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EFFECTIVENESS OF WHITE GUAVA LEAVES (*PSIDIUM GUAJAVA VAR. PYRIFERA L.*) IN REPAIR PROXIMAL TUBULE DAMAGE AND GLOMERULUS DIAMETER IN HYPERGLYCEMIC MICE

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ABSTRACT

Diabetes Mellitus (DM) is a global health problem with a high prevalence rate in Indonesia, ranking 5th out of 10 countries with the highest number of diabetes cases. In 2019, Indonesia had the highest prevalence rate of diabetes mellitus at 9.3% (463 million) and an estimated increase to 12.2% (783 million) by 2045. The kidney, the primary organ affected by high glucose levels, is the primary organ affected by a compound. Guava leaves, which contain alkaloids, flavonoids, saponins, polyphenols, tannins, and calcium, have been found to have anti-diabetic properties. This research aimed to investigate the effect of variations in the number of white guava leaves used in making waters tew on kidney histopathology in alloxan-induced mice (Mus musculus). The mice were divided into five groups, with initial blood glucose levels measured after being induced by alloxan and after treatment with white guava seeds. After treatment, kidney histopathological preparations were made using Hematoxylin Eosin (HE) staining. The results showed that the average size of the proximal tubule proximal and glomerular diameter was larger than the positive (+) control group. The average glomerular diameter at K0, P1, P2, and P3 was smaller than the positive (+) control. The results of the study suggest that boiled water from white guava leaves may have potential therapeutic benefits for diabetics.

I. INTRODUCTION

Diabetes mellitus (DM) is a non-communicable disease (PTM) that is a global health problem. Patients with diabetes mellitus, from year to year, continue to experience enhancement. According to the International Diabetes Federation (IDF) 2021, Indonesia ranks 5th out of 10 countries with the highest number of diabetes cases, namely by the number of cases at around 19.5 million. The global prevalence rate of people with diabetes mellitus in 2019 was a big 9.3% (463 million) increase over 2021, becoming 10.5% (537 million). It is estimated that it will increase to 12.2% (783 million) by 2045 [1].

Results Research Health Base (Riskesdas) year 2018 shows the prevalence of diabetes mellitus in Indonesia based on doctor's diagnosis population aged 15 years by 2%. This figure shows an increase compared to the prevalence of diabetes mellitus in 2013, which was 1.5% [2]. Based on health profile, Central Java In 2019, people with diabetes mellitus took second place in PTM cases, with a total of 652,822 people with diabetes [3].

Diabetes Mellitus (DM) is a metabolic disease characterized by hyperglycemia (high blood sugar levels) that occurs when the pancreas fails to produce enough insulin or when the body fails to use the insulin that is produced effectively. Insulin is a hormone that regulates blood glucose levels. There are three types of diabetes, namely type 1 diabetes, type 2 diabetes, and gestational diabetes [4,5]

The kidney is the primary organ that is often disturbed by the effects of a compound. Kidneys have their own genre volume of blood, which tall filters toxic substances in the glomerular filtrate and carries them through the cellstubules [6]. High levels of glucose in the blood result from diabetes and make the kidneys filter too much blood. Glucose and high blood pressure can

damage the blood vessels in the kidneys [4]. Rate High glucose is the main cause of structural changes in the kidney. Mesangial cells produce TGF-β1 under hyperglycemia conditions, leading to an increase in consumption and transport, resulting in an excess of GLUT-1 mRNA and protein. These conditions cause metabolic abnormalities in mesangial cells. Impaired kidney function in diabetics is indicated by increasing serum creatinine, acid tendon, and nitrogen blood urea [7].

Use waters Tea leaf guava seed (*Psidium guajava*) can be used as a therapy herb to lower blood sugar in diabetics. According to Rosalina's research (2013), guava leaves can lower blood glucose levels in conditions of hyperglycemia [8]. Leaf guava white seeds (*Psidium guajava var. Pyrifera L.*) proved It has antidiabetic activity and is high in antioxidants. Several active compounds are contained in leaf guava seed white (*Psidium guajava var. Pyrifera L.*) that have anti-diabetic activity, including alkaloids, flavonoids, saponins, polyphenols, tannins, and calcium [8, 9]. The content of these compounds can be found in young leaves of guava seed, which are located on orders of 1–4 from shoots.

Based on research conducted by Darmawan (2021), giving water decoction of guava leaves has the effect of reducing glucose levels in the blood of mice with diabetes. Decline rate of glucose because there is a content compound active in leaf guava seed [10], whereas according to Jaya Chandra Netal's research on the observation of kidney histology in diabetic rats, leaf extract guava seed can reduce necrosis and swelling tubules [8].

