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Targeting Circumsporozoite Protein of Malaria with Norcaesalpinin E From Caesalpinia Crista: an in Silico Study for Antimalaria Herbal

Nur Pratiwi, Aryadi Arsyad and Ika Yustisia

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Targeting Circumsporozoite Protein of Malaria with Norcaesalpinin E From *Caesalpinia crista*: an *in silico* study for Antimalaria Herbal

Pratiwi A N, Arsyad A, Yustisia I dan Sulfahri
Biomedical Sciences, Graduate School, Hasanuddin University, Makassar, Indonesia
Department of Biology, Faculty of Mathematics and Natural Sciences, Hasanuddin University, Makassar, Indonesia

Email: anurpratiwi@gmail.com

Abstract. Malaria is a parasitic sickness that is commonly found in developing countries and tropical climates such as Indonesia. The pint of the study was to decide the bioactivity of Norcaesalpinin E from Caesalpinia crista for antimalarials based on a switch docking studies. Circumsporozoite protein in Plasmodium falciparum is one of the new targets of antimalarial drugs being developed. In this study, molecular docking analysis was carried out to describe the interaction of Norcaesalpinin E with circumsporozoite protein using PyRx 0.8 programming. Prediction and significant descriptor of Physicochemical Properties, Lipophilicity, Pharmacokinetics and Druglikeness properties of compounds were predicted using Swissadme. The results showed that the Norcaesalpinin E compound in Caesalpinia crista had potential as an antimalarial based on its binding affinity and intermolecular interactions. The binding affinity of Norcaesalpinin E with Circumsporozoite Protein is -7.6, while the binding affinity of Circumsporozoite Protein with the control compound Quinine Sulphate is -7.1. The druglikeness prediction shows that Norcaesalpinin E meets Lipinski, Ghose, Veber, Egan and Muegge rules with 0.55 Bioavailability score.

1. Introduction

Malaria is the maximum crucial parasitic infectious disorder withinside the world. It is predicted that there had been 229 million instances of malaria in 2019 with a death toll from malaria of 409,000 (WHO, 2021). Indonesia holds the second-highest-ranking (after India) in Southeast Asia for the best range of malaria instances, primarily based totally on the WHO document withinside the World Malaria Report 2020 (Kemenkes, 2021). In 2010 fantastic instances of malaria reached 465.700 with 65% of endemic districts in which most effective 45% of the populace withinside the district became susceptible to contracting malaria (Kemenkes RI, 2013). Meanwhile, in 2020 there had been 235.700 malaria instances in Indonesia (Kemenkes, 2021). Malaria is an infectious disorder because of a protozoan of the genus *Plasmodium sp* that is transmitted to people via the chunk of an Anopheles mosquito (Prakash, 2010).

Indonesia as the tropical country has excessive organic wealth. Indonesian human beings are acquainted with the use of natural flowers in treating diseases, especially malaria. One of the natural flowers to be an

opportunity medication for malaria is a fried plant with the clinical call *Caesalpinia crista* (Kaloni et al., 2006). Use *Caesalpinia crista* as a natural medication through boiling all elements of the plant (each fruit, stems, leaves) Method after which ingesting boiled water (Mufidah & Zuhrotun, 2020). One compound remoted from seed extract *Caesalpinia crista* and might have an antimalarial hobby is Norcaesalpinin E (Linn et al, 2005).

2. Materials and Method

2.1. Ligands Preparation

The chemical compound shape of *Caesalpinia crista* (Norcaesalpinins E) became accumulated from the posted literature. Chemical 3-d systems and SMILES ligands (Norcaesalpinins E) had been retrieved from the PubChem compound database (https://pubchem.ncbi.nlm.nih.gov/compound/11773291) with ID range: CID 11773291 with Canonical SMILES CC(=O)OC1CCC(C2(C1(C3CC4=C(C=CO4)C(=O)C3C(C2)O)C)O)(C)C. Structure two-dimensional (2D) and three-dimensional (3-d) ligand chemistry had been sketched with the use of Avogadro and Discovery Studio and stored in PDB format.

