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# Spike Protein Covid-19 –Mahagoni's (Swietenia Mahogany) Secondary Metabolite Interaction Using In-Silico Analysis

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**Abstract**

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2) Outbreak destroy every particular aspect of global society. SARS-CoV2 infect humans thereby attaching their dreadful particle spike S1 protein to angiotensin-converting enzyme 2 (ACE2). Inhibition toward Spike S1- ACE2 interaction has been suggested to be significant target. One of the effective strategies to cure disease by secondary metabolites from potential plants such as Swietenia mahagony. This research aims at investigating the interaction between S1 protein with Some secondary metabolites from Swietenia mahagony (flavonoid, alkaloid, and Saponin) by molecular docking. The method carried in this study were experiment and descriptive. All ligand was obtained from PubChem and constructed by using PyMol, Biovia Discovery PyRx for visualization. The interaction was investigated using Autodoc vina then the docking skor from several probabilities is ranked by number of parameters namely binding affinity. The result showed binding affinity from saponin with S1 protein has the lowest value (-8.0), van der Waals, while the other two (Flavonoid and Alkaloid) have binding affinity higher namely -6.7 and 6.2 respectively. Those three ligands were interacting with AA located on 886, 1031 and 1036. In conclusion, secondary metabolites could be intrusive for viral particles to interact with ACE2 in human lung. This study revealed that secondary metabolite from Swietenia mahagony has potential as medication for Covid-19-infected patients.

**Keywords:** Sars-Cov2; ACE2; Docking; Binding Affinity

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## 1. Introduction

SARS-CoV-2 2019 (COVID-19) is currently one of the crucial problems facing the world today. The latest data as of July 1, 2021, reported by WHO shows the number of cases of the spread of COVID-19 to date has reached 248 million people while the number of patients who died is 5.02 million. Coronavirus particles contain four main structural proteins, namely S protein (spike protein) which is shaped like a spike, M protein (membrane protein), E protein (envelope protein), and N protein (nucleocapsid protein) [1]. Protein S (spike protein) is the outermost protein of COVID-19 which functions to infect host cells with the very fast transmission. In addition to functioning to infect cells, protein S (spike protein), mRNA is used as the strongest candidate to be used as a vaccine [2]. The main components of spike protein are S1 and S2 proteins. The main function of the S1 protein is to bind to the host cell. The binding of the S1 protein to the host cell receptor triggers the fusion of the viral membrane to the host cell membrane. COVID-19 uses protein S to enter host cells. When the S protein enters the host cell, it attaches to the ACE-2 (Angiotensin-converting enzyme-2) receptor [3].

The potential for secondary metabolic substances from medicinal plants as drugs to overcome the problem of body immunity against the spread of COVID-19 is very large. Secondary metabolites of flavonoids, alkaloids, and saponins can suppress the spread of COVID-19. This is reinforced by research from [4]; [5]; [6]; [7], that secondary metabolites have antiviral activity for HIV, Herpes, and Hepatitis B/C and can increase immunostimulants that are predicted to be able to prevent infection with the SARS-CoV-2 virus.

Mahogany plants (Swietenia mahogany) have flavonoid, alkaloid, and saponin compounds [8]. These flavonoid, acolloid, and saponin compounds are widely found in the mahogany bark, these compounds have physiological and pharmacological effects [9]. The content of antioxidant, anti-

inflammatory, antifungal, antimalarial properties in mahogany (Swietenia mahogany) is useful as an antiviral and immunostimulant which has not been developed, so it needs initial testing in the form of molecular docking.

Flavonoids act as antioxidants by donating hydrogen atoms or through their ability to chelate metals, in the form of glucosides (containing glucose side chains) or in free forms called aglycones [10]. Saponins have various biological properties such as hemolytic ability [11]; [12], antibacterial activity [13]. antimollus [14}. Antiviral activity [15], cytotoxic or anti-cancer activity [16], [17], hypocholesterolemic effect [18] and antiprotozoa.

The use of computers in the discovery of new drugs aims to increase the efficiency of the simulation and calculation processes in drug design (drug design) [19]. The great potential of protein docking applications in predicting compatibility or minimizing infection. We have conducted a research investigation entitled "Covid-19 Spike Protein Interaction with In-silico Mahogany (Swietenia mahogany) Secondary Metabolite Compounds".

