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Research Article

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Effect of Malacca Leaf (*Phyllanthus emblica*) Infusion on Sperm Quality in Streptozotocin-Induced Diabetic Rats (*Rattus norvegicus*)

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ABSTRACT

Background: Diabetes mellitus (DM) not only disrupts metabolic functions but also causes various complications, including reproductive disorders. Malacca (*Phyllanthus emblica*) leaves are known for their medicinal properties and may have beneficial effects on spermatozoa quality in diabetic conditions.

Aims: This study aimed to evaluate the effect of Malacca leaf infusion on sperm quality in streptozotocin (STZ)-induced diabetic rats.

Methods: Twelve male rats were randomly assigned into four groups (n=3): a positive control group receiving distilled water, a negative control group induced with STZ at 30 mg/kg BW, and two treatment groups induced with STZ followed by Malacca leaf infusion administration at doses of 100 mg/kg BW and 150 mg/kg BW. The infusion was administered orally via gastric gavage. Sperm motility, viability, morphology, and concentration were evaluated 22 days after treatment. Data were analyzed using analysis of variance (ANOVA).

Results: STZ-induced diabetic rats exhibited significant reductions in sperm motility, viability, and concentration ($P<0.05$), accompanied by a significant increase in abnormal sperm morphology ($P<0.05$) compared with the positive control group. Administration of Malacca leaf infusion improved all sperm quality parameters, with the greatest improvement observed in the group receiving 150 mg/kg BW. These findings indicate a dose-dependent beneficial effect of Malacca leaf infusion on spermatozoa quality under diabetic conditions.

Conclusion: Malacca leaf infusion has the potential to ameliorate spermatozoa quality in STZ-induced diabetic rats. The results suggest that this herbal preparation may serve as a promising therapeutic agent for managing diabetes mellitus-associated reproductive dysfunction.

INTRODUCTION

Hyperglycemia, characterized by elevated blood glucose levels, is a major clinical manifestation of diabetes mellitus (DM), which is a metabolic disorder resulting from insufficient insulin production or impaired insulin utilization (Putri et al. 2019). Diabetes mellitus is primarily classified into type 1 and type 2, with type 1 resulting from absolute insulin deficiency and type 2 from relative insulin deficiency or insulin resistance (Saputra et al. 2018; Yulizal et al. 2021).

Diabetes mellitus is associated with various complications, including reproductive dysfunction. Reduced insulin levels and increased oxidative stress caused by excessive free radical production contribute to testicular damage and impaired spermatogenesis,

leading to decreased sperm concentration, motility, and viability, as well as increased abnormal morphology (Meliyana et al. 2016; Bulqis et al. 2020). This disorder causes blood flow to the penis to be impaired so that the nutrients for the development of spermatozoa inside the seminiferous tubules are disrupted (Parhizkar et al. 2013).

Experimental DM is commonly induced using streptozotocin (STZ), a diabetogenic agent that damages pancreatic β-cells through free radical formation, thereby reducing insulin production (Munjiati et al., 2021). The use of herbal-based therapies has gained attention as a strategy to mitigate DM-induced reproductive disorders. One such plant is Malacca (*Phyllanthus emblica*), which is rich in vitamin C, minerals, amino acids, and bioactive compounds such as flavonoids, tannins, and saponins (Dhale, 2012; Syahputri et al. 2021). These compounds have been reported to support testosterone synthesis and spermatogenesis and are considered non-toxic (Lefaan, 2014; Zakwan et al., 2023).

Previous studies have reported the benefits of the Malacca plant as a chemoprotective (Singh et al. 2011), antidiabetic, anti-dioxide, anticancer, anti-inflammatory (Kaur et al. 2013), and antibacterial (Elangovan et al. 2015; Syahputri et al. 2021). The ethanol extract of malacca leaves can reduce the carrageenan-induced edema in male mice (Asmilia et al. 2020). The administration of ethanol extract of malacca leaves at a dose of 600 mg/kg body weight was able to restore the number and differential leukocytes of white rats infected with Trypanosoma evansi (Ramadhani et al. 2023). However, data regarding the effects of Malacca leaf infusion on spermatozoa quality under diabetic conditions remain limited. Therefore, this study aimed to evaluate the effects of Malacca leaf infusion on sperm quality in streptozotocin-induced diabetic rats.

