ABSTRACT

Fatimah Usfatina. 24020121120030. In Silico Study of the Antihypercholesterolemic Activity of Black Rice (*Oryza sativa* L. var. *indica*) Anthocyanins as Inhibitors of the NPC1L1 Protein. Under the guidance of Sunarno and Rasyidah Fauzia Ahmar.

Hypercholesterolemia is a disorder characterized by an increased level of total cholesterol in the blood. One of the key proteins involved in lipid metabolism is Niemann-Pick C1-Like 1 (NPC1L1), which functions in cholesterol absorption in the small intestine. Inhibition of NPC1L1 activity was reported shown to reduce blood cholesterol levels. Black rice (*Oryza sativa* L. var. *indica*) contains anthocyanin bioactive compounds known to possess various pharmacological activities, including antihypercholesterolemic effects. However, studies investigating the potential of black rice anthocyanins as NPC1L1 inhibitors through in silico approaches remain limited. This study aimed to analyze the inhibitory potential of antihypercholesterolemic bioactive compounds from the anthocyanin group of black rice as inhibitors of the NPC1L1 protein using an in silico approach. The methods used included the prediction of physicochemical properties, pharmacokinetic profiles (ADME), and toxicity of six anthocyanin test ligands (cyanidin-3-O-glucoside, delphinidin-3-O-glucoside, malvidin-3-O-glucoside, pelargonidin-3-O-glucoside, peonidin-3-O-glucoside, and petunidin-3-O-glucoside) and a control ligand (ezetimibe), as well as molecular docking between the six anthocyanin test ligands and the control ligand against the NPC1L1 target protein to obtain binding energy affinity and RMSD values for each tested ligand–protein complex. The results showed that all six anthocyanin test ligands exhibited strong binding affinity toward the NPC1L1 protein, with the highest binding affinity observed for pelargonidin-3-O-glucoside at -7.69 kcal/mol. Physicochemical predictions indicated that all six anthocyanin compounds had low bioavailability; however, they were considered relatively safe due to favorable ADME predictions and relatively low toxicity. Based on these findings, it was concluded that pelargonidin-3-O-glucoside had potential as an antihypercholesterolemic drug candidate and could be used as an inhibitor of NPC1L1 protein activity.

***Keywords**: Hypercholesterolemia, cholesterol, molecular docking, ezetimibe*