## 2. Materials and methods

### *2.1. 3D conformation of RCSB PDB and PubChem*

Design of 3D conformation of RCSB PDB Spike Protein on RCSB website PDB, Flavonoid Compounds, Alkaloids, Saponins on PubChem website. The 3D conformation of RCSB PDB and Pubchem is part of the first step to initiate molecular docking.

The use of the RCSB PDB and PubChem 3D websites aims to determine the conformational shape of the COVID-19 Spike Protein and secondary metabolites of Flavonoids, Alkaloids and Mahogany Saponins in a cartoon configuration.

### *2.2. igand and Receptor Preparation The ligand and receptor*

The preparation was carried out using the AutoDock-Vina software and the Biovia Discovery 2021 client. Making Gridbox in Autodock-Vina software which aims to cover the two molecules to be interacted. Gridbox closure that is done must cover the area of the two molecules so that the ligand and receptor can be interacted and the scale of the interaction is known.

### *2.3. Molecular Docking*

Docking of the ligands is done to find the 3D conformation of the ligand to the receptor by taking into account the coordinates of the center of mass of the structure and the gridbox size of the binding site pocket in angstroms (Å) or number of points. The conformation of the docking results obtained is aligned with the ligand conformation of the crystallographic measurement results expressed in the root mean square deviation (RMSD) value. The smaller the RSMD value, the greater the potential for interaction between the two molecules [20]. After getting the docking score for each combined molecule, the next step is to visualize the results of the docking with the PyMOL application, Biovia Discovery 2021 client and Chimera-1.15 rc.

Prediction of energy in the interaction of the two molecules with the root mean square deviation (RMSD) value provided that the smaller the distance value of the root mean square deviation, the greater the potential for closeness between the two molecules and the formation of complexes between the interacting molecules.

## 3. Results and discussion

### *3.1. Bonding of Ligands Test*

Ligands used in the form of secondary metabolites of flavonoids (11439), alkaloids (102115598) and saponins (158965316) in mahogany (Swietenia mahogany) whose structure was taken from PubChem. From the results, it was docking found that the shown binding affinity of the ligands test as in table 1. The ligand is tethered to the active site of the 6VSB receptor, to determine the anchorage site, the help of the Grid Box is used, namely the algorithm size x = 206.629275, size y = 223.020510, size z = 227.182716. then set the value of the docking step at 200 with 9 repetitions (Ratu et al., 2021). The results of the molecular docking of flavonoid secondary metabolite ligands with spike protein COVID-19 (6VSB) obtained a binding affinity value of -6.7, for ligands of alkaloid secondary metabolites to spike protein receptors, the binding affinity value was -7.2 and ligands for secondary metabolites of saponins obtained value -8.0. According to Saputri, the lower the binding affinity value, the stronger the ligand bond with the tethered receptor [21].

The ligands of alkaloid secondary metabolites are bound to the receptor binding Conventional Hydrogen Bond LYS41, Carbon Hydrogen Bond GLY283, and Pi-Sigma PHE43 bonds. Meanwhile, the ligands for secondary metabolites of saponins from Conventional Hydrogen Bonds GLU1031, GLN1036, and Pi-Sigma TRP886 bonds. The strength of hydrogen bonds in molecules is influenced by their electronegativity with other atoms, hydrogen bonds generally form interactions with dotted lines that are difficult to observe [22]. While the Pi-Sigma bond is two different bonds, the strength of the Pi bond is weaker than the Sigma bond, this is because the hybridization in the Pi bond occurs laterally. This type of hybridization does not cause paired electrons in one hybrid orbital so that the atoms interact more easily with other more electropositive atoms.