2.2. Target Selection

The goal protein candidate makes use of the 2018 Indonesian Biology magazine reference, entitled "Anotasi Domain Protin *Plasmodium sp.* Circumsporozoite Protein menggunakan Perangkat *Hidden Markov Model*". Furthermore, the goal protein became tested with the use of Uniport (https://www.uniprot.org). Protein became tested with PDB (Protein Data Bank https://www.rcsb.org/pdb) and proteins had been organized through cleansing water molecules from the shape. Water molecules and ligands had been eliminated by the use of PyMOL v2.5.2 Software. In this have a look at, the goal protein used became Circumsporozoute Protein (CSP) with the code 6AZM from PDB, due to the fact CSP is a crucial protein of *Plasmodium sp*. which paperwork a dense layer at the floor of the parasite.

2.3. Molecular Docking

Molecular docking experiments had been done with the use of PyRx 0.8 software program. Docking evaluation became done the use of the Vina Wizard function incorporated into the PyRx 0.8 software program which reacts to the herbal compound Norcaesalpinins E, CSP goal protein, and the control compound (Antimalarial Drugs). The control compound may be positive control withinside the docking process. The control compound became Quinine Sulfate. Quinine Sulphate is an antimalarial drug endorsed through the Indonesian Ministry of Health (Kemenkes RI, 2013).

2.4. Visualization of Molecule and Small Molecule Interaction

The interactions among the ligand (Norcaesalpinins E), goal protein (CSP), and control ligand (Quinine Sulfate) had been visualized and analyzed with the use of PyMol v2.5.2 software program.

2.5. Compound's Properties and ADMET Predictions

Swissadme (http://www.swissadme.ch) and admetSAR (HTTP:// lmmd.ecust.edu.cn) became used to expect predictions and significant descriptors of Physicochemical Properties, Lipophilicity, Pharmacokinetics and Druglikeness homes of the compounds.

3. Results and Discussion

Herbal plant called antimalarials are Gorek plant with clinical names *Caesalpinia crista*. One of the compounds located in *Caesalpinia crista* is Norcaesalpinin E (Mufidah & Zuhrotun, 2020). Norcaesalpinin E is understood to have an antimalarial activity (Linn et al, 2005). In addition, the outcomes of the seed extract. *C.crista* confirmed significant inhibition of malaria parasite increase *Plasmodium sp* (Kant Kaloni et al., 2006). The shape of herbal compounds with control compounds and goal proteins became visualized in three dimensions (3D) by the use of PyMol (Figure 1). Through the opposite docking technique, the capability of Norcaesalpinin E may be recognized as an antimalarial. The interplay of Norcaesalpinin E with CSP became as compared with Quinine Sulfate as a control compound. Based on the docking outcomes, the binding affinity of CSP to Norcaesalpinin E became decrease than that of CSP with Quinine Sulfate.

The range of binding affinities describes the capability of a compound or ligand to have interaction with its protein (goal protein). The binding affinity of Norcaesalpinin with CSP became -7.6, even as the binding affinity of CSP with control compound Quinine Sulphate became -7.1. This shows that Norcaesalpinin E is stronger in inheriting the goal protein than Quinine Sulfate. Norcaesalpinin E can have interaction higher with CSP than Quinine Sulfate.

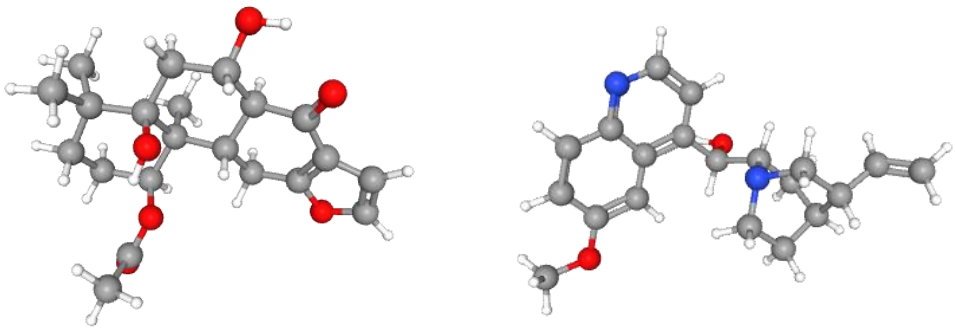

Figure 1. (a) Struktur 3D Kimia Norcaesalpinin E dan (b) Quinine Sulphate were showed *Software* PyMol

