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In Silico Analysis of Secang Wood Compounds (*Caesalpinia Sappan* L.) as Antibacterial Candidates Against Salmonella typhi Causing Typhoid Fever

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Abstract. Typhoid fever represents a significant global health issue, as it causes gastrointestinal infections in humans and is primarily associated with inadequate sanitation. Which encourages the search for natural remedies as an alternative option. This study investigates the antibacterial potential of Secang wood (Caesalpinia sappan L.), a widely used traditional medicinal plant in Indonesia. Through in silico approach, this study investigated the chemical interaction and binding affinity of the main compounds in Secang wood are Brazilin, Brazilein, Sappanchalcone, Caesalpiniaphenol, Quercetin, Sappanone-A, Sappanone-B, Hematoxylin, Butein with Salmonella typhi protein. Molecular docking analysis showed that Sappanone A showed high binding affinity energy of -9.2 kcal/mol, Butein and Sappanchalcone of -9.0 kcal/mol, then Quercetin and Brazilein showed binding affinity of -8.9 kcal/mol indicating significant potential as DNA gyrase inhibitors. Compounds that have high binding affinity above have the potential to be candidates antibacterial. Drug similarity analysis confirmed that Sappanone A, Butein, Sappanchalcone, Quercetin, and Brazilein have suitable characteristics to be further developed as therapeutic agents. The results of this study indicate that compounds from Secang Wood (Caesalpinia sappan L.) have the opportunity to become viable antibacterial agent candidates. The bioactivity value shown were Sappanone-A of 0.69, Butein 0.57, Sappanchalcone 0.33, Quercetin 0.58, and Brazilein 0.23. Further research is needed to isolate and test the effectiveness of these compounds in preclinical and clinical studies. These findings strengthen the role of traditional Indonesian herbal medicine as a natural therapeutic approach in dealing with typhoid fever infection.

Keywords : Antibacterial, Secang wood, DNA gyrase, molecular docking

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Introduction

Bacterial infections are one of the significant global health problems in the world [1]. Various pathogenic bacteria are capable of causing gastrointestinal infections in humans [2]. One of the diseases caused by bacteria is typhoid fever [1]. Indonesia has a prevalence of typhoid fever cases reaching 55,098 people with a mortality rate of 2.06% of the number of sufferers so typhoid fever is one of the top 10 causes of death in Indonesia [2].

The cause of typhoid fever is the bacterium Salmonella typhi, which belongs to the enterica subspecies of Salmonella enterica [3] This bacterium has a rod shape, is classified as gram-negative, does not produce spores, can to move (motile), is encapsulated, and has flagella (moves with the help of vibrating hairs) [4]. Typhoid fever is an acute systemic infectious disease that affects the reticulo-endothelial system, gastrointestinal lymph nodes, and gall bladder [5]. Treatment of typhoid fever generally involves the use of antibiotics. One of the effective antibiotics and the first line for treating typhoid fever is Ciprofloxacin [6].

The mechanism of action of this antibiotic is to inhibit bacterial DNA Gyrase activity and disrupt bacterial cell wall compounds, and it can cause a reduction in the amount of bacterial DNA, RNA, and protein [7]. Although antibiotics have become the main choice in the treatment of typhoid fever, new challenges arise in controlling this disease, namely antibiotic resistance [3].

Ciprofloxacin resistance in Salmonella typhi has increased in the last decade [8], leading to worse outcomes for patients and having major implications for the health system [8]. Therefore, it is necessary to develop new antibacterial therapies.

Antibacterial therapy is a treatment effort aimed at dealing with bacterial infections by utilizing bactericidal agents, because these substances are effective in eradicating bacteria and destroying biofilms that form and accelerating the healing of wounds infected with bacteria [9]. The parameters used in this research are affinity energy values, interacting amino acid residues, similarity of drug compounds based on Lipinki's law of 5, and toxicity of compounds. One of the antibacterial therapies is by utilizing plants [10].

One of the efficacious plants as an antibacterial is Caesalpinia sappan L. Caesalpinia sappan is a plant from the Caesalpiniaceae family which is found abundantly in Indonesia and has been empirically proven to have many properties in health as an antibacterial [11]. The part of Caesalpinia sappan that has antibacterial ability are primarily found in the heartwood [10]. Bioactive compounds of Caesalpinia sappan including Brazilin, Brazilein, Sappanchalcone, Caesalpiniaphenol, Quercetin, Sappanone -A, Sappanone-B, Hematoxylin, and Butein [11].

