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HISTOLOGICAL DESCRIPTION OF SKELETAL MUSCLES OF WISTAR RATS GIVEN NEPHELIUM LAPPACEUM EXTRACT

Lukman Fajar Setyawan[1]*, Elvin Clara Angmalisang[2], Sonny John Ruddy Kalangi[2]
[1]Medical Education Study Program, Faculty of Medicine, Universitas Sam Ratulangi Manado, Jl. Kampus UNSRAT Bahu, Malalayang, Manado, sulawesi Utara 95115, Indonesia
`Department of Anatomy and Histology, Faculty of Medicine, Universitas Sam Ratulangi Manado, Jl. Kampus UNSRAT Bahu, Malalayang, Manado, sulawesi Utara 95115, Indonesia
*lukmansetyawan011@student.unsrat.ac.id

ABSTRACT
Hyperglycemia is a condition characterized by elevated blood sugar levels, which can trigger oxidative stress and cause cellular damage, including to skeletal muscle cells. The antioxidant content in rambutan leaf extract can lower blood sugar levels. This study aims to determine the histological features of skeletal muscle of Wistar rats given rambutan leaf extract after alloxan induction. Method: This study used a laboratory experimental design with a post-test only control group design. A total of 20 Wistar rats were randomly divided into four groups: a negative control group, a positive control group, and treatment groups administered rambutan leaf extract at doses of 25 mg/kg body weight and 50 mg/kg body weight. Data were collected through blood glucose level measurements, examination of histopathological specimens of skeletal muscle stained with hematoxylin and eosin (H&E), and measurements of muscle fiber diameter. The data were analyzed descriptively by comparing histological findings, blood glucose levels, and mean muscle fiber diameters across groups. Group A experienced a decrease in the average diameter of muscle fibers to 49.06 mm (longitudinal) and 70.45 mm (transverse) accompanied by morphological changes in the form of wavy skeletal muscle fibers. Group B showed improvements in muscle fiber structure with an average diameter approaching normal, namely 59.35 mm (longitudinal) and 91.35 mm (transverse). Group C saw an increase in the average diameter of muscle fibers to 100.97 mm (longitudinal) and 130.21 mm (transverse) indicating a tissue protective effect. Group D showed an average diameter of muscle fibers of 29.47 mm (longitudinal) and 54.34 mm (transverse) accompanied by wavy skeletal muscle fibers. Administration of rambutan leaf extract at a dose of 25 mg/kgBW to Wistar rats increased the average diameter of skeletal muscle fibers and maintained the basic structure of skeletal muscle tissue. Administration of rambutan leaf extract at a dose of 50 mg/kgBW showed wavy skeletal muscle fibers and a decrease in the average diameter of skeletal muscle fibers.

Keywords: alloxan; rambutan leaf extract; skeletal muscle histology

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INTRODUCTION

Hyperglycemia is a chronic and progressive condition characterized by elevated blood sugar levels and impaired carbohydrate, lipid, and protein metabolism. This condition is closely related to diabetes mellitus. Diabetes mellitus can occur due to damage to pancreatic beta cells that causes insulin deficiency (Type 1 Diabetes Mellitus) or insulin resistance that is often found in obesity (Type 2 Diabetes Mellitus) (Baynest, 2015). Diabetes mellitus increases free radical production through glucose autooxidation and protein glycation (Ardiani et al. 2021; IDF, 2021). In patients with diabetes mellitus, hyperglycemia induces oxidative stress that can trigger cell damage, including skeletal muscle cells (Serang & Bani, 2017).

The global prevalence of diabetes mellitus continues to increase and has a significant impact on public health, especially related to damage to skeletal muscle cells (Serang & Bani, 2017). In 2019, the International Diabetes Federation (IDF) reported that as many as 463 million people in the world suffer from diabetes aged 20-79 for a prevalence rate of 9.3% of the total population of the same age. This figure is projected to increase to 578 million diabetes sufferers in 2030 and 700 million sufferers in 2045. Indonesia is recorded as the country in Southeast Asia with the largest contribution to the prevalence of diabetes cases (Wardhani & Astuti, 2020). In 2018, the Basic Health Research (Riskesdas) reported that the prevalence of diabetes mellitus in Indonesia increased from 6.9% in 2013 to 8.5% in 2018. The four provinces with the highest prevalence during the 2013-2018 period were DI Yogyakarta, DKI Jakarta, East Kalimantan, and North Sulawesi (Kementerian Kesehatan Republik Indonesia, 2020). In North Sulawesi, the number of diabetes mellitus cases increased from 3,652 cases in 2015 to 5,083 cases in 2016. In 2013, diabetes mellitus cases in North Sulawesi ranked fourth nationally at 6.9%. In 2018, the prevalence of diabetes mellitus sufferers actually increased to 8.5% (Paseki et al., 2021).