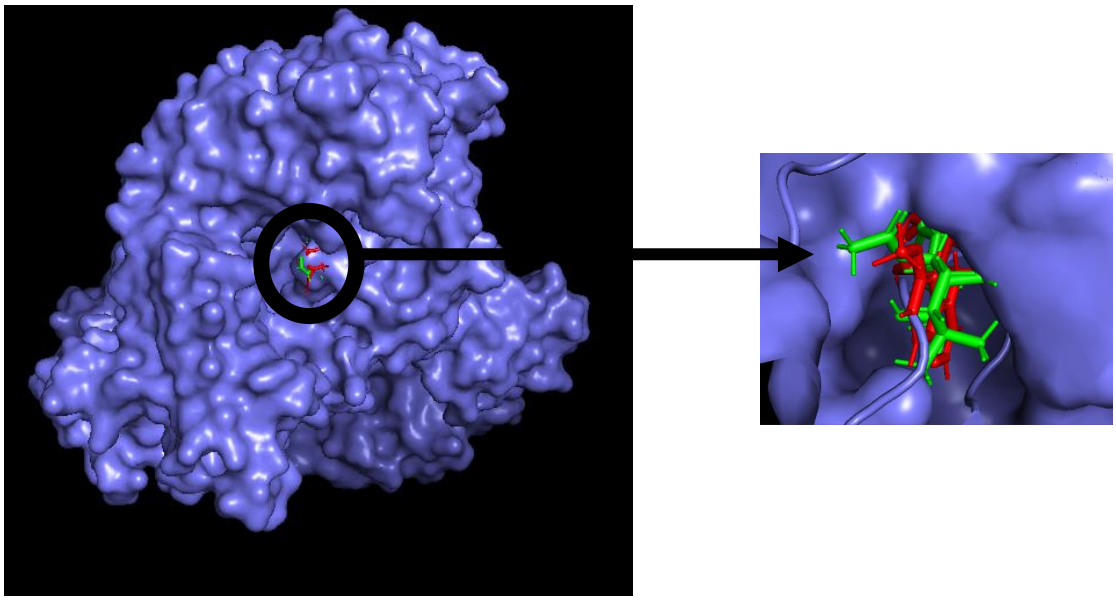

Figure 2. Binding Site of Norcaesalpinin E (Green), Quinine Sulphate (Red) with CSP (blue)

Tabel 1. The result of Reverse Docking CSP with ligand and control ligand

Ligand	Binding Affinity
CSP and Norcaesalpinin E	-7,6
CSP and Quinine Sulfate	-7,1

Most capsules are supposed to deal with the disorder. So the attention of a drug ought to be consistent. The facet results of Norcaesalpinin E compounds at the frame were located through ADMET predictions evaluated and related to molecular permeation, metabolism process, and bioavailability. As found out through the outcomes of this have a look at (AMES Test), the outcomes display that Norcaesalpinin E is neither a capability mutagen and carcinogen. Plant ligands can go into molecular membranes and be absorbed through the frame due to the fact they agree to Lipinski's guidelines. The seek outcomes confirmed that Norcaesalpinin E met the guidelines of Lipinski, Ghose, Veber, Egan, and Muegge with a Bioavailability Score of 0.55. Meanwhile, the control ligand, Quinine Sulfate, no longer met Lipinski, Gose, Veber, Egan, and Muegge guidelines with a Bioavailability Score of 0.17.

4. Conclusion

This has a look at proved that Norcaesalpinin E is an antimalarial primarily based totally on its binding affinity with -7.6 and intermolecular interactions. *Caesalpinia crista* containing Norcaesalpinin E is a natural medication in keeping with the guidelines of Lipinski, Ghose, Veber, Egan, and Muegge with a Bioavailability Score of 0.55. But it is higher to consume *Caesalpinia crista* withinside the shape of simplicia to keep away from overreaction withinside the frame if most effective eating plant extracts.

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