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Analysis of the Effects of Palm Oil Fruit Extract (*Elais Guineensis Jacq*) with Histopathological Evaluation of the Liver Tissue of Male Wistar Rats (*Rattus norvegicus*) with Diabetes Mellitus After Streptozotocin Induction

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Abstract

Hyperglycemia is a chronic condition that can cause serious complications, such as liver damage and elevated SGOT and SGPT enzyme levels, which are closely related to Diabetes Mellitus (DM). Palm fruit (*Elaeis guineensis* Jacq.), which is rich in antioxidants such as carotenoids, vitamin E, flavonoids, alkaloids, saponins, and tannins, has antidiabetic and hepatoprotective potential. Streptozotocin selectively damages pancreatic β-cells, causing oxidative stress and decreased blood insulin levels. This research aims to analyze the effect of palm fruit extract (*Elaeis guineensis* Jacq.) by observing steatosis, inflammation, fibrosis, and necrosis. This study is a laboratory experimental study with a post-test–only control group randomized experimental design. There were five groups that received treatment for 28 days, namely KN (negative control, pellet feed), KP (positive control, streptozotocin), P1 (treatment 1, streptozotocin 30 mg/kg BW and palm fruit extract dose 100 mg/kg BW), P2 (treatment 2, streptozotocin 30 mg/kg BW and palm fruit extract dose 200 mg/kg BW), and P3 (treatment 3, streptozotocin 30 mg/kg BW and palm fruit extract dose 300 mg/kg BW). The results of this study were analyzed using the Kruskal–Wallis test and the Mann–Whitney test for comparisons between two independent groups. The Kruskal–Wallis test showed that the group comparison results obtained a value of $p = 0.000$. The Mann–Whitney test showed significant differences in the comparisons of KP with P1, P2, and P3 ($p = 0.015 < 0.05$; $p = 0.007 < 0.05$; $p = 0.005 < 0.05$). The dose of 300 mg/kg BW of palm fruit extract was the most optimal dose for improving the histopathological appearance of liver tissue in male Wistar rats (*Rattus norvegicus*).

INTRODUCTION

The phenomenon of hyperglycemia is one of the urgent health problems affecting global society, with incidence and prevalence continuing to rise, particularly in developing countries (Alberti et al., 2020; Forouhi & Wareham, 2021). Serious complications related to diabetes mellitus (DM) can affect many vital organ systems, making diabetes mellitus one of the major chronic diseases of global concern (Jiang et al., 2021; Sun et al., 2021). This condition can lead to severe and irreversible pathological conditions, including cardiovascular disease, retinopathy, nephropathy, neuropathy, and hepatopathy (Janson et al., 2022; Li et al., 2020). The number of DM patients in Indonesia continues to increase. According to the International Diabetes Federation (IDF) data in 2017, Indonesia ranked sixth in the world in the number of people with diabetes mellitus, with approximately 10.3 million cases (IDF, 2017; Chen et al., 2020). Estimates by the International Diabetes Federation indicate a continued surge in cases. There were approximately 425 million people worldwide suffering from diabetes mellitus, with about 48% undiagnosed (Ng et al., 2021). The data are expected to continue increasing if preventive efforts are not implemented, and it is predicted that by 2045 the number will rise to

629 million DM patients (Jiang et al., 2021). In 2017, the mortality rate was estimated at 3.2–5 million deaths caused by DM among individuals aged 20–79 years (Zheng et al., 2018; Yang et al., 2020).

The prevalence of diabetes mellitus diagnosed by physicians in Indonesia, based on PERKENI 2015 guidelines for individuals aged ≥15 years, was reported in Riskesdas 2018 data at 10.9%. Compared with data from 2013, this represents an increase (Sari et al., 2020; Nugroho et al., 2021). According to Riskesdas 2018 data, the prevalence of DM in North Sumatra was 1.75%. The liver is a target organ commonly used in toxicological studies. It is also one of the organs susceptible to damage resulting from increased blood glucose levels or hyperglycemia (Singh et al., 2021; Kaur et al., 2020). Hyperglycemia in DM patients contributes to impaired glucostatic liver function (Zhao et al., 2020). Tissue damage caused by hyperglycemia interferes with insulin activity in target organs such as the liver and muscles (Jiang et al., 2021; Iqbal et al., 2019). The liver is also one of the major organs in the digestive system where carbohydrate, protein, and fat metabolism occur, and it functions as a storage site for nutrients absorbed from the digestive tract (Gao et al., 2020). Normal hepatocytes form plates of cells with a rounded nucleus and bright cytoplasm. Liver cell damage may initially begin with degeneration, which can return to normal because it is reversible. By controlling the mechanism of glycogen synthesis, the liver plays an important role in maintaining (buffering) postprandial hyperglycemia (El-Sayed & Ali, 2021; Li et al., 2022).

Hyperglycemic conditions in patients with diabetes mellitus (DM) cause significant changes in the histopathological appearance of liver tissue (Al-Shaeli et al., 2022; Işıldar & Koyutürk, 2025; Khales et al., 2024; Oyouni et al., 2022; Rajabi et al., 2025). These changes are characterized by the presence of inflammatory cell infiltration, fatty degeneration, and necrosis. Inflammatory cell infiltration refers to the infiltration of mononuclear cells such as lymphocytes, macrophages, and plasma cells, accompanied by tissue damage and blood vessel proliferation. The infiltration of inflammatory cells, including lymphocytes and Kupffer cells in the liver, indicates chronic or transitional inflammation. Fatty degeneration is characterized by morphological alterations and decreased liver function due to lipid accumulation in the cytoplasm. Necrosis is a condition of injury caused by cell death in normal tissue and is irreversible.

