CHAPTER I INTRODUCTION

1.1 Background

Cholesterol is one of the main fat components needed by the body. The substance is synthesized in the liver. In the blood, the cholesterol content of 70% is derived from the synthesis in the liver, while the remaining 30% comes from food consumed (Naim *et al*., 2019). Based on the type of cholesterol is classified into 2, namely low-density lipoprotein (LDL) and high-density lipoprotein (HDL). LDL is the bad cholesterol that can form plaque of cholesterol on the walls of the blood vessels that causes constriction of blood vessels. HDL is one type of cholesterol that has benefits for the body because it can remove bad cholesterol from the vascular endothelium into the digestive tract, so there is no accumulation of cholesterol in the vascular endothelium (Rafsanjani *et al*., 2019).

Hypercholesterolemia is a condition characterized by very high cholesterol levels in the blood (Nevenka and Milev, 2016). The causes of hypercholesterolemia are unhealthy lifestyle, obesity, diabetes, and excessive consumption of a high-fat diet (Hill & Bruno, 2021). In patients with hypercholesterolemia, no clinical symptoms are found, because hypercholesterolemia can only be known by the sufferer through the results of a cholesterol test.

One of the important organs in the body that functions to filter and remove waste substances from the body's metabolism is the kidney (Kurniawati and Adhiyanti, 2018). Impaired kidney function can cause interference with fluid and electrolyte balance in the

body. The causes of impaired kidney function are diabetes, obesity, hypertension, and an unhealthy lifestyle. In animals, impaired kidney function is often occurs in cats and dogs, especially in older animals (Bartges, 2012). Disorders of kidney function can be detected by examining creatinine levels and blood urea nitrogen (BUN) levels.

Creatinine, uric acid, and urea are metabolic products that must be excreted by the body through the kidneys (Gounden *et al*., 2021). If BUN and creatinine are both increased and followed by a decrease in GFR, it is a sign that there is a disturbance in kidney function (Barsanti, 2012).

In this modern era, the development of science, especially in the field of medicine, is growing rapidly. People's knowledge about health is also increasingly widespread, especially in the field of medicine. People are starting to realize the negative effects of chemical drugs, and therefore researchers attempt to make drugs derived from natural materials.

One of the fruits that are often consumed by people and are a medicinal plant is dragon fruit (*Hylocereus sp*). According to Hernawati *et al*. (2018), there are three types of dragon fruit that are generally consumed, namely red dragon fruit (*Hylocereus polyrhizus*), white dragon fruit (*Hylocereus undatus*), and yellow dragon fruit (*Hylocereus megalanthus*). Red dragon fruit has high moisture content and is rich in calcium, fiber, phosphorus, and vitamin C (Hernawati *et al*., 2018). Red dragon fruit is known to contain betacyanin, vitamin B3 (niacin), vitamin C, and fiber (Prakoso *et al*., 2017). In addition to

red dragon fruit flesh which has many benefits, red dragon fruit peels is known to contain saponins, flavonoids, alkaloids, and steroids (Noor *et al*., 2016).

Based on the background above, it is necessary to do research on the effect of red dragon fruit (*Hylocereus polyrhizus*) peels extract on the levels of blood urea nitrogen and creatinine in white rats with hypercholesterolemia.

1.2 Problem Statement

Based on the background above, the problem statement of my research are :

1. Can the extract of red dragon fruit (*Hylocereus polyrhizus*) peels reduce the blood urea nitrogen levels in white rat (*Rattus norvegicus*) hypercholesterolemia?.
2. Can the extract of red dragon fruit (*Hylocereus polyrhizus*) peels reduce the creatinine levels in white rat (*Rattus norvegicus*) hypercholesterolemia?.

1.3 Research Purpose

1.3.1 General purpose

The general purpose of this research is :

To discover the potential of the red dragon fruit (*Hylocereus polyrhizus*) peels extract as a medicinal plant in assisting the healing process of hypercholesterolemia white rats (*Rattus norvegicus*) and impaired kidney.

1.3.2 Special Purpose

The special purpose of this research are :

1. To discover the potential of the red dragon fruit (*Hylocereus polyrhizus*) peels extract in lowering the levels of blood urea nitrogen (BUN) towards the healing process of hypercholesterolemia white rats (*Rattus norvegicus*).
2. To discover the potential of the red dragon fruit (*Hylocereus polyrhizus*) peels extract in lowering the levels of creatinine towards the healing process of hypercholesterolemia white rats (*Rattus norvegicus*).

1.4 Research Benefits

1.4.1 Theoretical Benefit

The theoretical benefit is to provide information regarding the potential use of the red dragon fruit (*Hylocereus polyrhizus*) peels extract in helping the healing process of hypercholesterolemia white rats (*Rattus norvegicus*) as well as to provide data for future research purposes.

1.4.2 Practical Benefit

The results of this research is expected to provide alternative therapies derived from natural ingredients which can help the healing process of hypercholesterolemia and impaired kidney.

