were analyzed by visualization of the ligand to the receptor (SSCMec) in two dimensions using the biovia program. Analysis obtained from molecular interactions, namely hydrogen hydrogen bonds which are illustrated with dotted lines and hydrophobic interactions which are illustrated with arcs. Next, the ligand and receptor were analyzed with three-dimensional visualization using the Biovia program.

Pharmacokinetic and Toxicity Prediction (Modification)

Pharmacokinetic and Toxicity predictions were carried out using the method referring to the report by Ochieng et al., 2017; Yusriani, 2019; Farhan, 2019 with modifications. A number of ligands that have been declared to have passed the virtual screening stage, one comparison ligand and one natural ligand, are then carried out by searching for the canonical SMILES structure of the ligand by opening the Pubchem database (https://pubchem.ncbi.nlm.nih.gov/) . Next, the canonical SMILES structure of the ligand was copied and then pasted through the SWISSADME database (http://www.swissadme.ch/) (Daina et al., 2017) to perform pharmacokinetic prediction analysis. The parameters in this analysis are molecular weight, acceptor hydrogen, donor hydrogen, MLogP, and molar refractivity. Next, the

canonical SMILES structure was accessed in the ADMETSAR database (http://lmmd.ecust.edu.cn/admetsar1) (Cheng et al., 2012) to perform toxicity prediction analysis. The parameters in the analysis are Human ether-a-go-go-Related Gene (hERG) inhibition, carcinogenicity, and acute oral toxicity.

RESEARCH RESULT

Preparation of Ligand and Receptor Structures

A total of 15 test ligands and one comparison ligand as a negative control used were three-dimensional structures obtained from the PubChem database. Preparation and optimization of the structure of all ligands using the Discovery Studio 2016, VegaZZ, and AutoDockTools programs. All ligands were prepared using the Discovery Studio 2016 program by adding hydrogen ions and optimized using the AutoDockTools program by calculating the number of torsion bonds. Next, all ligands that have been prepared and optimized can be saved (extension *.PDBQT (Protein Data Bank, Partial Charge (Q), & Atom Type (T)). Preparation of all ligands aims to calculate the interaction energy between the ligand and the receptor so that it can produces flexibility of a ligand by increasing the number of bonds that can be rotated by a ligand (Meng et al., 2011). The receptor in the study is the enzyme butyrylcholinesterase (SSCMec) with the PDB (Protein Data Bank) code 4FAK. The 4FAK PDB code was obtained from the downloaded Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB) database (*.PDB extension) and is a three-dimensional structure. The code has a full name, namely Ribosomal RNA large subunit methyltransferase H. The molecule that is also attached to the receptor, namely s-adenosylmethionine, is a natural ligand for the receptor that will be used in the validation process of the docking area (gridbox) and molecular docking. The resolution of the receptor in the study was 2.8 Å. The natural receptors and ligands used in the research are the single chain and natural ligand s-adenosylmethionine. Preparation and optimization of the receptor structure using the Discovery Studio 2016 program and AutoDockTools. The preparation process for the receptor involves removing water molecules, ions, and molecules attached to the receptor that are not needed in the molecular docking process. Optimization of the receptor structure was carried out by adding polar ions, nonpolar ions, and calculating the number of Gasteiger charges. Adjusting the number of Gasteiger charges aims to obtain and estimate the results of calculations between ligand and receptor interactions precisely (Novriadi et al., 2020). Meanwhile, for natural ligands, preparation and optimization are carried out in the same way as for the preparation of the ligand structure. Receptors and all ligands that are ready to be prepared and optimized are saved (extension *.PDBQT) so they can be used for the next process (Figure 1).

The comparison ligand used in the research is a commercial drug that has been approved by the Food and Drug Administration (FDA), namely Paracetamol. The purpose of negative control as a negative control in the process is to provide a comparison that allows assessment of the quality of predictions or interactions between target molecules (such as proteins) and other molecules (such as ligands). Negative control in docking can include several aspects, including method verification, by using a ligand that is known not to bind to the

target, researchers can verify whether the docking method used is able to distinguish between positive (ligand that binds to the target) and negative (ligand that does not bind) interactions. with targets). As an assessment of specificity, negative controls help in evaluating how specific docking predictions are to a particular target. If the negative control shows an unexpected interaction, this can indicate that the prediction may have errors or weaknesses in determining specificity. As an accuracy assessment, by using known negative ligands, researchers can evaluate the level of accuracy of docking predictions. If a negative ligand obtains a positive result in the prediction, this may indicate an error in the method or parameters used.