Research by Agustini et al (2023) shown Caesalpinia sappan extract has antibacterial activity against Streptococcus mutans bacteria. In silico testing is a test conducted with the help of a computer to determine the interaction between an antibacterial compound and the target molecule [12]. In silico assays employ computational tools and molecular databases to model interactions between candidate compounds and target proteins [13]. This approach offer substantial benefits in antibacterial research by enabling efficient prediction of antibacterial activity with reduced time and cost [14].

The supporting tests in this study include drug-likeness evaluations based on Lipinski's Rule of Five, compound toxicity assessments based on LD_{50} values, toxicity class, hepatotoxicity, and carcinogenicity parameters, as well as bioactivity tests based on pharmacological activity [13]. Toxicity testing needs to be done to identify potential side effects of compounds [22]. However, until now there has been no research on the antibacterial effect of Caesalpinia sappan in silico. Therefore, researchers are interested in conducting research with the title "In Silico Analysis of Secang Wood Compounds (Caesalpinia sappan L.) as Antibacterial Candidates Against Salmonella typhi Cause of Typhoid Fever"

Experimental

The Sample Preparation of Ligand and Target Protein. The software used in this research are Pyrx and Biovia Discovery Studio. Pyrx serves as a docking engine for structure-based drug design [12]. Biovia Discovery Studio serves as a molecular structure visualization engine [16]. The webservers used in this research are SwissADME, protox online tool and passonline. The databases used were RCBS protein data bank (PDB) and PubChem. SwissADME is a web-based tool used to predict the drug-likeness and pharmacokinetic properties of a compound

[21]. ProTox Online Tool is a web server designed to predict the toxicity and potential health risks of a compound [22]. PASS Online is a tool for predicting the biological activity of a compound based on its chemical structure [24]. The RCSB PDB is a database that provides three-dimensional structures of macromolecules [12]. PubChem is a database containing structural and chemical information on small molecules [13].

Bioactive compounds of Secang wood (Caesalpinia sappan L) including Brazilin (CID_73384), Brazilein (CID_ 6453902), Sappanchalcone (CID_5319493), Caesalpiniaphenol (CID_ 71452598), Quercetin (CID_5280343), Sappanone A (CID_ 9817274), Sappanone B (CID_13888976), Hematoxylin (CID_ 442514), Butein (CID_ 5281222) were downloaded through PubChem, then saved in sdf format and preprocessed by separating water molecules and ligand groups through Biovia Discovery Studio software [13]. Next, the target DNA gyrase (PDB ID: 6J90) with chain A was retrieved from the protein data bank (PDB). The protein was first processed using Biovia Discovery Studio, then given a polar charge and hydrogen atoms using autodock tools, then saved in pdbqt format. Target receptor preparation is important to do in order to get optimal docking results [14].

Target Receptor Validation. Receptor validation is an important thing to do before starting molecular docking [15]. Validation of the target receptor aims to know the receptor binds precisely to the active side and shows little deviation by paying attention to the RMSD (Root Mean Square Deviation) value [16]. Validation of the target receptor, 6J90, was done by redocking the native ligand Adenosine 5'-triphosphate (ATP_52) with the target receptor 6J90 using Discovery Studio software.

Molecular Docking. The molecular docking process was carried out using PyRx software with coordinates that have been adjusted in receptor validation [17]. Receptor 6J90 with binding site center X: -16,0064, Y: 50,2545, Z: 30.3858, Dimension (Angstrom) X: 25,0015 Y: 19,1140, Z: 21,9192.

Interaction and Visualization. The molecular docking results are then integrated with the protein complex structure through Discovery Studio software to obtain visualization in the form of chemical bond interactions to determine the interaction position and type of chemical bonds formed in the ligand-protein complex such as hydrogen bonds, hydrophobic bonds, and electrostatic at the binding site [18].

Drug Compound Similarity Test. This test aims to identify the ability of a compound to be a promising drug candidate by fulfilling the parameters of Lipinski's Law of Five [19]. Lipinski's five law parameters include Molecular Weight (BM) value, Log P value, Hydrogen Bond Acceptors (HBA), and Hydrogen Bond Donors (HBD) [20]. Each compound was tested for drug similarity using SwissADME (http://www.swissadme.ch/). SwissADME can predict data on the ability of a test compound to be a promising drug candidate [21].