### *3.2. Binding Site Analysis*

From the results of the binding site analysis that has been carried out on flavonoid secondary metabolites with amino acid residues of VAL 320, they are able to interact in the Pfam region of instances A, B, and C as well as the region that interacts with instance C with the binding site bCoV_S1_N-terminal, RBD (Receptor Binding Domain). The binding analysis is presented in Table 2. In testing secondary metabolites of flavonoid compounds with amino acid residues of VAL 551, it was found that the interaction results of Pfam, instances A, B, C with the binding site bCoV_S1_C. Then site domain, instance A, B, with binding site BetaCoV_S1_CTD and region, instance A, B with binding site RBD (Receptor Binding Domain). The LYS 41 amino acid residue is able to interact in the Pfam region, instances A, B, C with the bCoV_S1_N-terminal binding site. The region site of the LYS 41 amino acid has a BetaCoV_S1_CTD binding site in instance B. While the LYS 41 amino acid residue only interacts in the region, instance B with the RBD (Receptor Binding Domain) binding site. PHE 43 amino acid residues of interacting alkaloid compounds were found in the Pfam region with instances A, B, C with the binding site bCoV_S1_N-terminal.

The S2 unit in the spike protein are responsible mainly for the fusion of the host cell membrane, S2 contains two heptad repeat regions known as HR-N and HR-C, which form a helical structure by the protein ectodomain. The amino acid GLU 1031 interacts with Pfam instances A, B, C with the binding site CoV_S2, then interacts with the B instance domain site with the BetaCoV_S1_CTD binding site and the A, B, C region instances with the binding site RBD (Receptor Binding Domain).

## 4. Conclusions

The study examined weather any probability of interaction between Spike Protein and Secondary Metabolite of Swietania Mahogany thereby performing in-silico analysis. From all those result explained, we could revealed that there is interaction binding site between both substances. Among all, Spike Protein and saponin appeared to be strongest interaction. We suggested that Swietania Mahogany has potential to be medication of covid-19.

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**Table 1.** Binding Affinity Ligand Results Flavonoid, Alkaloids, Saponins and Spike Protein Ligands With COVID-19 Receptors (6VSB)

| Ligand Compounds | Ligand Compounds |
|---|---|
| Flavonoid | -6.7 |
| Alkaloid | -7.2 |
| Saponin | -8.0 |
| Ligan Spike Protein | -5.8 |