Mooring Area Validation (gridbox)

Validation of the mooring area (gridbox) is the first step used based on the assessment function when docking. Validation of the docking area is obtained from the structural ability of the natural ligand that has been tethered to the receptor (original natural ligand). Where it can resemble the original natural ligand pose again. In this process, the parameter used as a benchmark is RMSD (Root Mean Square Deviation). The gridbox validation process used in the research uses the natural ligand s-adenosylmethionine. This validation process obtained a gridbox zone of; namely center X -5.563, Y -8.699, Z 4.3 and the coordinate dimensions of the and this process was carried out 100 repetitions. The validation process can be accepted if the RMSD calculation obtained by a ligand is less than or equal to 2.0 Å (Sari et al., 2020). The validation results obtained in this study were an average binding free energy of -7.79 kcal/mol. The lowest RMSD was obtained at 1.767Å (Figure 2), so it can be stated that the resulting RMSD is <2.0 Å and is acceptable.

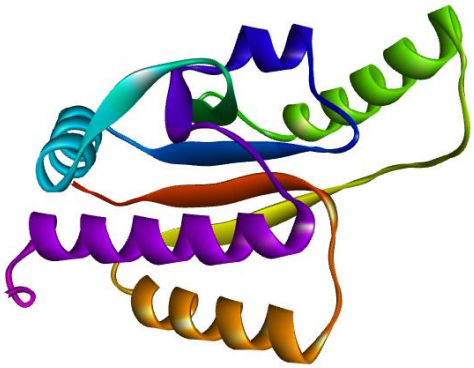


Figure 3. Preparation of Receptor Structure (BChE Enzyme) (Source: Personal Documentation Using the Discovery Studio 2016 program).

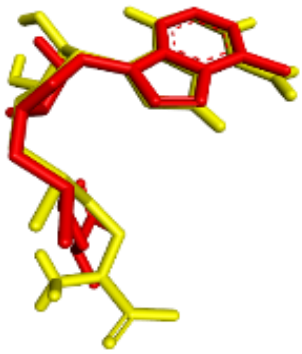


Figure 4. (A) Validated Natural Ligand (Yellow) and (B) Original Natural Ligand (Red) (Source: Personal Documentation Using the Discovery Studio 2016 Program)

Molecular Docking

Molecular docking can be interpreted as the most suitable orientation of a ligand that binds a particular receptor and is used to predict the structure of intermolecular complexes or similar molecules. Based on the assessment function in docking, the docking process involves two basic steps, namely: 1) prediction based on the conformation of the ligand as well as the position and orientation of the ligand binding or what is known as the pose; 2) based on binding free energy assessment (Meng et al., 2011 ; Vijesh et al., 2013). The first stage can be called redocking or what is known as the process of searching for validation of the mooring area (gridbox). The second stage can be called the scoring stage, namely predicting the binding of the ligand to the receptor (protein) by considering the highest binding free energy or the one that shows the most negative value (Boittier et al., 2020; Sari et al., 2020; Tallei et al., 2020). Molecular docking aims to screen a number of compounds that carry out virtual screening based on binding free energy and predict small molecules that can inhibit important amino acids in the target protein.

The molecular docking used in the research is through the AutoDockTools program. The natural ligand used is s-adenosylmethionine, a total of 15 test ligands are used. Molecular docking can be visualized using two-dimensional and three-dimensional programs using biovia. The research results show that the test ligand has a good interaction with the SSCMec protein which can be seen from the binding energy value with an average binding energy value of -9.395333333, the most negative binding energy is the Elucanainones A ligand with a value of -11.91 kcal/mol and Eleucanainones B with a binding energy value of -11.66 kcal/mol. The more negative the binding energy value, the better the bond between the ligand-protein, this is because the ligand that has a more negative value has more amino acid bonds and then the ligand with the best

value will be selected to proceed to the molecular dynamics simulation (Kurczab, 2017) compounds that have lower binding energies and interact with amino acid residues similar to the natural ligand Eleucanainones A have the lowest binding free energy values in the SCCMec protein. The value of the test ligand is smaller when compared to the native ligand (s-adenosylmethioni) (Table), because there are more amino acid residues that interact with the two test ligands when compared to the natural ligand (figure 1).