To date, no drug has been found that can completely cure diabetes mellitus, so diabetes mellitus sufferers generally use insulin or oral antidiabetic drugs for life (Alotaibi et al., 2019). However, the use of oral antidiabetic drugs and insulin often causes side effects (Puspitasari & Choerunisa, 2021). Therefore, many studies have turned to natural ingredients in the form of plants as an alternative therapy for diabetes mellitus (Saleh, 2019). Indonesia is rich in traditional plants with medicinal properties, such as rambutan leaves (Nephelium lappaceum). Rambutan leaves have long been used in traditional medicine and are known to contain bioactive compounds, such as flavonoids, tannins, and saponins that have antioxidant, anti-inflammatory, and antidiabetic properties (Glukosa, 2020).This provides a strong basis for exploring the use of rambutan leaf extract in an effort to protect and restore skeletal muscle damaged by oxidative stress (Thitilertdecha et al., 2008).

Alloxan is a chemical agent frequently used in laboratory animal studies. Alloxan induction in Wistar rats is a common method used to mimic human diabetes mellitus, which is known to cause significant damage to various body tissues, including skeletal muscle (Wardhani & Astuti, 2020; Lenzen, 2008; Ahmad et al., 2018). Alloxan works by damaging pancreatic beta cells, resulting in prolonged hyperglycemia. This hyperglycemia triggers high oxidative stress, which can damage cellular structures in skeletal muscle, resulting in decreased muscle mass, changes in muscle fiber morphology, and ultimately, muscle dysfunction. 5,15–17 (Wardhani & Astuti, 2020; Rena et al., 2017; Ryall et al., 2008).

In this context, rambutan leaf extract (Nephelium lappaceum) is expected to provide positive effects by reducing oxidative stress and inflammation due to alloxan induction (Zainuri, 2019; Mustaqim & Habibul, 2022). Previous research results, the active compounds of rambutan leaves have the potential to neutralize free radicals, protect muscle cells from further damage, and help the regeneration process of damaged muscle tissue (Ramasamy & Sivasithamparan, 2013; Rasyad, 2021). Therefore, this study aims to determine the histological characteristics of the skeletal muscle of Wistar rats administered rambutan leaf extract following alloxan induction. Thus, this study is expected to show how rambutan leaf extract can improve the histological appearance of skeletal muscle in alloxan-induced Wistar rats and provide a basis for the development of new therapies based on natural ingredients for prophylaxis in overcoming muscle complications due to diabetes mellitus (Wardhani & Astuti, 2020).

METHOD

This study is a laboratory-based experimental study using a post-test-only control group design. Conducted between September and November 2024, the research took place across three facilities at Sam Ratulangi University: the Faculty of Medicine's Testing Laboratory for animal housing, the Faculty of Mathematics and Natural Sciences for rambutan leaf extraction, and the Anatomical Pathology Laboratory for preparing and analyzing histological specimens. The study population consisted of male Wistar rats (Rattus norvegicus). The study sample comprised 20 male Wistar rats that were randomly divided into four groups, each consisting of five rats. Group A served as the negative control and was induced with alloxan at a dose of 170 mg/kg body weight. Group B served as the positive control and was induced with alloxan at a dose of 170 mg/kg body weight and administered glibenclamide at a dose of 0.09 mg/200 g body weight. Group C was the treatment group induced with alloxan at a dose of 170 mg/kg body weight and administered rambutan leaf extract at a dose of 25 mg/kg body weight, while Group D was the treatment group induced with alloxan at a dose of 170 mg/kg body weight and administered rambutan leaf extract at a dose of 50 mg/kg body weight.