Based on the description, researchers want to know how variations in the number of white guava leaves (*Psidium guajava var. Pyrifera L.*), which are used in making water tea, affect the kidney histopathology of alloxan-induced mice (Mus musculus). Research This study uses animal mice (Musmuscle) because their structure, anatomy, physiology, and genetics are similar to humans [11]. Circumstances diabetes in experimental animals is done by inducing alloxan. Alloxan is a material chemistry that is used to induce diabetes. Use alloxan on the test. This is because fasting causes permanent hyperglycemia within 2–3 days [12]. This research is expected to add new information about the effectiveness of giving boiled water from white guava leaves (*Psidium guajava var. Pyrifera L.*) to histopathology kidneys.

II. MATERIALS AND METHODS

This research was carried out experimentally at the Experimental Animal Laboratory, Faculty of Medicine, Diponegoro University (UNDIP) in March 2023 and has passed ethical eligibility from the Semarang Ministry of Health Polytechnic with number 0566/EA/KEPK/2023.

This study used 25 samples of mice (Mus musculus) aged 8–12 weeks and weighing 20–40 grams. The mice used had been adapted and conditioned to hyperglycemia using alloxan (blood sugar level> 120 mg/dL). 25 mice were divided into 5 groups (K0: control group without treatment, K+: control group induced by alloxan). P1: treatment group induced by alloxan and given boiled water of white guava leaves with a 35-gram content; P2: treatment group induced by alloxan and given boiled leaves of white guava with a 45-gram content; and P3: the treatment group was induced by alloxan and given boiled water of white guava leaves with a 55-gram content. Initial blood glucose levels were measured after being induced by alloxan and after treatment with white guava seeds. After the treatment, kidney histopathological preparations were made using hematoxylin and eosin (HE) staining. Observations were made in the area of the proximal tubule and glomerulus with a magnification of 400x.

The data obtained were processed using SPSS version 25.0 to be tested for normality and homogeneity. After that, the One-Way Anova test was carried out with a significance value of 95%, while the data on histopathological changes in the kidneys were presented descriptively.

III. RESULTS AND DISCUSSIONS

This research was conducted using experimental mice (Mus musculus) with a total of 25 mice divided into five groups, namely K0: control group without treatment, K+: alloxan-induced control group. P1: an alloxan-induced treatment group was given boiled white guava leaf water with a concentration of 35 grams; P2: the treatment group was induced by alloxan and given boiled water of white guava leaves with a concentration of 45 grams, and P3: the treatment group was induced by alloxan and given boiled water of white guava leaves with a concentration of 55 grams. Preparations of mice's kidney organs (Mus musculus), which were treated with boiled water from white guava leaves, were then observed for the size of the narrowing tubule proximal and diameter glomerulus obtained results as follows:

Table 1: Mean Results of Proximal Tubule Size and Glomelurus Diameter.

Variable	**Group**					***p-values* (ANOVA)**
	K0 n=5 mean±SD	**K+ n=5 mean±SD**	**P1 n=5 mean±SD**	**P2 n=5 mean±SD**	**P3 n=5 mean±SD**	
Proximal Tubule	16.85±0.54	16.02±0.18	16.24±0.42	16.53±0.77	16.89±0.79	0.120
Shapiro wilk	0.236	0.273	0.866	0.273	0.853	
Levene test	0.134					
Glomelurus diameter	51.15±2.98	55.03±2.60	53.53±3.37	53.28±2.84	52.20±3.55	0.193
Shapiro wilk	0.858	0.337	0.570	0.157	0.163	
Levene test	0.145					

Source: Authors, (2023).

Based on Table 1, it can be seen that the average size of the tubules proximal to the group K0, P1, P2, and P3 was larger compared to the positive (+) control, while the average glomerular diameter at K0, P1, P2, and P3 was smaller than the positive (+) control.

From the results of reading the size of the proximal tubule and glomerulus, we carried out statistical tests using SPSS. Results of the normality test obtained mark significance >0.05 in the proximal tubule and glomerulus, which means the data distribution is normal. Then, using Levene's test, the homogeneity test results obtained on tubular size and glomerular diameter significance >0.05 can be interpreted as homogeneous. Furthermore, a hypothesis test was carried out on the tubules proximal and glomerulus using the analysis of variances (ANOVA). Mark significance obtained in the size of the proximal tubule was 0.120 more than 0.05 (>0.05) and on the glomerular diameter was 0.193 more than 0.05 (>0.05). It can be concluded that there is a difference but not significant in the administration of tew leaf guava seed white (*Psidium guajava var. Pyriferous L.*) to histopathology tubule proximal and glomerulus. Data histologically is also viewed descriptively (Figure 1).