MATERIALS AND METHODS

Tool and Materials

The equipment used in this research concists of animal cages and wire mesh, *EasyTouch GCU*, filter paper, analytical scales, glass beakers, stomach probes, Erlenmeyer flasks, microscopes, stirring rods, tweezers, scalpels, Petri dishes, watch glasses, droppers, object glasses, and cover glasses.

The materials used in this research included rats, chloroform, pellets, Malacca leaf infusion, distilled water, ethanol solvent, eosin dye, 0.3% NaCl, and physiological NaCl.

Ethical Approval

All animal procedures performed in this study were registered in the Research Ethics Committee at Faculty of Veterinary Medicine of Universitas Syiah Kuala Number: 332/KEPH/2024.

Research Methods

This study used the Complete Random Design (RAL) method using sample of 12 male rats and malacca leaves taken from Bha Ulee Tutu village, Simpang Tiga Aceh Besar, Aceh. Before starting the study, the experimental animals were randomly taken and then divided into four experimental groups (n=3): positive control (P1) resived distilled water, negative control (P2) was administered STZ at a dose of 30 mg/kg BW and two treatment groups receving STZ followed Malacca leaf infusion at doses of 100 mg/kg BW (P3) and 150 mg/kg BW (P4). The Malacca leaf infusion was delivered orally via gastric gavage. Each treatment was carried out for a week consecutively, after which the quality of spermatozoa could be assesed on 22 days post-treatment (Munjiati et al. 2021).

Research Procedure

Making Malacca Leaf Infusion

The dried malacca leaves are ground into powder, then the malacca leaves are weighed as much as 0.1 g, plus 100 ml of aquades, put in a bath, after which they are heated to make infusion of malacca leaves 100 mg/kg BW and weighed 0.15 g plus 100 ml of aquades to make infusion of malacca leaves 150 mg/kg BW. Heating is carried out for 15 minutes calculated after the temperature reaches 900 C. Then it is filtered using filter paper/flannel (Zuhrawati et al. 2015).

Diabetic Mellitus Rats Manufacturing

Streptozotocin injections were administered intraperitoneally and the dose was determined based on the weight of the rats. The dose of STZ given was 30 mg/kg BW (Munjiati et al. 2021). Rats'blood glucose levels were checked using *EasyTouch GCU*.

Giving Malacca Leaf Infusion

Malacca leaf infusion was given to rats through a gastric sonde with a dose of 1 ml for 7 consecutive days after the rats were DM, on 15 to 21 days.

Sprem Collection

Seven days after administration of malacca leaves infusion, the rats were euthanized and dissected, then the testes and cauda epididymis organs were collected and placed in a watch glass containing physiological NaCl. Next, the proximal part of the cauda is slightly cut

with scissors and then pressed slowly until the semen comes out and is suspended with NaCl. Observations were carried out including checking the quality of spermatozoa.

Microscopic Examination of Sperm Quality

Sperm Motillity

Observation of spermatozoa motility was observed by dripping semen on an object glass and adding one drop of physiological NaCl, then observed under a microscope with a magnification of 40 x 10. The assessment was carried out by looking at the percentage of individual motility and movement. Motility is assessed in percentages, which is the ratio of spermatozoa that move vibrate in place (vibrator), spermatozoa movement that move in a circular, spermatozoa movement that is reversed, and spermatozoa that are dead or floating. The motile sperm count is based on spermatozoa movements such as rapid progressive (A), slow progressive (B), circular (C), and fibration (D) (Arifiantini 2012). The determination of the percentage of spermatozoa motility is carried out, with the formula:

$$\text{Motility (\%)} = \frac{A}{A+B+C+D} \text{ x 100\%}$$

Sperm Viability

One drop of semen is dripped on the object glass and one drop of eosin solution (2%) staining is added. The smear preparation is made, then fixed on a spiritus lamp, then examined under a microscope with a magnification of 40 x 10. Living spermatozoa do not absorb the color eosin or are white in color while dead spermatozoa will absorb the color eosin or are red. After that, the living spermatozoa are counted, and divided by the number of all visible spermatozoa in one field of view and expressed in percent (Arifiantini 2012).