Data were collected by measuring blood glucose levels before and after treatment using a glucometer. After the treatment period ended, the rats were euthanized, and skeletal muscle tissue was collected to prepare histopathological sections stained with hematoxylin and eosin (H&E). The sections were examined under a light microscope at 100× and 400× magnification to evaluate the histological features of the tissue. Subsequently, muscle fiber diameters were measured in longitudinal and transverse sections using image analysis software to obtain the average diameter values for each group. The data were analyzed descriptively by comparing the histological features, blood glucose levels, and average muscle fiber diameters between the control and treatment groups. The research results are presented in the form of a descriptive narrative, histological images, and average muscle fiber diameter values to illustrate the morphological changes in the tissue following administration of rambutan leaf extract.

RESULT

Histological Image of Normal Wistar Rat Skeletal Muscle

The blood sugar of the mice measured on day 0, after going through an acclimatization period, showed a normal value of 86 mg/dL.

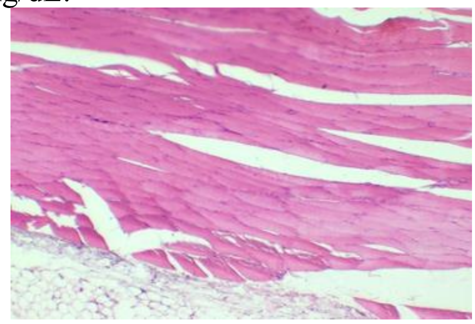

Figure 1. Histology of Wistar Rat Skeletal Muscle in Longitudinal View. (X100;H&E)

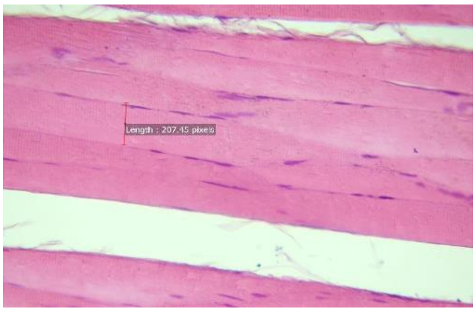

Figure 2. Histology of Wistar Rat Skeletal Muscle in Longitudinal View. (X400; H&E)

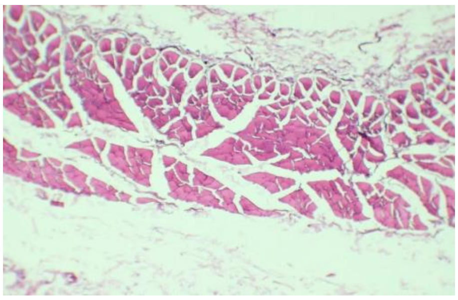

Figure 3. Histology of Wistar Rat Skeletal Muscle in Transverse View. (X100;H&E)

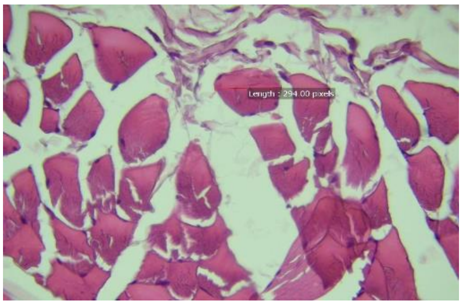

Figure 4. Histology of Wistar Rat Skeletal Muscle in Transverse View. (X400; H&E)

The histological image of the skeletal muscle of Wistar rats shows the typical structure of skeletal muscle tissue, namely the presence of patterned muscle fibers, a key characteristic of this tissue. These muscle fibers are elongated, cylindrical, and neatly arranged. Furthermore, the cell nuclei of the muscle fibers appear to be located at the periphery, consistent with the general characteristics of skeletal muscle cells. Muscle fiber diameter measurements were performed to provide quantitative information regarding the size of these histological structures. In longitudinal views of muscle fibers, the average diameter was 207.45 pixels, which, when converted, is equivalent to 73.15 mm (see Figure 15). Meanwhile, in transverse views of muscle fibers, the average diameter was recorded at 294 pixels, equivalent to 103.72 mm (see Figure 17). These results provide a more in-depth understanding of the dimensions of the skeletal muscle structure of Wistar rats observed in this study.