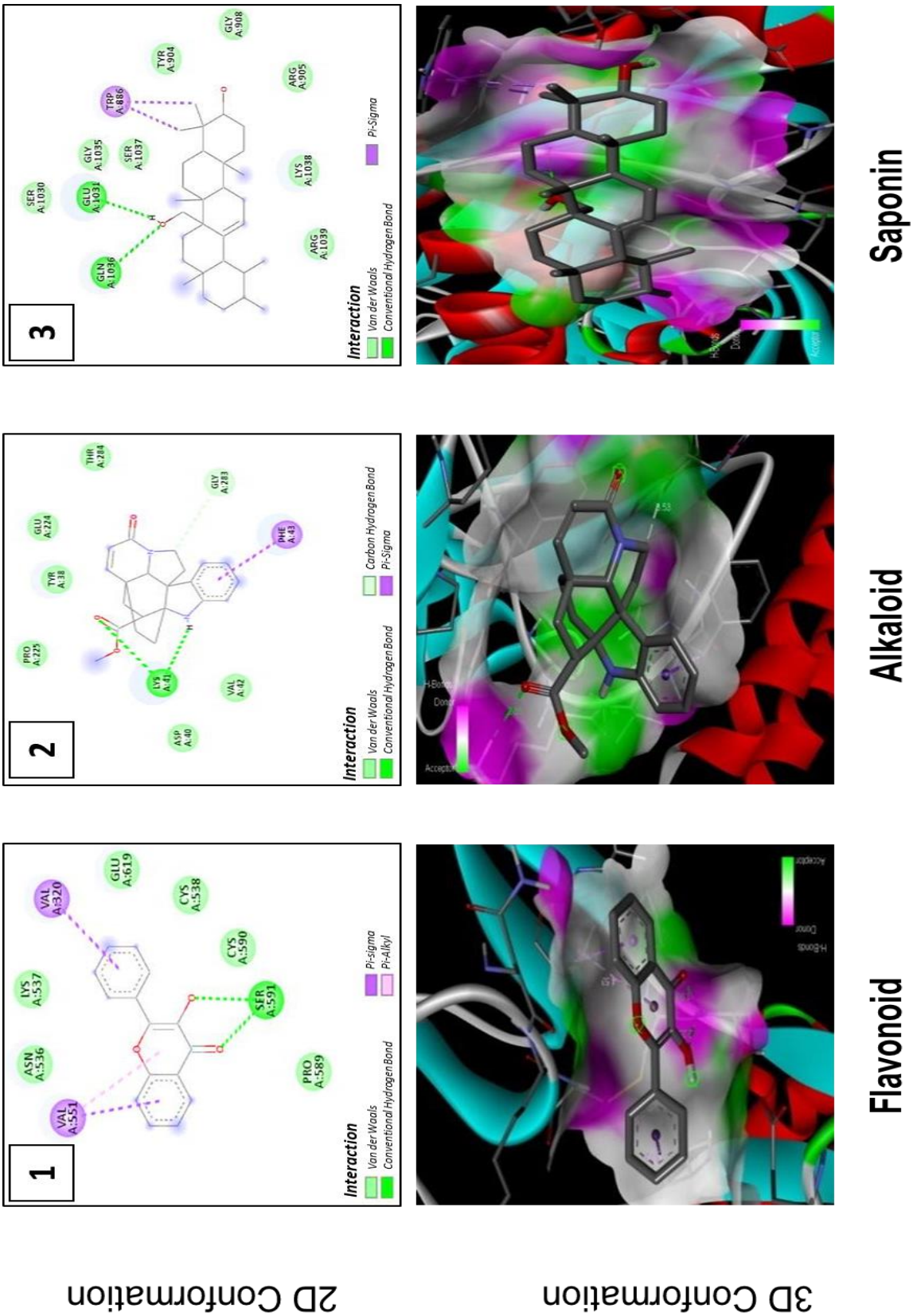


**Figure 1.** Molecular docking visualization of Receptor to Ligand on 3D and 2D

**Table 2.** Binding Site Analysis

| Metabolit Sekunder | Residu Interkasi | Region | Varian | | | Binding Site |
|---|---|---|---|---|---|---|
| | | | A | B | C | |
| | | Bond Outlier | - | - | - | - |
| | | Pfam | √ | √ | √ | bCoV_S1_N |
| | VAL 320 | Glycostation | - | - | - | - |
| | | Site Domain | - | - | - | - |
| | | Region | - | - | √ | RBD |
| | | Bond Outlier | - | - | - | - |
| | | Pfam | √ | √ | √ | bCoV_S1_C |
| Flavonoid | VAL 551 | Glycostation | - | - | - | - |
| | | Site Domain | √ | √ | - | BetaCoV_S1_CTD |
| | | Region | √ | √ | - | RBD |
| | | Bond Outlier | - | - | - | - |
| | | Pfam | √ | √ | √ | bCoV_S1_C |
| | SER 591 | Glycostation | - | - | - | - |
| | | Site Domain | - | - | - | - |
| | | Region | - | - | - | - |
| | | Bond Outlier | - | - | | - |
| | | Pfam | √ | √ | √ | bCoV_S1_N |
| | TYR 38 | Glycostation | - | - | - | - |
| | | Site Domain | - | - | - | - |
| | | Region | - | - | - | - |
| | | Bond Outlier | - | - | - | - |
| | | Pfam | √ | √ | √ | bCoV_S1_N |
| Alkaloid | LYS 41 | Glycostation | - | - | - | - |
| | | Site Domain | - | √ | - | BetaCoV_S1_CTD |
| | | Region | - | √ | - | RBD |
| | | Bond Outlier | - | - | - | |
| | | Pfam | √ | √ | √ | bCoV_S1_N |
| | PHE 43 | Glycostation | - | - | - | - |
| | | Site Domain | - | - | - | - |
| | | Region | - | - | - | - |
| | | Bond Outlier | - | - | - | - |
| | | Pfam | √ | √ | √ | CoV_S2 |
| | TRP 886 | Glycostation | - | - | - | - |
| | | Site Domain | - | - | - | - |
| | | Region | - | - | √ | RBD |
| | | Bond Outlier | - | - | - | - |
| | | Pfam | √ | √ | √ | CoV_S2 |
| Saponin | GLU 1031 | Glycostation | - | - | - | - |
| | | Site Domain | - | √ | - | BetaCoV_S1_CTD |
| | | Region | √ | √ | - | RBD |
| | | Bond Outlier | - | - | - | - |
| | | Pfam | √ | √ | √ | CoV_S2 |

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