1.5 Theoretical Base

Cholesterol is an essential substance that has physical properties such as fat and has a steroid group (Anggraini and Lily, 2018). That substance has an important role in the formation of hormones, vitamin D, and bile salts. Lipoproteins are particles that transport cholesterol in the blood. Cholesterol is classified into two types, namely high-density lipoprotein (HDL) and low-density lipoprotein (LDL). Changes in the levels of high-density lipoprotein (HDL), low-density lipoprotein (LDL), and total cholesterol can be used as a sign that there has been impaired function of organs in the body. One of the organs that experience impaired function due to changes in cholesterol levels in the blood is the kidney. In patients with chronic kidney disease, lipid fraction abnormalities occur in the form of an increase in LDL levels and a decrease in HDL levels (Ahmad *et al*., 2018).

The condition where the plasma cholesterol levels are high and followed by an increase of low-density lipoprotein (LDL) is called hypercholesterolemia or dyslipidemia (Martinez-Hervaz & Juan, 2019). The occurrence of hypercholesterolemia can potentially accelerate the decrease in kidney function. In this condition the increased levels of low-density lipoprotein (LDL) and triglycerides, as well as decreased levels of high-density lipoprotein (HDL) commonly experienced by patients with chronic kidney failure (Senge *et al*., 2017). The mechanism of decreased kidney function due to hypercholesterolemia is through reabsorption of phospholipids, fatty acids, and cholesterol followed by accumulation of lipoproteins in the glomerular mesangium (Ahmad *et al*., 2018).

A study conducted by Bhagaskara *et al*., (2015) stated that statistically there was a strong correlation between LDL cholesterol levels with urea and creatinine levels. However, in this study, there was no correlation between HDL cholesterol levels with urea and creatinine levels. Another study conducted by Yang *et al*., (2020) showed that in patients with chronic kidney disease there was an increase in LDL cholesterol levels followed by an increase in serum creatinine and urea levels. The study also explained that patients with chronic kidney disease reported having lower or higher LDL cholesterol levels. High LDL cholesterol levels have a greater potential to cause atherosclerosis (Yang *et al*., 2020).

A study by Kaur et al., 2021 stated that the correlation between hypercholesterolemia and the increase of BUN and sCr was seen in activation of the renin-angiotensin system, glomerular hyperfiltration, and structural changes in the kidneys associated with prolonged obesity. Kaur et al. also stated that binding and trapping lipids by extracellular matrix (ECM) molecules would lead to the accumulation of ROS, such as superoxide anions and hydrogen peroxide. An increase in ROS levels followed by a decrease in antioxidant enzyme activity will cause cellular antioxidant defences in the rat kidney not to work efficiently (Kaur et al., 2021).

Dragon fruit (*Hylocereus sp*) is one of the tropical plants that provide financial benefits for farmers in Indonesia. Dragon fruit is also known to have many benefits for the body. There are three types of dragon fruit, namely white dragon fruit (*Hylocereus undatus*), red dragon fruit (*Hylocereus polyrhizus*), and yellow dragon fruit (*Hylocereus megalanthus*) (Hernawati *et al*., 2018; Hoa *et al*., 2006; Nerd *et al*., 2002). Red dragon

fruit (*Hylocereus polyrhizus*) has better nutritional content than other types of dragon fruit because, red dragon fruit (*Hylocereus polyrhizus*) contains higher levels of vitamin C, vitamin B3, and betacyanin (Prakoso *et al*., 2017). The red dragon fruit (*Hylocereus polyrhizus*) peel content includes vitamin C, vitamin E, vitamin A, flavonoids, and polyphenols (Kongkham *et al*., 2013). In addition, the peels of red dragon fruit (*Hylocereus polyrhizus*) can be used as a medicinal plant because it contains pectin, betacyanin, and fiber (Irmayanti and Marta, 2016).

Antioxidant compounds such as flavonoids, phenols, and anthocyanins, can prevent the oxidation of LDL in the blood (Irmayanti & Marta, 2016). This causes a decrease in cholesterol absorption so that cholesterol levels in the blood decrease (Heryani, 2016).

Many studies have proved that the red dragon fruit (*Hylocereus polyrhizus*) can lower cholesterol levels in the blood. A study conducted by Irmayanti *et al*., (2016) stated that the administration of red dragon fruit peel extract could significantly reduce LDL cholesterol levels in rats with hypercholesterolemia. In this study, it was explained that phenolic compounds can affect LDL cholesterol levels so that LDL cholesterol levels are reduced.

A study conducted by Sahin *et al*. (2021) proved that the extract of red dragon fruit (*Hylocereus polyrhizus*) peels could lower creatinine serum and BUN. They also mentioned that antioxidants such as polyphenols and flavonoids could scavenge alkyl and hydroxyl radicals. Another research conducted by Jun *et al*. (2012) stated that antioxidant therapy using vitamins A, C, E, beta carotene, and N-acetylcysteine could reduce serum

creatinine levels and improve kidney function. In this context, flavonoid, polyphenol, and anthocyanin demonstrate protective effects through increased endothelium relaxation via ROS production inhibition.

1.6 Hypothesis

According to the formulation of the problem and the theoretical base of the research above, the hypothesis of this research are:

1. The extract of the red dragon fruit (*Hylocereus polyrhizus*) peels can reduce the levels of blood urea nitrogen (BUN) in white rats (*Rattus norvegicus*) hypercholesterolemia.
2. The extract of the red dragon fruit (*Hylocereus polyrhizus*) peels can reduce the levels of creatinine in white rats (*Rattus norvegicus*) hypercholesterolemia.