Histological Description of Skeletal Muscle of Wistar Rats Group A

In group A, two mice survived until day 18 of the entire study. Before the mice in this group received alloxan induction, their average fasting blood sugar level was recorded at 89 mg/dL, which is within the normal range. Three days after induction, on day 3, the mice's blood sugar levels were checked again, and the results showed that the mice's blood sugar was at the Hi level, which is more than 599 mg/dL. Before the termination procedure was carried out, the mice's blood sugar levels were still detected at the Hi level, which is more than 599 mg/dL.

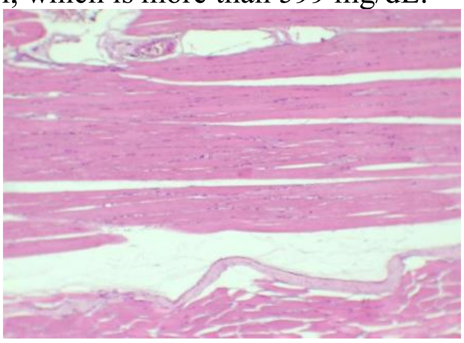
Figure 5**.** Longitudinal View of Histology of Wistar Rat Skeletal Muscle After Alloxan Induction. (X100;H&E)

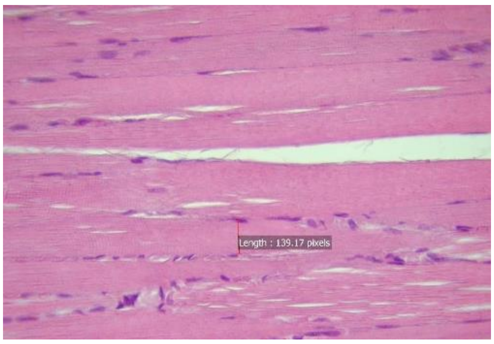

Figure 6. Longitudinal View of Histology of Skeletal Muscle of Wistar Rats After Alloxan Induction. (X400; H&E)

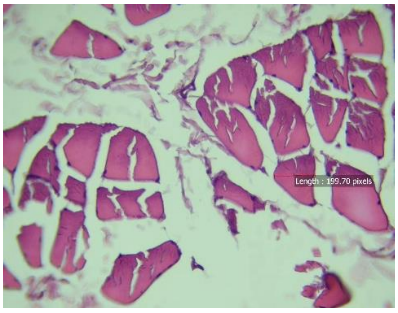

Figure 7. Histological Transverse View of Skeletal Muscle of Wistar Rats After Alloxan Induction. (X400; H&E)

The histological appearance of skeletal muscle in treatment group A showed striking changes compared to normal skeletal muscle. Some muscle fibers appeared wavy, but retained their characteristic pattern, with cell nuclei still visible at the edges of the muscle fibers. This indicates that despite the morphological changes, the basic structure of skeletal muscle remains recognizable (see Figure 5). Measurements of the average muscle fiber diameter revealed a significant decrease in size compared to normal muscle fibers. In longitudinal view, the average muscle fiber diameter was 139.17 pixels, equivalent to 49.06 mm (see Figure 6). Meanwhile, in transverse view, the average muscle fiber diameter was recorded at 199.70 pixels, equivalent to 70.45 mm (see Figure 7).

Histological Description of Skeletal Muscle of Wistar Rats Group B

In group B, two mice survived to day 18 of the entire study. Group B served as a positive control in this study. Mice in this group were induced with alloxan at a dose of 170 mg/kg body weight on day 0 to induce hyperglycemia. Three days after induction, on day 3, the mice's blood sugar levels were checked and the result was 517 mg/dL, indicating a significant increase. On day 4, glibenclamide was administered at a dose of 0.09 mg/200 g body weight to lower blood sugar levels, followed by 14 consecutive days of feeding. On day 18, the mice were euthanized for skeletal muscle harvesting. Before euthanasia, the mice's blood sugar levels were checked again. The results showed that the mice's blood sugar levels had decreased to 262 mg/dL, although still higher than normal.