Analysis of docking results can be found through the AutoDockTools program. AutoDockTools is a program that can predict the free energy of ligand binding to a receptor based on the docking scoring function. The assessment function used is at the scoring stage. The scoring stage is a stage that combines the predicted results of the binding free energy with the experimentally generated binding free energy (based on ranking). To evaluate the free energy of binding, it can be obtained through the free energy formula (ΔG) in the laws of thermodynamics by finding the value of the inhibition constant. This formula can be described as follows (Shityakov and Forster 2014; Du et al., 2016; Salsabila, 2019; Boittier et al., 2020): The binding free energy will reach equilibrium if it is negative. The binding free energy is directly proportional to the inhibition constant. The greater the negative value of the binding ΔG of a compound, the more spontaneous its ability to interact with the target receptor. Thus, the lower the inhibition constant of a compound will reduce the concentration required for a compound to inhibit enzyme action, and vice versa (Du et al., 2016). According to Zheng and Polli (2010), the inhibition constant can be declared strong if it has a value of ≤100 μM, and conversely, the inhibition constant can be declared weak if it has a value of ≥100 μM.

It can be seen that the test ligand that has the lowest binding free energy and the lowest inhibition constant is Eleucanainones A of -11.91 kcal·mol-1 and 1.87 μM. Meanwhile, it can also be seen that all the test ligands analyzed stated that all ligands were at relatively strong inhibition constants. Apart from these two factors, the number of hydrogen bonds and the number of hydrophobic interactions are also parameters for docking analysis. These parameters become a reference in finding drug candidates. The greater the number of hydrogen bonds and hydrophobic interactions in a ligand-receptor complex, the more stable and stronger the conformation of the two structures will be, as well as increasing the interfacial binding of the ligand-receptor complex and increasing biological activity in designing drug candidates (Patil et al. 2010)

Amino Acid Bonding

Amino acid bonding in the context of docking refers to the interaction between the amino acid side chains of the target protein and the ligand molecule being analyzed. When performing molecular docking, one of the important things is to take into account possible interactions between various amino acid residues within the protein binding site and adjacent sites of the ligand.

