THESIS

THE EFFECT OF RED DRAGON FRUIT (*Hylocereus polyrhizus*) PEELS EXTRACT ON BLOOD UREA NITROGEN AND CREATININE LEVELS IN HYPERCHOLESTEROLEMIA WHITE RATS (*Rattus norvegicus*)

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DECLARATION

Hereby, I declare that in the thesis entitled:

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There is no other work ever published to obtain bachelor degree in any other universities before and as I have ever known that there are no papers or opinions which have been written or published by somebody else, besides the writing which is referre in this paper and mentioned in the references.

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SUMMARY

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. Hypercholesterolemia is a condition characterized by very high cholesterol levels in the blood and caused by unhealthy lifestyle, obesity, diabetes, and excessive consumption of a high-fat diet. One of the important organs in the body that functions to filter and remove waste substances from the body's metabolism is the kidney. 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. 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. Red dragon fruit has high moisture content and is rich in calcium, fiber, phosphorus, betacyanin, vitamin B3 (niacin), vitamin C, and fiber. In addition to red dragon fruit flesh which has many benefits, red dragon fruit peels is known to contain saponins, flavonoids, alkaloids, and steroids. A study conducted by Sahin *et al*. (2021) proved that the extract of red dragon fruit (*Hylocereus polyrhizus*) could lower creatinine serum and BUN levels also they mentioned that antioxidants such as polyphenols and flavonoids could scavenge alkyl and hydroxyl radicals. Flavonoids and phenolic acid are a group of secondary metabolites produced by plants that are included in the large group of polyphenols. Flavonoids can

capture ROS/ RNS, suppress the formation of ROS/ RNS by inhibiting several enzymes involved in the production of free radicals, and regulate antioxidant defense. It is known, that high-fat diet could significantly increase BUN and serum creatinine levels and promote renal injury by inducing oxidative stress and mitochondrial dysfunction. Oxidative stress can also inhibit blood circulation due to vascular smooth muscle cell contraction and improper functioning of endothelial NO synthase, resulting in a decrease in GFR levels. Oxidative stress can affect all aspects of the kidney, including vascular reactivity and renal hemodynamics, glomerular filtration, and tubular reabsorption and secretion in all nephron segments

This study aims to examine the effect of red dragon fruit (*Hylocereus polyrhizus*) peels extract on blood urea nitrogen and creatinine levels in hypercholesterolemia white rats (*Rattus norvegicus*). Twenty white rats were induced with a high-fat diet made from a mixture of boiled duck egg yolk (1 gr) and lard (3 ml) via oral gavage for 14 days. On day 15th, 20 rats that had been induced with a high-fat diet were divided into five groups which were T0 (Rats with hypercholesterolemia treated with CMC-Na1% via oral gavage), T1 (Rats with hypercholesterolemia treated with simvastatin 0.013 mg via oral gavage), T2 (Rats with hypercholesterolemia treated with red dragon fruit (*Hylocereus polyrhizus*) peels extract of 100 mg dosage via oral gavage), T3 (Rats with hypercholesterolemia treated with red dragon fruit (*Hylocereus polyrhizus*) peels extract of 150 mg dosage via oral gavage), and T4 (Rats with hypercholesterolemia treated with red dragon fruit (*Hylocereus polyrhizus*) peels extract of 200 mg dosage via oral gavage). All groups were treated for 14 days, from day 15th to day 28th. On the 29th day, all groups

were given ketamine (90 mg/kg BW) and xylazine (10 mg/kg BW) intraperitoneally in order to take the blood samples through intracardiac, which then proceeded to make blood serum and examined.

The examination of blood urea nitrogen (BUN) and creatinine levels in hypercholesterolemic white rats induced by a high-fat diet in the negative control group showed an increase in BUN and creatinine levels. The positive control group showed no significant effect on BUN and creatinine levels. Based on this study, administration of red dragon fruit extract at doses of 100, 150, and 200 mg/kg BW can reduce creatinine and BUN levels. Based on the Duncan test, the best dose of red dragon fruit peels extract to reduce levels of BUN or creatinine is 200 mg/kg BW. It can be concluded that the extract of red dragon fruit (*Hylocereus polyrhizus*) peels extract could reduce the blood urea nitrogen and creatinine levels in white rats (*Rattus norvegicus*) hypercholesterolemia.

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Fitriana Putri Anwar

ABSTRACT

This research was conducted to discover the potential of the red dragon fruit (*Hylocereus polyrhizus*) peels extract in lowering the levels of blood urea nitrogen (BUN) and creatinine towards the healing process of hypercholesterolemia induced by high fat diet in white rats (*Rattus norvegicus*). High fat diet made from a mixture of boiled duck egg yolk (1 gr) and lard (3 ml) and administered via oral gavage for 14 days. Twenty male hypercholesterolemia white rats were divided into five groups and were administered via oral gavage with different treatments for 14 days. The groups consisted of C- (CMC Na 1% + aquadest), C+ (Simvastatin 0.013 mg/200 g BW), T1, T2, and T3 (100, 150, 200 mg/kg BW of red dragon fruit peels extract respectively). The results of the blood serum examination were carried out at the Laboratorium Klinik Hewan Sehat Indonesia Malang using chemical analyzer. Then, the data were analyzed using Duncan Test. The result of statistical analysis showed significant difference ($p<0.05$) between treatment groups for creatinine and BUN levels. This research showed that red dragon fruit peels extract could reduce BUN and creatinine levels in the blood in hypercholesterolemia white male rats (*Rattus norvegicus*). The effective dose of red dragon fruit peels extract on this research was 200 mg/kg BW.

Keywords : *Hylocereus polyrhizus*, High Fat Diet, Blood Urea Nitrogen, Creatinine, *Rattus norvegicus*

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Author

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SYMBOLS AND ABBREVIATIONS

ADH	: Antidiuretic Hormone
AKI	: Acute Kidney Injury
ANOVA	: *Analysis of Variance*
BUN	: Blood Urea Nitrogen
CKD	: Chronic Kidney Disease
cm	: Centimeter
CoA	: Coenzyme A
CO2	: Carbon dioxide
dL	: Deciliter
EPO	: Erythropoietin
Et al.	: *et alli*
GFR	: Glomerular Filtration Rate
G	: Gram

HDL	: High-Density Lipoprotein
HMG-CoA	: 3-Hydroxy-3-methylglutaryl-Coenzyme A
Kg	: Kilogram
L	: Liter
LDL	: Low-Density Lipoprotein
MDA	: Malondialdehyde
mg	: Milligram
mL	: Milliliter
mol	: Mole
RDF	: Red Dragon Fruit
ROS	: Reactive Oxygen Species
sCr	: Serum Creatinine
SPSS	: Statistical Package for the Social Sciences
ß$_2$	: beta-2