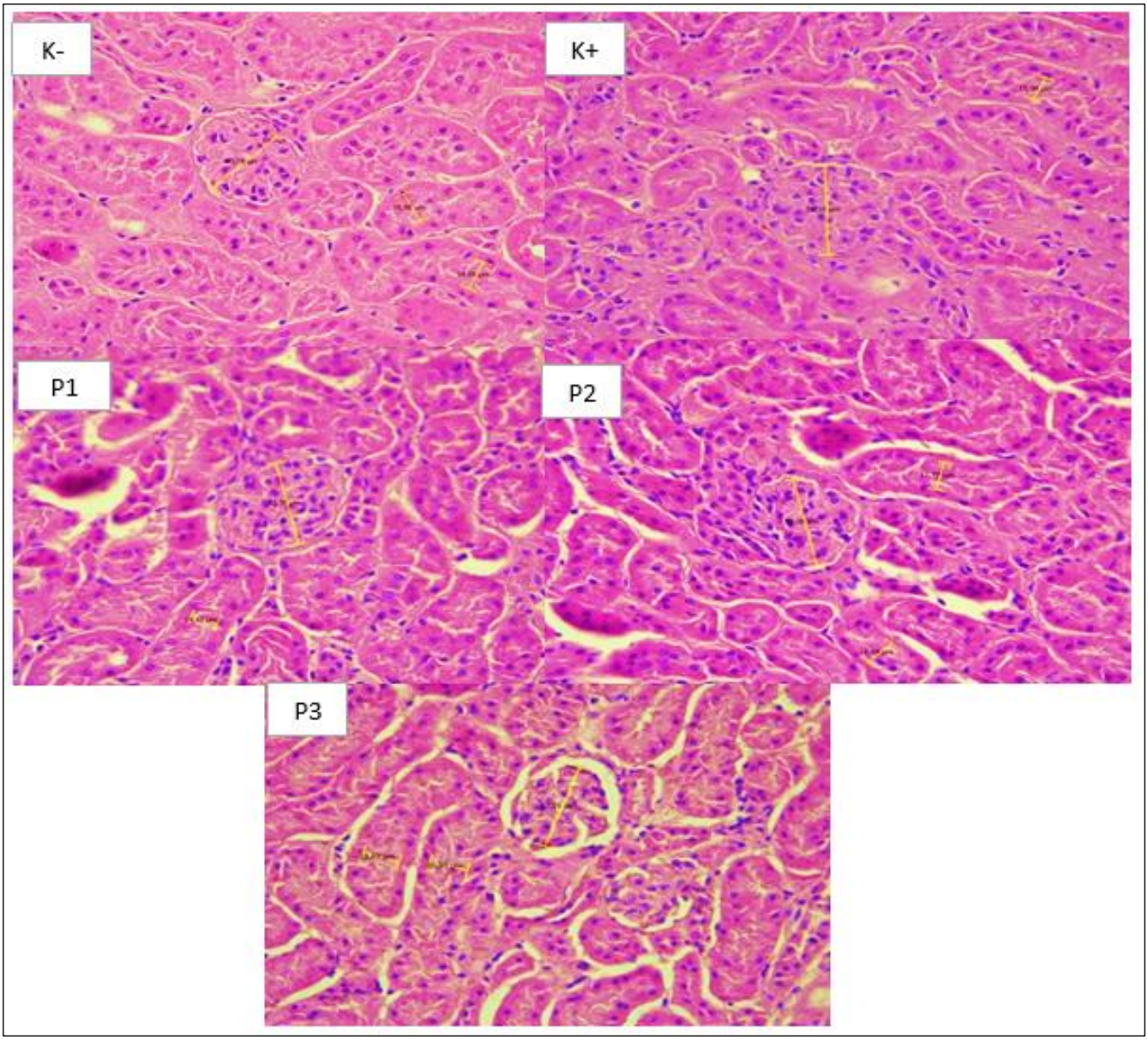

Figure 1: Histopathology glomerulus And tubule proximal mice magnification 400x.
Source : Authors, (2023).

In Figure 1, it can be seen that the proximal tubules in the Control + group (alloxan-induced) appeared to shrink and began to experience improvement or enlargement, best when given 55 grams of white guava treatment. In the control group, the glomerular border was damaged due to alloxan induction, so that the cells inside experienced irregular enlargement. The P3 group, when compared to the K0, P1, and P2 groups, experienced improvement with a reduction in glomerular diameter, and the glomerular borders had begun to be clearly visible.