Toxicity Test. Toxicity testing is conducted to evaluate the toxicity and potential risk of test compounds that may harm the human body. [22]. Toxicity prediction using LD50 parameters, toxicity class, hepatotoxicity, and carsonogenic using Protox Online Tools (https://tox.charite.de/) to obtain toxicity data and the impact on the human body [23].

Bioactivity Test. Bioactivity tests are conducted to predict the characteristics, pharmacological, bioactivity and potential and metabolic pathways of a compound [24]. The antibacterial potential of each compound was estimated by utilizing the Way2Drugs PASSOnline online tool (https://www.way2drug.com). This tool can estimate the possibility of a compound having certain pharmacological activities, including antibacterial, antiviral, anticancer, and other activities [25].

Data Analysis. The data analysis technique used in this research is the interpretation of molecular docking results based on the binding energy value, and the type of molecular interaction between the ligand and the target protein, then the data is analyzed descriptively by comparing the results of each ligand interaction with the target protein. The results of molecular docking between bioactive compounds of Secang Wood (Caesalpinia sappan L.) against the target protein DNA gyrase (PDB ID: 6J90) were visualized in three dimensions using Biovia Discovery studio software. This visualization aims to determine the interaction and form of bonds produced by ligands and proteins [26].

Result and Discussion

Validation of the target receptor is a very important first step before molecular docking. Vali-

Table 1. Receptor validation results using Discovery Studio software

Ligand	DNA gyrase (6J90)			Average
	Replication I	Replication II	Replication III	
RSMD Value (Å)	0.0632	0.0589	0.02055	0.04755

dation of the target receptor, 6J90, was done by redocking the native ligand Adenosine 5'-triphosphate (ATP_52) with the target receptor 6J90 using Discovery Studio software. Validation of the target receptor is done to know the receptor binds precisely to the active side and shows little deviation by paying attention to the RMSD (Root Mean Square Deviation) value [16]. Target receptor validation also aims to ensure that the receptor used is able to recognize the ligand with high accuracy on its active site [17]. The results of receptor validation are shown in Table 1.

Root Mean Square Deviation (RMSD) value is used as the main parameter in assessing receptor validity [27]. The smaller the RMSD value, the smaller the deviation of ligand position, which means the higher docking accuracy [28]. Receptor is declared valid and can be used for docking process if it has RSMD value ≤ 2 Å [29]. Receptor validation was replicated three times by re-docking between native ligand and 6J90 target receptor [30].

Based on Table 1, the results of receptor validation using Discovery Studio software obtained an average RMSD value of 0.04755 Å. Based on Table 1, the RMSD value of redocking results carried out in three replications, namely 0.0632 Å, 0.0589 Å, and 0.02055 Å with an average value of 0.04755 Å. This value is well below the threshold limit of 2 Å, which indicates that the 6J90 receptor has been very well validated and can be used in further molecular docking processes. This shows that the target receptor used has met the criteria for receptor validation, namely RMSD value ≤ 2 Å. Furthermore, the ligand was tethered to the 6J90 receptor into the binding site with Grid coordinates at the binding site center X: -16,0064, Y: 50,2545, Z: 30.3858, Dimension (Angstrom) X: 25,0015 Y: 19,1140, Z: 21.9192.

Setting consistent coordinates in each docking is important so that the results of ligand interactions with receptors can be compared objectively, because differences in position or dimension can affect the affinity value and interpretation of molecular interactions [31]. The docking results between the test compounds and the 6J90 receptor are presented in Table 2.

The compounds selected for further visualization are those that demonstrate higher binding affinity values than the comparator drug, Ciprofloxacin. A higher binding affinity suggests a stronger compound, indicating a potentially greater antibacterial effect [33]. Therefore, compounds with superior binding profiles compared to Ciprofloxacin are prioritized for visualization to further assess their molecular interactions and potential as drug candidates. Visualization and interaction of docking results are shown in the Figure 1.