$$\text{Live (\%)} = \frac{Number\ \ of\ \ live\ \ spermatozoa}{Number\ \ of\ \ live\ \wedge\ dead\ \ spermatozoa} \text{ x 100\%}$$

Sperm Abnormalities

Observation is carried out by making a review preparation, by dripping one drop of semen on the object glass, then dripping the eosin solution and then fixing it with a spritus lamp, after which make observations under a microscope with a magnification of 40 x 10. The examination was carried out by looking at morphology and deformities or primary abnormalities (small/large head size, double head/double tail, and abnormal head shape) and secondary abnormalities (broken head, broken tail in the neck or middle and folded tail) (Arifiantini 2012). A minimum of 200 spermatozoa were observed and the calculation was carried out using the formula:

$$\text{Abnormality (\%)} = \frac{Abnormality}{Total\ \ cell\ \ observed} \text{ x 100\%}$$

Sperm Concentration

The calculation of spermatozoa concentration, was carried out with semen sucked up to a scale of 0.5 then added with a 3% NaCl solution to mark 101, then homogenized to form a figure of eight to 2-3 minutes. A few drops of the solution are discarded. Then the Neubauer counting room was covered with a glass cover, then the sample was filled into the Neubauer counting room. The spermatozoa count was carried out in five large boxes, with a magnification of 40 x 10. The concentration of spermatozoa obtained was Y x 5 x 10^6 (Y = the number of spermatozoa in 5 boxes) (Arifiantini 2012).

Research Parameters and Data Analysis

The study parameters were spermatozoa quality examination including motility (%), viability (%), concentration (Y x 10^6/ml) and abnormality (%) spermatozoa. The data from the results of the study obtained from the results of the spermatozoa quality examination will be statistically analyzed by *analysis of variants* (Anova).

RESULTS AND DISCUSSION

The identification of diabetic rats was based on blood glucose level measurements across all treatment groups. The results indicated that the blood glucose level in the control group (P1) was 85.75 ± 17.83 mg/dL, whereas STZ-induced groups (P2–P4) exhibited markedly elevated glucose levels (299 ± 109.57 mg/dL), confirming the diabetic condition. Detailed hematological data have been reported separately and submitted to another journal.

The results showed that the highest spermatozoa motility was observed in the non-STZ-induced control group (P1; 92.97 ± 1.55%), while the lowest motility occurred in the STZ-induced group (P2; 28.05 ± 0.84%). Treatment with Malacca leaf infusion significantly improved sperm motility in a dose-dependent manner,

with values of 30.19 ± 0.70% in P3 and 38.88 ± 1.23% in P4. These results are summarized in Table 1.

Table 1 shows significant differences in spermatozoa viability among all groups ($P < 0.05$). The STZ-induced group (P2) exhibited the lowest viability compared with P1, P3, and P4. The 150 mg/kg BW Malacca leaf infusion (P4) produced the greatest improvement, resulting in a spermatozoa viability of 59.24 ± 2.26%. Statistical analysis confirmed significant differences ($P < 0.05$) in spermatozoa viability between the treatment groups (P1, P3, and P4) and the negative control group (P2).

Abnormal spermatozoa were observed in all groups, with the highest incidence in the STZ-induced group (P2; 14.02 ± 1.66%). In contrast, the P4 group exhibited a level of abnormalities comparable to the positive control (P1; 2.00 ± 0.50% vs. 0.83 ± 0.76%), indicating that Malacca leaf infusion at 150 mg/kg BW restored sperm morphology to near-normal levels. Representative microscopic images of spermatozoa from all groups are shown in Figure 1.

As shown in Table 1, spermatozoa concentration was highest in the P4 group (310.0 ± 20.0 million/mL) compared with P3 (213.3 ± 15.2 million/mL) and P2 (90.0 ± 20.0 million/mL). These findings indicate that Malacca leaf infusion at a dose of 150 mg/kg BW effectively increased spermatozoa concentration in diabetic rats to near-normal levels.