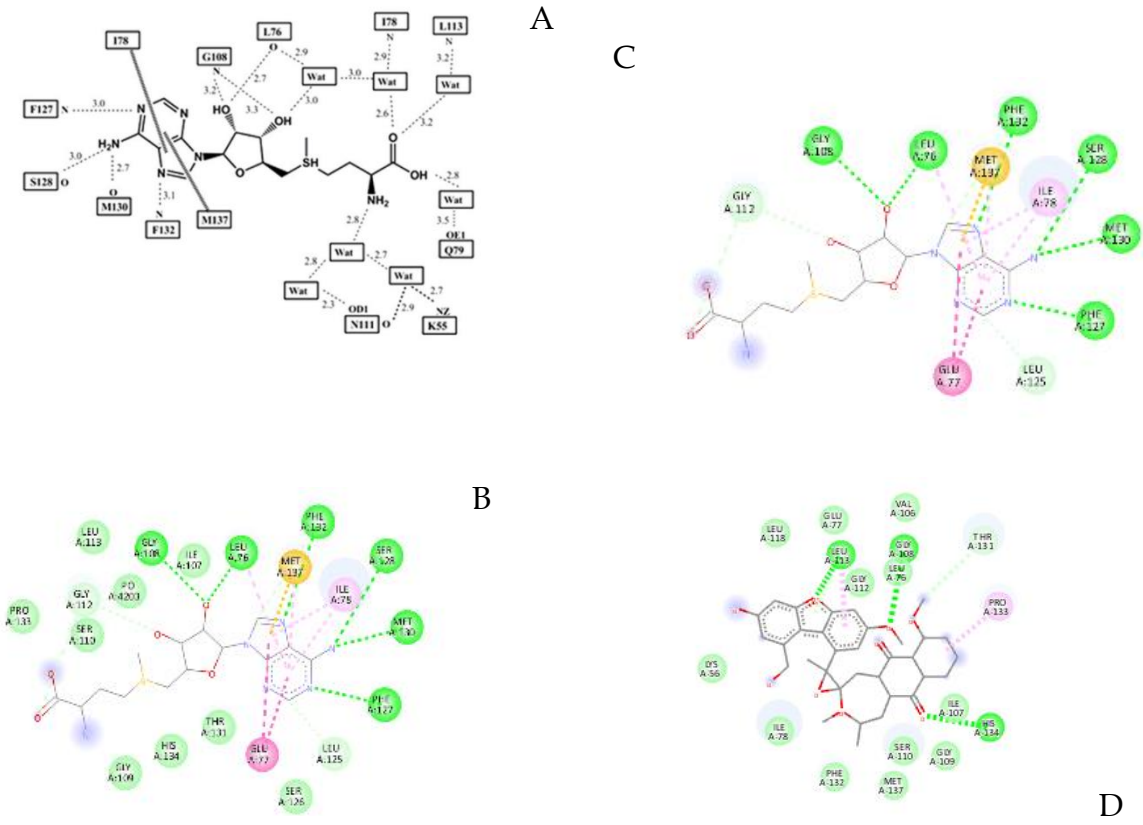


Figure 5. A: interaction of s-Adenosylmethioni and Proteins from The Journal. B: Interaction of S-Adenosylmethioni and Proteins From pdb. C: interaction of s-Adenosylmethioni and The Proteins Involved. D: Interaction of Eleucannones and Proteins

It can be seen in the picture that the test ligand has the same amino acid bonds as the native ligand. s-adenosylmethionine which is an inhibitor and natural ligand of SCCMec (4FAK) interacts with amino acid residues in the active site via hydrogen bonds, van der Waals bonds and π-alkyl bonds (Figure 3). According to Boundy. (2013) the natural ligand in 4FAK forms hydrogen bonds with G:108, P:132, S:128 L:76, M:130, P:127, P:133, G:108, I:107, A:111, S:110, H:134, G:109, G:112, L:125, G:77, M:137, S:126, T:131, L:113, P:4203, I:78, M: 137. In the docking results of the eleucananones compound with protein, it can be seen that the amino acids L:113, G:108, H:134, G:77, T:131, G:112, L:76, I:78, P:132, M:137 are similar. , S:110, G:109, I:107 with a similarity percentage of 56%. Pocket site Pocket site docking is a molecular docking technique in which the primary focus is on binding molecules into a "pocket" (pocket) within the target protein structure. These pockets are often regions with special properties that allow for a variety of chemical interactions with appropriate ligands. The process involves placing a ligand molecule into a protein pocket and then evaluating potential interactions between the ligand and surrounding amino acid residues. This can provide valuable information about the affinity and potential biological activity of the ligand towards the target protein. “Pocket site docking” techniques are

important in drug design because many drugs work by interacting with specific binding sites on their target proteins. By using molecular docking to evaluate potential interactions between drug candidates and these pockets, researchers can estimate the drug's activity and affinity before conducting further biological testing. It can be seen in the picture that s-adenosylmethionine and the eleucananones compound occupy the same pocketed site, even though they do not have similar grid values, they have the same position, this is influenced by different binding energy values and different amino acid bonds .