Table 2 shows the docking results between the test compounds and the DNA gyrase receptor (6J90) showing variations in binding affinity values as well as the type and number of interactions formed, which illustrates the ability of the ligand to bind to the active site on the target. The binding affinity value is expressed in units of kcal/mol, where the more negative the value, the stronger the affinity of the ligand to the receptor [32] Based on table 2, it is found that the ligand that has a better binding affinity value than ciprofloxacin is the Sappanone A compound with a binding affinity value of -9.2, kcal/mol followed by Butein and Sappanchalcone with a binding affinity value of -9.0 kcal/mol, followed by Quercetin and Brazilein compounds with a binding affinity value of -8.9 kcal/mol. Meanwhile, the binding affinity value of the comparator drug, ciprofloxacin, is -8.7 kcal/mol. Good binding affinity value are those with the lowest (negative) binding affinity values. [33]. This shows that there are 5 compounds, namely the compounds Sappanone A, Butein, Sappanchalcone, Quercetin, and Brazilein are the best ligands that have a more negative binding affinity than the comparison drug ciprofloxacin.

Table 2 also shows the ligand-receptor complex binding interactions. Some key residues such as GLY102, THR165, LYS103, and ASN46 frequently appear in the hydrogen interactions, indicating that they are important parts of the active site or ligand-binding region [34]. For example, Sappanone A formed three hydrogen bonds with residues VAL118, GLY119, THR165 which showed strong and

stable interactions. Hydrophobic interactions were also observed to be quite dominant, especially with residues ILE78, VAL120, and ILE94 indicating the involvement of the hydrophobic part of the compound in the stabilization of the complex. Almost all the test compounds showed hydrophobic interactions with ILE78, indicating that this residue plays an important role in non-polar binding of ligands [35]. Some compounds such as Sappanone A, Quercetin, and Ciprofloxacin also showed electrostatic interactions, especially with charged residues such as LYS103 and GLU50. These interactions make an additional contribution to ligand affinity, especially in compounds with charged groups [36]. The docking results show that the test compounds Sappanone A and Butein have strong potential as DNA gyrase inhibitors, with high affinity values and complex interaction patterns. This study provides a strong basis for further research into these compounds in the development of new antibacterial agents.

Furthermore, physicochemical properties were predicted on the SWISSAdme webserver (http://www.swissadme.ch/) using the parameters of Lipinski's Law of Five. The results of the drug compound similarity test are shown in the Table 3.

Lipinski's law of five is a law used to determine chemical compounds with oral bioavailability and pharmacological activity [19]. Lipinski's five law parameters include Molecular Weight (BM) values, Log P values, Hydrogen Bond Acceptors (HBA), and Hydrogen Bond Donors (HBD) [20]. This test was carried out by entering the SMILES code of each com-

Table 2. *Docking* Results and Chemical Interactions between Test Compounds with Receptor 6J90

Ligand	*Binding affinity* (kcal/mol)	Hydrogen Bond	Hydrophobic Bond	Electrostatic
Native Ligand Adenosine 5'-triphosphate	-10,7	ASN46, TYR109, LEU115, HIS116, GLY117, VAL118, VAL120, LYS337, ASP73, GLY101, GLY114, GLY119, GLU50	ASN46, ASN47, ILE78, VAL120	GLU42
Sappanone A	-9,2	VAL118, GLY119, THR165	ILE78.	LYS103, GLU50
Butein	-9,0	GLY102, SER121, GLU50, THR165,	GLY101, ASN46, ILE94, VAL120, ILE78	-
Sappanchalcone	-9,0	GLY102, LYS103, VAL120, THR165	ASN46,	LYS103, VAL120, ILE78
Quercetin	-8,9	GLY77, PRO79, THR165.	TYR109, ILE78, ILE94, VAL120	LYS103, GLU50
Brazilein	-8,9	ASN46, TYR109, ALA100, LYS103, THR165	ASN46, ILE94, VAL120, ILE78	LYS103
Sappanone B	-8,7	GLY102, GLU50, GLY101, LYS103	TYR103, ILE78, PRO79, LYS103	-
Hematoxyln	-8,2	LYS103, GLY119.	ILE78, VAL120	-
Brazilin	-8,1	LYS103	ILE78,	-
Caesalpiniaphenol	-8,0	ASP73, ALA100, ILE78, PRO79	ASN46, ILE78, ILE94.	LYS103
Ciprofloxacin	-8,7	GLY77, GLY102, TYR109, GLY117, ASN46, ILE94	ASN46, ILE78, ILE94,	LYS103

pound obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) on the SWISSAdme online tool (http://www.swissadme.ch/) [21].