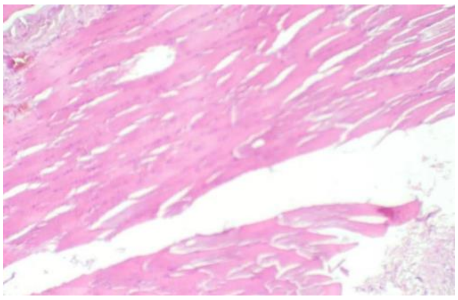

Figure 8. Longitudinal View of Histology of Skeletal Muscle of Wistar Rats After Alloxan Induction and Administration of Glibenclamide at a Dose of 0.09 mg/200 g Rat Body Weight for 14 Days. (X100; H&E)

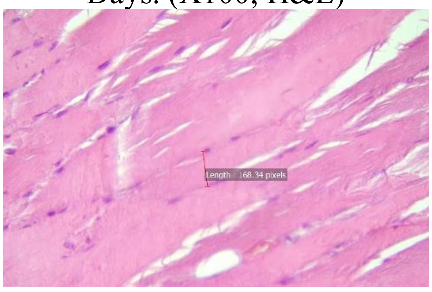

Figure 9. Longitudinal View of Histology of Skeletal Muscle of Wistar Rats After Alloxan Induction and Administration of Glibenclamide at a Dose of 0.09 mg/200 g Rat Body Weight for 14 Days. (X400; H&E)

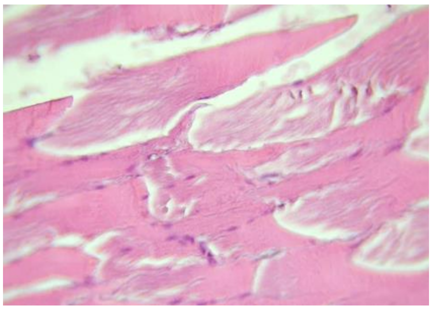

Figure 10. Longitudinal Histological View of Wistar Rat Skeletal Muscle Showing Necrosis After Alloxan Induction and Glibenclamide Administration at a Dose of 0.09 mg/200 g Rat Body Weight for 14 Days. (X400; H&E)

Figure 11. Histological Transverse View of Skeletal Muscle of Wistar Rats After Alloxan Induction and Administration of Glibenclamide at a Dose of 0.09 mg/200 g Rat Body Weight for 14 Days. (X400; H&E)

The histological features of skeletal muscle in group B showed that most muscle fibers remained within normal limits, with a regular fiber structure and a characteristic skeletal muscle pattern (see Figure 21). However, in several areas, necrosis was observed in some muscle fibers (see Figure 10). The results of the measurement of the average diameter of muscle fibers revealed values that were beginning to approach the average diameter of normal muscle fibers. In the longitudinal view, the average diameter of muscle fibers was recorded at 168.34 pixels, or equivalent to 59.35 mm (see Figure 9). Meanwhile, in the transverse view, the average diameter of muscle fibers was 258.68 pixels, which is equivalent to 91.35 mm (see Figure 11).

Histological Description of Skeletal Muscle of Wistar Rats Group C

Group C was the first treatment group in this study. One mouse survived until day 18 of the research process. Three days after alloxan induction, on day 3, the mice's blood sugar levels were rechecked, and the results showed very high blood sugar levels (Hi), above 599 mg/dL, indicating severe hyperglycemia. On day 4, rambutan leaf extract was administered at a dose of 25 mg/KgBW per mouse. On day 18, a repeat blood sugar test was performed, which showed that the mice's blood sugar levels had decreased to 415 mg/dL.

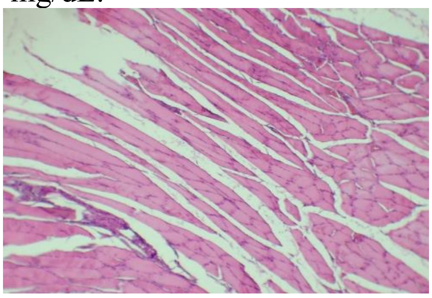

Figure 12. Longitudinal and Transverse View of Histology of Skeletal Muscle of Wistar Rats After Alloxan Induction and Administration of Rambutan Leaf Extract at a Dose of 25 mg/KgBW for 14 Days. (X100; H&E)

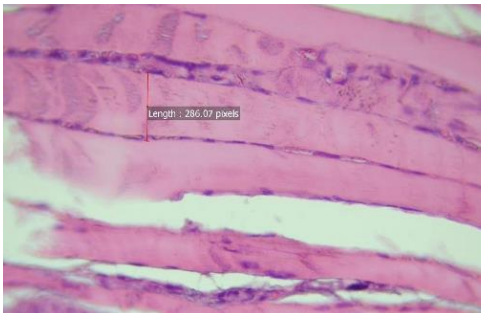

Figure 13. Longitudinal View of Histology of Skeletal Muscle of Wistar Rats After Alloxan Induction and Administration of Rambutan Leaf Extract at a Dose of 25 mg/KgBW for 14 Days. (X400;H&E)