III.1 DISCUSSION

Study This is an experimental study that aims to know the effect of fluence waters of tew leaf guava seed white (*Psidium guajava var. Pyrifera L*) on kidney histopathology in mice (Mus musculus) alloxan-induced. Alloxan is a fast way to produce a diabetic experimental (hyperglycemic) condition in animals. Diabetes is caused by the alloxan effect on damage to the cells

that make up the kidney tissue, such as degeneration and necrosis in tubules and glomeruli [13].

Leaf guava seed white has content that is good for lowering blood glucose rate with drinking water from the stew [10]. The content of active compounds found in guava leaves and seeds, such as flavonoids, tannins, and calcium, has antidiabetic activity. Tannins function as inhibitor enzymes of glucosidase, slowing down the release of glucose in the blood. Calcium is capable of raising cell production in the pancreas to produce insulin [7]. Flavonoid-sown antioxidants, which can ward off free radicals, Antioxidants are substances that can kill other substances, which makes cells brittle and unable to repair damaged cells [13].

The results showed that giving guava leaf, boiled water, and white seeds for 7 days had an effect on reducing glucose levels in the blood of mice (Musmuscle). This is in line with a study carried out by Darmawan, which found that water from boiling guava leaves can reduce blood glucose levels in diabetic mice [10]. Based on the results of observation in a microscopic manner on tubule proximal and glomerular diameter, measurement results in the form of data ratios were obtained. And tested statistics using Analysis of Variance (ANOVA) yielded proximal tubule size results of sig 0.162 and glomeruli sig 0.331 (P >0.05). Matter This means that, based on analysis statistics, giving white guava leaves boiled water has no significant effect on the size of tubules or the diameter of glomeruli.

Observation on tubule proximal done with measure constriction of the tubules, in the negative control group (K-) has an average size of 16.85 µm while the positive control (K+) or induced mice alloxan has the smallest average tubular constriction, namely 16.02 µm. This is in accordance with the study by Jaya Chandran et al. (2018), which stated that diabetic rats will experience swelling of the tubules [8]. Swelling on tubules is called albuminous or parenchymatous degeneration. Proximal tubular swelling causes lumen tubules to experience narrowing until they close [14]. While in the treatment group, the average in the P1 group was 16.2 ± 4 µm, in the P2 group 16.53 µm and the 16.89 µm P3 group. The third treatment group (P3) was given boiled water 25 sheets of guava leaves have an average tubule size that is close to that of the control negative (K-) ormice.

Observations on the diameter of the glomerulus obtained results showing that the negative control group (K-) has an average size of 51.15 µm positive control group (K+) or mice alloxan-induced have an average size of 55.03 m, and the largest glomerular diameter is 55.03 µm. Group positive control (K+) alloxan induced had the largest diameter; this is in line with research by Fanhriyansyah (2021), which stated that alloxan induced in mice will result in hyperglycemia, which furthermore will result in hypertrophy of the glomerulus because there is pressure on the glomerular cells [15]. Research done by Handani showed that mice induced with alloxan would have a widening glomerulus This results in adhesions between the glomerulus and Bowman's capsule [16]. Meanwhile, in the treatment group, the average flat on group P1 was 53,53 µm, group P2 was 53,28 m, and group P35 was 2.20 µm. Group treatment three (P3), given 25 sheets of guava leaves, has an average tubule size that is close to that of the control negative (K-) or healthy mice.

Based on the results of this study, it was shown that the water boiled leaves of 25 guava sheets had an effect on the histopathology of the mice's kidneys after alloxan-induced tubule size and glomerular diameter were close to those of the negative control group (K-). However, the influence exerted is not very significant.

IV. CONCLUSIONS

Based on the results of observation, the study concluded that a 25-sheet water decoction of white guava leaves (*Psidium guajava var. Pyrifer L.*) would better fix the damage to histopathology in kidney mice (Mus musculus). Compared to 15 sheets and 20 sheets of white guava leaves, Should study furthermore use extract leaf guava seed to take active substances like flavonoids, tannins, and similar substances that are expected to have an effect on histopathology of the kidney.

V. AUTHOR'S CONTRIBUTION

Conceptualization: Eko Naning Sofyanita and Anisa Rizky Yunianti.
Methodology: Eko Naning Sofyanita.
Investigation: Anisa Rizky Yunianti.
Discussion of results: Eko Naning Sofyanita and Anisa Rizky Yunianti.
Writing – Original Draft: Eko Naning Sofyanita.
Writing – Review and Editing: Anisa Rizky Yunianti.
Resources: Anisa Rizky Yunianti.
Supervision: Eko Naning Sofyanita and Anisa Rizky Yunianti.
Approval of the final text: Eko Naning Sofyanita and Anisa Rizky Yunianti.

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