Table 3 shows that Sappanone A, Butein, Sappanchalcone, Quercetin, and Brazilein compounds have sequential molecular weight values of 284.26 g/mol, 272.25 g/mol, 286.28 g/mol, 302.24 /mol, and 284.26 g/mol so that they fulfill Lipinski's law 5, namely molecular weight values <500 g/mol. Molecular weight is related to the process of drugs penetrating biological membranes by diffusion. Compounds that have a molecular weight > 500 g/mol will be more difficult to pass through biological membranes so that drugs require a longer absorption time. It is different when the compound has a molecular weight <500 g/mol, it will be easier to pass through the biological membrane so it does not require a long absorption time [37].

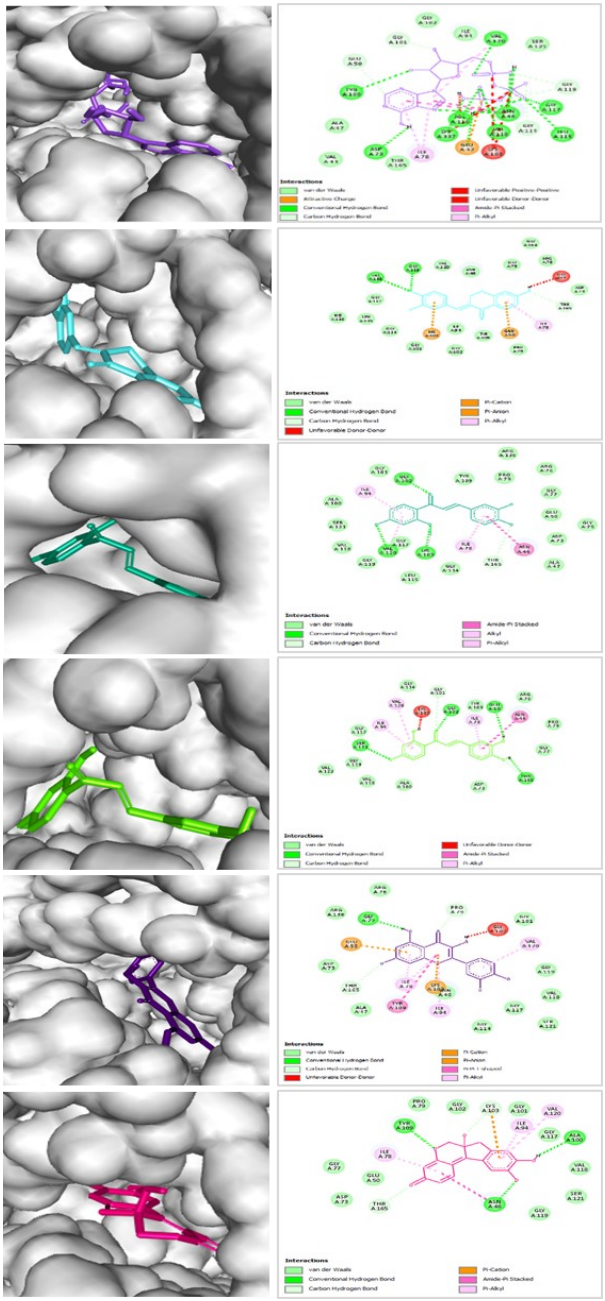

Figure 1. Visualization and Protein Interaction between target protein 6J90 with (A) Native ligand, (B) Sappanone A, (C) Butein, (D) Sappanchalcone, (E) Quercetin, (F) Brazilein

Table 3 shows that the compounds Sappanone A, Butein, Sappanchalcone, Quercetin, and Brazilein have log P values of 1.95, 1.96, 2.17, 1.23, and 0.97 respectively, thus fulfilling Lipinski's law 5, namely log P value <5. The log p value is related to the hydrophobicity or lipophilicity of a compound. A log P value that is too large can make the compound very hydrophobic, thus reducing its selectivity to the receptor and causing its toxicity to be higher [37]. Table 3 shows that the compounds Sappanone A, Butein, Sappanchalcone, Quercetin, and Brazilein have sequential HBA (Hydrogen Bond Acceptor) values of 5, 5, 5, 7, 5 so that they fulfill Lipinski's law 5, namely the HBA value < 10. Sappanone A, Butein, Sappanchalcone, Quercetin, and Brazilein compounds have sequential HBD (Hydrogen Bond Donor) values of 3, 4, 3, 5, 3 so that they fulfill Lipinski's law of 5, namely the HBD value < 5. The higher the donor and acceptor capacity, the higher the energy required for the absorption process to occur [38].