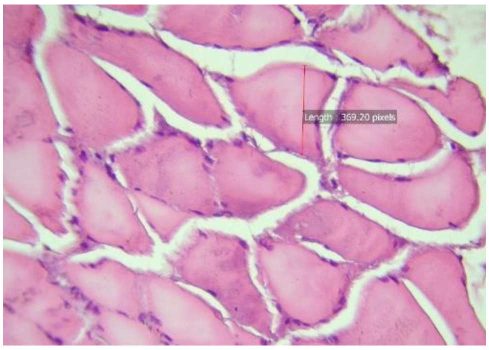

Figure 14. Histological Cross-Section of Wistar Rat Skeletal Muscle After Alloxan Induction and Administration of Rambutan Leaf Extract at a Dose of 25 mg/KgBW for 14 Days. (X400; H&E)

The histological features of skeletal muscle in group C showed that most muscle fibers remained within normal limits. The muscle fibers appeared organized with a pattern typical of skeletal muscle, indicating that the basic structure of this tissue was largely well preserved (see Figure 12). The results of the measurement of the average diameter of the muscle fibers provided quantitative information that supported the morphological observations. In the longitudinal view, the average diameter of the muscle fibers was recorded at 286.07 pixels, which is equivalent to 100.97 mm (see Figure 13). Meanwhile, in the transverse view, the average diameter of the muscle fibers was recorded at 369.20 pixels, or equivalent to 130.21 mm (see Figure 14).

Histological Description of Skeletal Muscle of Wistar Rats Group D

Group D, treatment group 2 in this study, consisted of two mice that survived to day 18 of the study. Three days after alloxan induction, on day 3, the mice's blood sugar levels were checked and showed a result of 502 mg/dL, indicating an increase in blood sugar levels, although not as high as in the other groups. On day 4, rambutan leaf extract was administered at a dose of 50 mg/kg body weight per mouse. After the extract and feed administration period, the mice's blood sugar levels were checked again and showed a significant decrease, reaching 370 mg/dL.

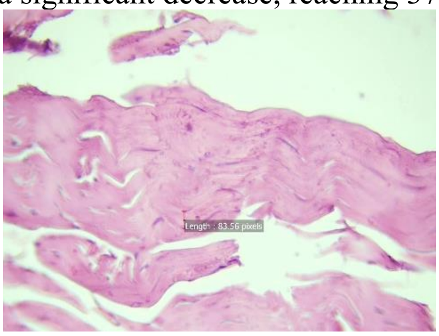

Figure 15. Longitudinal View of Histology of Skeletal Muscle of Wistar Rats After Alloxan Induction and Administration of Rambutan Leaf Extract at a Dose of 50 mg/KgBW for 14 Days. (X100;H&E)

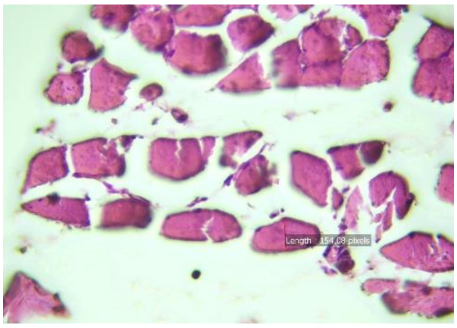

Figure 16. Histological Transverse View of Skeletal Muscle of Wistar Rats After Alloxan Induction and Administration of Rambutan Leaf Extract at a Dose of 50 mg/KgBW for 14 Days. (X100; H&E)

The histological features of skeletal muscle in group D showed that most muscle fibers remained within normal limits, with a regular fiber structure and a characteristic pattern characteristic of skeletal muscle tissue. However, there was a phenomenon of wavy muscle fibers in several areas (see Figure 15). The results of measurements of muscle fiber diameter showed a decrease in size compared to normal conditions. In the longitudinal view, the average diameter of muscle fibers was recorded at 83.56 pixels, which is equivalent to 29.47 mm (see Figure 15). Meanwhile, in the transverse view, the average diameter of muscle fibers was 154.08 pixels, which is equivalent to 54.34 mm (see Figure 16).