According to Mitruka and Howard as cited in Vincent et al. (2004), the normal blood glucose level in male rats ranges from 50 to 135 mg/dL. In the present study, streptozotocin (STZ)-induced rats exhibited blood glucose levels exceeding 200 mg/dL (299 ± 109.57 mg/dL), indicating the development of hyperglycemia or diabetes mellitus (DM) and confirming their suitability as experimental models. Streptozotocin induction causes selective damage to pancreatic β-cells, leading to impaired insulin secretion and reduced insulin production (Hammam, 2008; Tabatabaei et al. 2008). The mechanism β-cells damage in pancreas due to DNA mathylation alkylation inhibits insulin secretion, thereby causing high blood sugar levels leading to type one DM (Tanko et al. 2008). Insulin deficiency disrupts glucose homeostasis and the metabolism of carbohydrates, lipids, and proteins, which subsequently affects male reproductive function, including sperm quality (Jangid et al. 2025).

Diabetes mellitus reduces male infertility by inducing oxidative stress that damages sperm quality and hormonal balance (Dena et al. 2025). The low spermatozoa motility in this study was most likely due to an increase in Reactive Oxygen Species (ROS). Increased ROS is oxidative for spermatozoa (Hammam 2008). ROS decreases the frequency of spermatozoa tail movements, causing reduced energy for spermatozoa tail movement. In addition, spermatozoa abnormalities also play a role in influencing motility. Spermatozoa with abnormal morphology cause weakness in spermatozoa movement (motility) (Fitriani et al. 2009).

Decreased spermatozoa viability in diabetic conditions is closely related to impaired insulin production. Arundani et al. (2021) stated that the content of flavonoid compounds in malacca leaf infusion is an antioxidant that protects cells from free radical damage. If the structure of the spermatozoa cell membrane is not damaged, the viability of spermatozoa will remain good, besides that flavonoids in malacca leaf infusion that are high enough can cause testosterone

Table 1. Average±SD number of spermatozoa quality calculation results of male white rat spermatozoa

Group Treatment	Spermatozoa Quality			
	Motility (%)	Viability (%)	Abnormalitas (%)	Concentration (Yx10^6)
P1	92.97±1.55^c	83.74±0.83^d	0.83±0.76^a	373.3±20.8^d
P2	28.05±0.84^a	22.29±0.97^a	14.02±1.66^c	90.0±20.0^a
P3	30.19±0.70^a	41.00±2.26^b	9.09±0.52^b	213.3±15.2^b
P4	38.88±1.23^b	59.24±2.26^c	2.00±0.50^a	310.0±20.0^c

Note: ^{a,b,c,d} Different superscripts in the same column show significan differences ($P<0.05$). P1 (Positive control), P2 (Negative control), P3 (Infuse of malacca leaves 100 mg/kg BW and STZ) and P4 (Infusion of flacca-leaves 150 mg/kg BW and STZ)

production to change. Testosterone is an important hormone for spermatogenesis process so changes in testosterone levels will have a direct impact on spermatozoa number, morphology, and viability.

Elevated ROS levels are strongly associated with declining sperm quality through oxidative stress mechanisms that damage lipid membranes, DNA, and protein structures, ultimately contributing to male infertility (Kothari et al. 2010; Agarwal et al. 2014). The high level of free radicals in the reproductive organs causes tissue changes in the testicles which are characterized by damage to the mitochondrial membrane of Leydig cells so the spermatogenesis process is disrupted. Disruption of the spermatogenesis process will cause the quality of the spermatozoa produced to decrease (Kunu et al. 2020). The administration of malacca leaf infusion has an effect on reducing the abnormality of DM rat spermatozoa, this shows that the active compounds contained in malacca leaf infusion can ward off free radicals in DM sufferers thereby reducing spermatozoa abnormalities. According to Kunu et al. (2020), tannin compounds have the potential to lower blood sugar levels and are able to increase glucose transport by activating insulin. Saponins function as anti-DM because they are able to regenerate the pancreas so that they can increase insulin secretion.

Based on table 1, it can be seen that the P4 group has a higher concentration level compared to P3 and P2 (310.0±20.0 million/ml vs 213.3±15.2 million/ml vs 90.0±20.0 million/ml) this indicates that the administration of malacca leaf infusion at dose of 150 mg/kg BW can increase the spermatozoa concentration of DM-induced rat close to normal rats. The results of previous research by Meliyana et al. (2016) reported the same thing but using a decoction of binahong leaves (*Anredera cordifolia*) on the quality of mouse spermatozoa (*Mus musculus*) DM.