Bioavailability Score is an estimate of the probability that a compound will have good bioavailability when given orally in humans and optimally >10% [39]. Based on table 3, it is known that all ligands have a high bioavailability score with a value of 0.55 so that the ligand compounds are considered to have a high enough chance to be absorbed orally and become potential drug candidates. GI absorption (Gastrointestinal absorption) is a prediction of the level of absorption of compounds in the digestive tract after oral administration [40].

Furthermore, the toxicity prediction of ligand compounds and ciprofloxacin comparator drugs was carried out using the online tool Protox Online Tools. The results of the toxicity properties test of the ligand compound and the comparison drug ciprofloxacin are shown in the Table 4.

Based on the toxicity prediction results in table 4, it shows that the compounds Sappanone A, Butein, Sappanchalcone, Quercetin, and Brazilein have sequential LD50 of 3800 mg/kg, 1000 mg/kg, 3000 mg/kg, 159 mg/kg, and 2000 mg/kg, so that the compounds are included in the toxicity class in

Table 3. Drug Compound Similarity Test Results

Ligand	Lipinski's Law of Five Parameters				Lipinski's Law of Five	Bioavailability Score	GI absorption
	BM (g/mol)	Log P	HBA	HBD			
Native Ligand Adenosine 5'-triphosphate	507,18	-3,80	16	7	No.	0,11	Low
Sappanone A	284,26	1,95	5	3	Yes	0,55	High
Butein	272,25	1,96	5	4	Yes	0,55	High
Sappanchalcone	286,28	2,17	5	3	Yes	0,55	High
Quercetin	302,24	1,23	7	5	Yes	0,55	High
Brazilein	284,26	0,97	5	3	Yes	0,56	High
Sappanone B	302,28	1,30	6	4	Yes	0,55	High
Hematoxyln	302,28	1,21	6	5	Yes	0,55	High
Brazilin	286,28	1,51	5	4	Yes	0,55	High
Caesalpiniaphenol	258,23	1,56	5	3	Yes	0,55	High
Ciprofloxacin	331,34	1,10	5	2	Yes	0,55	High

Table 4. Test Results of Toxicity Properties of Ligand Compounds and Ciprofloxacin

Compound	Toxicity			
	LD_{50} (mg/kg)	Toxicity Class	*Hepatoxicity*	Carcinogenicity
Native Ligand Adenosine 5'-triphosphate	2000	IV	No.	Yes
Sappanone A	3800	V	No.	No.
Butein	1000	IV	No.	No.
Sappanchalcone	3000	V	No.	No.
Quercetin	159	III	No.	Yes
Brazilein	2000	IV	No.	Yes
Sappanone B	2000	IV	No.	No.
Hematoxyln	500	IV	No.	No.
Brazilin	800	IV	No.	No.
Caesalpiniaphenol	1500	IV	No.	Yes
Ciprofloxacin	2000	IV	No.	No.

order, namely class V, class IV, class V, class III, and class IV. This classification is based on Globally Harmonized System (GHS) which is class V means may be harmful if swallowed ($2000 < LD_{50} \leq 5000$ mg/kg), class IV means harmful if swallowed ($300 < LD_{50} \leq 2000$ mg/kg), class III means toxic if swallowed ($50 < LD_{50} \leq 300$ mg/kg) [31]. The next test parameter is the Hepatotoxicity test which is a test conducted to determine whether drug candidate compounds can cause damage to the liver [39]. Based on the results of the Hepatotoxicity test, the compounds Sappanone A, Butein, Sappanchalcone, Quercetin, and Brazilein are not toxic to the liver. Based on all the results of the toxicity test, it is known that Sappanone A and Sappanchalcone compounds belong to class 5 which has a relatively safe level of toxicity and is not toxic to the liver, Butein and Brazilein compounds belong to class 4 which has relatively low toxicity and is not toxic to the liver, and Quercetin compounds belong to class 3 which have moderate toxicity and are not toxic to the liver, and the comparison drug ciprofloxacin belongs to class 4 which has relatively low toxicity and is not toxic to the liver. This shows that Sappanone A and Sappanchalcone compounds are better than the comparison drug ciprofloxacin. The next parameter is the Carcinogenicity test which is a test conducted to determine the potential of a substance, such as a chemical or medical device, to cause cancer [25]. Based on table 4 the compounds Sappanone A, Butein, Sappanchalcone are not carcinogenic.