DISCUSSION

The results of the study showed that the skeletal muscle fibers of normal Wistar rats had a longitudinal, cylindrical, patterned, and neatly arranged muscle fiber structure. The cell nuclei were located at the edge of the muscle fibers, in accordance with the typical characteristics of skeletal muscle tissue (Mescher, 2024).The average diameter of skeletal muscle fibers in longitudinal (73.15 mm) and transverse (103.72 mm) views was in accordance with previous studies, indicating normal conditions and histological standards of skeletal muscle tissue in healthy Wistar rats (see Figures 14-17) (Maynard & Downes, 2019). These results provide an important basis for comparing histological changes that may occur in groups of Wistar rats that have been induced by alloxan and given rambutan leaf extract. These data confirm that Wistar rats that are only fed food have a normal muscle structure, which serves as a comparison for the treatment group. This picture also aligns with the theory that healthy skeletal muscle demonstrates muscle fiber integrity without degeneration or necrosis, which indicate tissue damage (Wardhani & Astuti, 2020).

The negative control group, induced by alloxan at a dose of 170 mg/kgBW, successfully induced severe hyperglycemia, characterized by blood sugar levels exceeding 599 mg/dL. This is consistent with the diabetogenic properties of alloxan, which trigger oxidative stress and damage to pancreatic beta cells. Alloxan is known to cause hyperglycemia by increasing the production of free radicals that damage cells through oxidative stress mechanisms. This oxidative stress leads to skeletal muscle protein degradation, characterized by changes in skeletal muscle structure (Lenzen, 2008). Histologically, skeletal muscle fibers exhibited morphological changes, with a wavy appearance in some areas (see Figure 18). A significant decrease in the average diameter of skeletal muscle fibers, both in longitudinal (49.06 mm) and transverse (70.45 mm) views, reflects the adverse effects of chronic hyperglycemia (see Figures 19 and 20). These results are consistent with studies showing that hyperglycemia can cause metabolic disturbances in skeletal muscle, such as muscle atrophy and changes in muscle structure, such as the appearance of wavy muscle fibers. These features are usually an early indication of degeneration (Dubuisson et al., 2022; Mann et al., 2011).

The group of mice receiving glibenclamide as a positive control after alloxan induction showed a significant decrease in blood sugar levels, from 517 mg/dL on day 3 to 262 mg/dL on day 18. Based on histological observations, the skeletal muscle fibers largely maintained their regular structure with a characteristic pattern. However, there were several areas of necrosis (see Figure 23). The presence of this necrosis indicates skeletal muscle tissue damage, likely caused by the hyperglycemia experienced by the mice prior to glibenclamide treatment. By controlling blood sugar levels, glibenclamide can mitigate skeletal muscle tissue damage. However, this protective effect depends on the initial condition of the tissue. 84 If the results show necrosis in the group receiving glibenclamide, this is likely due to other factors, such as the severity of the initial alloxan-induced damage or the individual mice's biological response to therapy (Alotaibi et al., 2019).

The variability in skeletal muscle histology in alloxan-induced experimental animals, even when using the same dose, is influenced by various biological and physiological factors, including age, metabolic status, individual immune response, and microcirculatory distribution. Alloxan induction is known to cause oxidative stress through the production of free radicals, which can trigger tissue damage. The extent of this damage varies between individuals, depending on the capacity of the body's antioxidant system and the tissue's sensitivity to oxidative stress. This variation may explain differences in histological appearance, such as the appearance of necrosis or other changes in skeletal muscle tissue (Obi et al., 2018). The average muscle fiber diameter in the positive control group was close to that in the normal group. In longitudinal views, the muscle fiber diameter reached 59.35 mm, while in transverse views it reached 91.35 mm (see Figures 22 and 24). Although still smaller than in the normal group, this increase was significant when compared with the negative control group.