Pocket site

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Dynamics Simulation

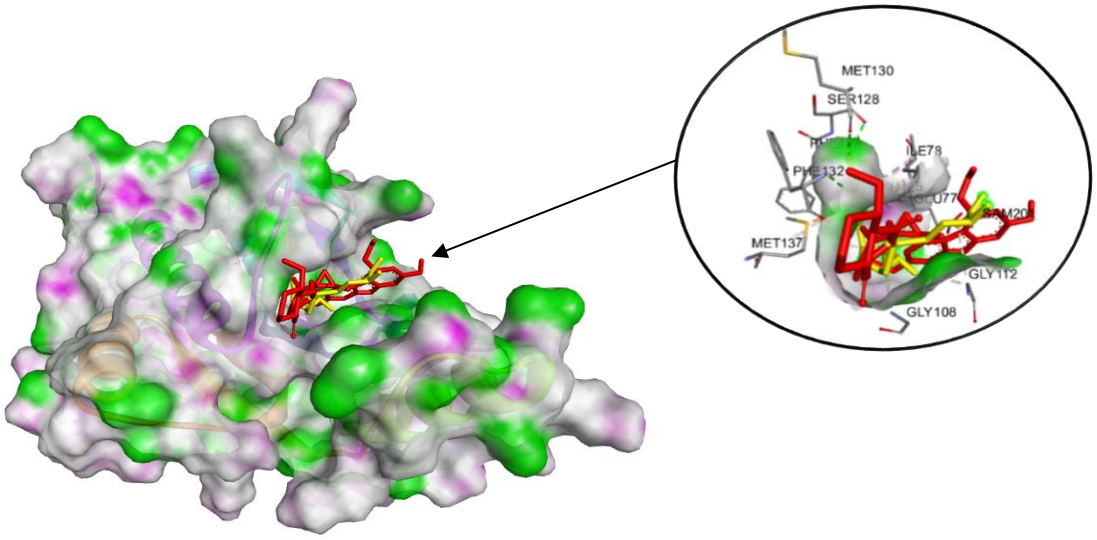

Figure 6. Dynamics Simulation

Based on the image, the natural protein-ligand complex is more stable than Eleucananones B. This result can also be proven by the average RMSD value of the natural ligand which is smaller than that of Eleucananones A (Table). Based on the graph and average results, it can be seen that the binding stability of the Eleucananones B ligand with the SSCMec protein is close to the binding stability of the natural protein-ligand complex, the binding stability is not as good as that of the natural ligand, this could be caused by conformational differences. In addition to environmental influences such as temperature and pH, ligand-protein interactions can also trigger structural conformational changes that can involve changes in torsional angles, atomic shifts, or distortion of the protein structure. These changes can be triggered by various factors, including different shapes, sizes, charges and chemical properties of the ligands (Oliwa & Shen, 2015). Based on the picture, the test ligand Eleucananones A has an RMSF graph that is almost the same as the test ligand. The natural protein-ligand complex had approximately the same stability as the test ligand as indicated by the average RMSF value (Table 8). Based on RMSF results, amino acid residues in natural ligands such as G:108, P:132, S:128 L:76, M:130, P:127, P:133, G:108, I:107, A:111, S:110, H:134, G:109, G:112, L:125, G:77, M:137, S:126, T:131, L:113, P:4203, I:78, M: 137 has not experienced any changes and remains stable. Likewise , the amino acid residues in the test ligand Eleucananones A are the same as the natural ligand, have not changed and remain stable.

ADMET Prediction Profile

Table 2. ADMET Prediction Profile

Distribution			
Compound	PPB	VD	BBB
Elucananones A	86.164%	0.279	---
Elucananones B	89.018%	0.346	---

Absorption					
Compound	P-Caco2	Pgp-sub	HIA	F20	F30
Elucananones A	-5,233	---	+	---	-
Elucananones B	-5,420	---	-	---	+

Metabolism					
The rent	CYPA12 Substrate	CYP219 Substrate	CYP2C19 Substrate	CYP2D6 Substrate	CYP3A4 Substrate
Elucananones A	+++	+	+++	+++	--
Elucananones B	+++	---	++	--	+++

Excretion		
Compound	Clerance	1/2
Elucananones A	9,304	0 .544
Elucananones B	2,022	0.151

Toxicity					
Compound	Hhrg	H-HT	DILI	FDMDD	LD50

Elucananones A	---	++	+++	+++	6,273
Elucananones B	--	-	+++	+++	6,207

--- : Very good
-- : Good
-: Currently
+ : Not good
+ + :Not Good
++ + : Very bad

Based on the table it can be seen that the absorption value of the three compounds has an optimal P-Caco2-2 value because it has a value of more than -5.151log cm/s and has very good Pgp-sub, in the parameter compound eleucainanones B has a better HIA than eleucainanones A and have F20 which are both good but F3 eleucainanones B is better. However, both compounds have a metabolic profile that is on average unfavorable for use as medicine. For the excretion parameter, the eleucanainones A compound has a clearance of 9.303 and eleucanainones B is 2.022 and the ½ parameter has a value of 0.544 and 0.151. The toxicity parameters for both compounds have an average value that is not good, but the eleucanainones B compound has a better H-Ht value than eleucanainones A. namely with a value that can still be accepted by the body.

DISCUSSION

This section allows you to describe your research findings academically. You may not enter figures related to your statistical tests here; instead, you should explain those numbers here. You should structure your discussion with academic support for your studies and a good explanation according to the specific area you are investigating.

CONCLUSIONS AND RECOMMENDATIONS

Dayak onion compounds have potential as candidates for MRSA antibacterial drugs with an energy value that exceeds and has an amino acid bonding pattern that resembles s-adenosylmethionine with an average binding energy value of -9.395333333, the most negative binding energy is the Elucanainones A ligand with a value of -11.91 kcal/mol and Eleucanainones B of -11.66 kcal/mol. With stability values shown by the RMSD and RMSF values approaching the native ligand s-adenosylmethionine

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