Furthermore, the bioactivity test of the ligand compound was carried out. Bioactivity tests are carried out to predict the characteristics, pharmacological, bioactivity and potential and metabolic pathways of a compound [24]. The antibacterial potential of each compound was estimated using the Way2Drugs online platform. PASSOnline (https://www.way2drug.com). This tool can estimate the

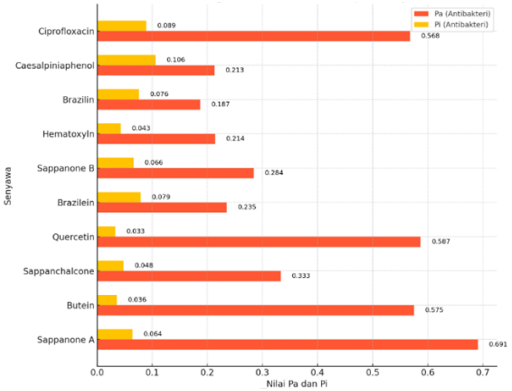

Figure 2. Compound Bioactivity Test Results

possibility of a compound having certain pharmacological activities, including antibacterial, antiviral, anticancer, and other activities [25]. The results of the compound bioactivity test are shown in the Figure 2.

Based on the results of the bioactivity test in Figure 2 which refers to the prediction of the general biological potential of a bioactive compound, it shows that there is an antibacterial compound activity that is higher than the Ciprofloxacin comparator drug where Pa (Probability of activity) exceeds Pi (Inhibitor Probability) in Sappanone A, Quercetin, and Butein compounds has a value of 0.691, 0.587, and 0.575 respectively which is higher than the antibacterial Pa on Ciprofloxacin comparator drug which is 0.568. This indicates that Sappanone A, Quercetin, and Butein compounds are active against the target and have a greater chance of antibacterial activity. The activity probability value (Pa) describes the ability of biological potential activity or the mechanism that the compound activates when it enters the body [25]. Furthermore, it can be seen that there is an inhibition probability value (Pi) which indicates the possibility of inactivity where the antibacterial Pi (inhibition probability) of Sappanone A, Quercetin, and Butein compounds has a value of 0.064, 0.033, 0.036 respectively which is lower than Ciprofloxacin's Pi which is 0.089. This indicates that Sappanone A, Quercetin, and Butein compounds have a lower chance of being inactive for certain biological properties. The value of Pa (probability of activity) should be greater than the value of Pi (probability of inhibition) with Pa > 0.3 indicating medium confidence (theoretical) prediction results aimed at screening.

Conclusion

Based on the results of the research that has been carried out, it can be concluded that the interaction that occurs between the bioactive compounds of Secang Wood (Caesalpinia sappan L.) against the Salmonella typhi DNA gyrase receptor shows a strong chemical bond in the mechanism of DNA gyrase inhibition. The types of bonds formed include hydrogen bonds, hydrophobic interactions, and electrostatic bonds that contribute to the stability of the complex between the bioactive compound of Secang Wood (Caesalpinia sappan L.) and the target protein. This shows the potential of the bioactive compound of Secang wood (Caesalpinia sappan L.) as an antibacterial agent through the mechanism of DNA gyrase inhibition. Then the bioactive compounds of Secang Wood (Caesalpinia sappan L.) showed varying affinity energy against DNA gyrase of Salmonella tyhpi. Sappanone A compound has the highest binding affinity value of -9.2 kcal/mol, followed by Butein and Sappanchalcone -9.0 kcal/mol, and Quercetin and Brazilein -8.9 kcal/mol compared to Ciprofloxacin antibiotic -8.7 kcal/mol. This indicates that the bioactive compounds of Secang Wood (Caesalpinia sappan L.) show good potential as DNA gyrase inhibitors and have the opportunity to be developed as alternative antibacterial agents against Salmonella typhi.

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