These findings indicate that glibenclamide administration contributes to improved muscle metabolism, which subsequently impacts muscle fiber size recovery (Obi et al., 2018; Alotaibi et al., 2019). The histological image of skeletal muscle in Wistar rats administered rambutan leaf extract at a dose of 25 mg/kg body weight after alloxan induction shows that skeletal muscle fibers maintained their normal structure, with a characteristic pattern characteristic of skeletal muscle tissue. The integrity of this pattern indicates that the underlying structure of skeletal muscle was largely preserved, despite the rats experiencing severe hyperglycemia prior to administration of rambutan leaf extract. Measurement of muscle fiber diameter provided quantitative evidence of significant improvement. In longitudinal views, the average muscle fiber diameter reached 100.97 mm, while in transverse views, the average muscle fiber diameter reached 130.21 mm. This value was not only greater than that of the positive control group but also exceeded that of normal Wistar rats. This indicates a repair effect on skeletal muscle tissue. The antioxidant compounds, such as flavonoids, in rambutan leaves play a role in suppressing oxidative stress and promoting skeletal muscle cell regeneration, as well as supporting the tissue repair effects of flavonoids on tissue damage caused by hyperglycemia (Riyanto & Rohman, 2017; Alam et al., 2014).

The reduction in blood sugar levels of up to 415 mg/dL after administration of rambutan leaf extract supports the hypothesis that this extract has antidiabetic potential and a protective effect against tissue damage caused by hyperglycemia (Durry, 2016; Riyanto & Rohman, 2017). These results are consistent with previous research demonstrating the antioxidant activity of rambutan leaves (Nephelium lappaceum) that can reduce oxidative stress and inflammation. This activity likely plays a role in protecting muscle fibers from degeneration that typically occurs in chronic hyperglycemia (Nisa, 2017; Durry, 2016; Farikatulibrizah, 2017). However, the rats' blood sugar levels remained high, suggesting that the dose or duration of extract administration may not have been optimal for fully restoring the rats' metabolism. These findings underscore the need for further research to explore the potential of rambutan leaves in treating metabolic complications caused by hyperglycemia (Durry, 2016; Farikatulibrizah, 2017).

The histological image of the skeletal muscle of Wistar rats receiving rambutan leaf extract at a dose of 50 mg/kgBW shows that most muscle fibers retained their characteristic pattern and regular structure. However, some areas with wavy muscle fibers were observed (see Figure 28). This phenomenon indicates tissue damage, albeit unevenly, which may be related to initial hyperglycemia or the effect of the higher extract dose compared to the group receiving rambutan leaf extract at a dose of 25 mg/kgBW (Alotaibi et al., 2019; Rohman, 2017).

The average diameter of skeletal muscle fibers in this group decreased more significantly than in the positive control group and the group receiving rambutan leaf extract at a dose of 25 mg/kgBW. In longitudinal views, the average muscle fiber diameter reached only 29.47 mm, while in transverse views it was 54.34 mm (see Figures 28 and 29). This value indicates that although rambutan leaf extract at a dose of 50 mg/kgBW was able to reduce blood sugar levels from 502 mg/dL to 370 mg/dL, the protective effect on skeletal muscle tissue was not as good as in the treatment group given rambutan leaf extract at a dose of 25 mg/kgBW. This finding could suggest a suboptimal effect of high doses or even potential toxicity to skeletal muscle tissue. The bioactive activity of rambutan leaf extract, which acts as an antioxidant and anti-inflammatory, likely has a threshold of effectiveness, so high doses provide no additional benefit and may cause side effects (Rohman, 2017).

The decrease in muscle fiber size likely indicates that the metabolic stress caused by hyperglycemia has not been fully resolved, despite decreased blood sugar levels.84 These results highlight the importance of adjusting the dosage of rambutan leaf extract to achieve a balance between antihyperglycemic effects and tissue protection. Further research is needed to understand the mechanisms underlying the effects of high doses of rambutan leaf extract on skeletal muscle tissue, as well as its potential toxicity (Alotaibi et al., 2019; Rohman, 2017).

CONCLUSION

BASED on the results of a study on the histological appearance of skeletal muscle in Wistar rats given rambutan leaf extract after alloxan induction, the following conclusions were obtained: 1)Administering rambutan leaf extract at a dose of 25 mg/kgBW to alloxan-induced Wistar rats showed an increase in the average diameter of skeletal muscle fibers and a well-maintained basic skeletal muscle tissue structure. 2)Administering rambutan leaf extract at a dose of 50 mg/kgBW to alloxan-induced Wistar rats showed wavy skeletal muscle fibers and a decrease in the average diameter of skeletal muscle fibers.

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