Overall, administration of malacca leaf infusion improved spermatozoa quality, as evidenced by increased motility, viability, and concentration, accompanied by a reduction in abnormal sperm morphology. Ballester et al. (2004) stated that the improvement in spermatozoa quality is influenced by increased insulin production. The hormone insulin will lower blood sugar levels and launch the action of the pituitary hypothalamus as a function of the endocrine system in increasing the production of reproductive hormones. Increased insulin will increase the effects of gonadotropins (Luteinizing Hormone/LH and Follicle Stimullating Hormone/FSH) on Sertoli cells and Leydig cells in the testes. The hormone insulin will stimulate Leydig cells so that it will increase the function of Leydig cells and cause an increase in FSH receptors. Increased

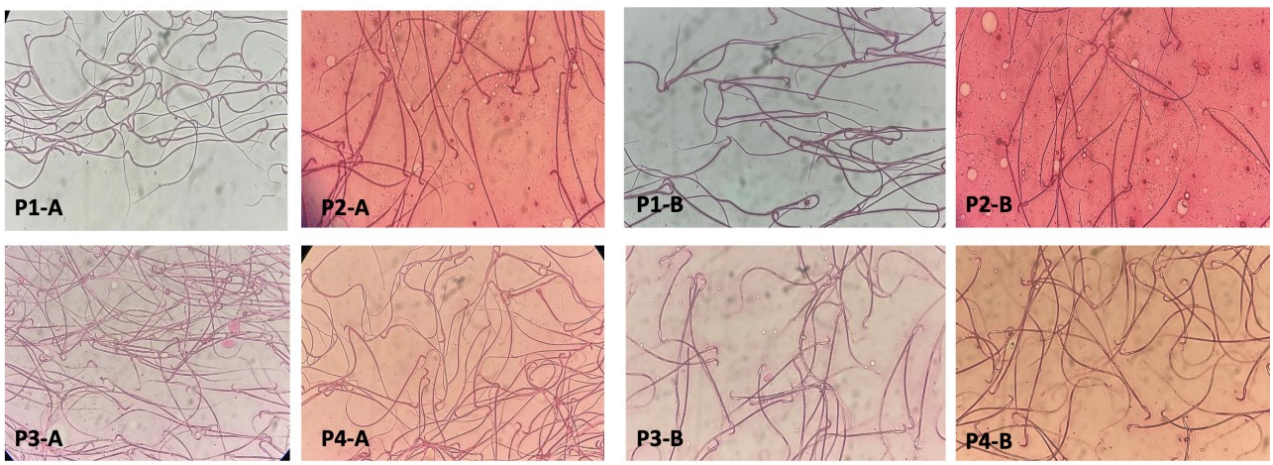

Figure 1. Micriscopic image of male rats spermatozoa. A. Viability, B. Abnormality. P1= Male rats + aquadesta as control positif, P2= Male rats + STZ 30 mg/kg BW as control negative, P3=Male rats + STZ 30 mg/kg BW + 100 mg/kg BW malacca leaf infusion, P4= Male rats + STZ 30 mg/kg BW + 150 mg/kg BW malacca leaf infusion (40x10 magnification)

FSH receptors increase FSH levels which also affect the increase in LH levels, further Sabirosi et al. (2014) stated that the increase will trigger an increase in the production of testosterone and Androgen Binding Protein (ABP) hormones used in the spermatogenesis process. The hormone testosterone will activate a gene in Sertoli cells that triggers spermatogonia differentiation to initiate spermatogenesis. The uninhibited process of spermatogenesis will produce spermatozoa of better quality.

CONCLUSION

Malacca leaf infusion demonstrates potential in ameliorating spermatozoa quality in diabetic rats, suggesting its therapeutic role in DM-induced reproductive dysfunction.

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AUTHORS CONTRIBUTION

J.M. and R.Z.S. carried out the animal experiment, collected samples, evaluated sperm quality parameters, and prepared the initial manuscript draft. M.A., C.N.T., B.P., and D.A. contributed to laboratory analyses, data collection, and interpretation of the results. N. supervised the research activities, assisted in study design and data interpretation, and critically reviewed the manuscript. N.A., as the corresponding author, conceived the study, coordinated the project, supervised the overall research process, and finalized the manuscript. All authors read and approved the final version of the manuscript.

"The author declares that there is no conflict of interest with parties involved in this research".

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