Tissue damage caused by hyperglycemia in DM patients occurs through various mechanisms, such as autooxidation, protein modification, and activation of the polyol metabolic pathway, which further accelerates the release of reactive oxygen species. One of the important organs in the human digestive system is the liver. The liver is an organ that is highly susceptible to the effects of hyperglycemia, which can result in oxidative stress and subsequently trigger liver damage. Liver damage caused by hyperglycemia is usually accompanied by abnormalities in carbohydrate, protein, and fat metabolism. Consequently, oxidative stress increases and triggers an inflammatory response in liver tissue. Another response resulting from disruption of carbohydrate, protein, and fat metabolism is the induction of apoptosis in hepatocyte cells and the release of inflammatory cytokines, which leads to increased expression of adhesion molecules and leukocyte infiltration. Ultimately, this can result in large-scale liver tissue damage and elevated levels of the enzymes serum glutamate pyruvate transaminase (SGPT) and serum glutamate oxaloacetate transaminase (SGOT).

Cases of diabetes mellitus (DM) in Indonesia continue to increase, highlighting the need for proper treatment to lower blood glucose levels and prevent complications associated with DM. Several non-pharmacological management strategies are recommended, such as lifestyle modifications, increased physical activity, and improved dietary choices. Pharmacological management includes the use of drugs that help lower blood glucose levels, such as sulfonylureas, biguanides, and acarbose. However, because these drugs are chemically based, they may produce side effects in the body. As a result of these side effects, research and

development related to herbal medicines have increased, as they are expected to have minimal side effects in future therapeutic applications.[8]

Due to the minimal side effects associated with herbal treatments, which are often considered anti-hyperglycemic therapies, several studies have shown favorable results in patients receiving herbal treatment. Oil palm (*Elaeis guineensis Jacq.*) is one of the plants that can be utilized.[10] Oil palm (*Elaeis guineensis Jacq.*) is one of the dominant commodity crops cultivated globally and is highly valued by the plantation industry. It plays an important role in agricultural trade. Indonesia is one of the largest palm oil producers in the world and ranks first as the leading producer of palm oil globally. Oil palm is one of the most strategic plantation commodities for strengthening the national economy because it is a major source of foreign exchange through agricultural exports and contributes significantly to the country's economic growth.

Palm oil produces various materials such as edible oils, industrial oils, and biofuels that provide numerous benefits. In addition to oil, palm fruit contains various compounds with potential applications in the food, health, and pharmaceutical sectors. Among the bioactive compounds present, phenolics and flavonoids have attracted considerable attention from researchers because of their strong antioxidant properties and potential health benefits. Antioxidant compounds can inhibit or prevent the oxidation of lipids, nucleic acids, or other molecules by blocking the formation or propagation of oxidative chain reactions. In the body, antioxidant compounds function as defenses against free radicals, protecting the body from the risk of degenerative diseases and slowing the aging process (anti-aging). Natural antioxidants are generally easier for the body to absorb, have better biological activity, and are considered relatively more effective in cancer prevention compared with synthetic antioxidants. The antioxidant compounds contained in oil palm fruit are diverse.

Previous studies have demonstrated the potential of palm oil fruit extract in alleviating oxidative stress and improving liver function. Research by Sasidharan et al. (2009) showed that palm oil fruit extract exhibited significant hepatoprotective effects, reducing inflammation and promoting tissue regeneration. Furthermore, studies by Faramayuda et al. (2024) highlighted the antioxidant properties of palm oil fruit, which could help mitigate the harmful effects of hyperglycemia on liver tissues. However, there is a gap in the literature regarding the specific histopathological effects of palm oil fruit extract on liver tissue in diabetes-induced animal models, particularly with respect to steatosis, inflammation, fibrosis, and necrosis.

The novelty of this research lies in its focus on evaluating the histopathological effects of palm oil fruit extract on the liver of male Wistar rats (*Rattus norvegicus*) with diabetes mellitus induced by streptozotocin (STZ). While previous studies have explored the antioxidant potential of palm oil fruit, few have examined its specific impact on liver tissue damage in DM models, especially with histopathological assessments. This study aims to fill this gap by investigating the effects of varying doses of palm oil fruit extract (100 mg/kgBW, 200 mg/kgBW, and 300 mg/kgBW) on liver tissue in diabetic rats.

The objectives of this research are to analyze the effects of palm oil fruit extract on liver histopathology, specifically examining steatosis, inflammation, fibrosis, and necrosis in Wistar rats with DM after STZ induction. This research will provide valuable insights into the hepatoprotective potential of palm oil fruit extract, which could serve as a promising alternative therapy for managing liver damage in DM patients.

The benefits of this research are twofold. Theoretical benefits include contributing to the understanding of the mechanism of action of palm oil fruit extract in mitigating oxidative stress and liver damage in DM, potentially enhancing current knowledge of herbal treatments for diabetes and its complications. Practically, the findings may offer a safe, effective, and low-cost alternative for DM management, particularly in preventing liver complications associated with the disease. Additionally, the results may guide future studies on the use of palm oil fruit

extract in clinical settings, providing a foundation for further research on its potential therapeutic applications.

METHOD

This study is laboratory experimental research with a research design in the form of a randomized post-test-only control group design to determine the effect of administering oil palm fruit extract (*Elaeis guineensis Jacq.*) with histopathological assessment of liver tissue in male Wistar rats (*Rattus norvegicus*) after streptozotocin induction. The research was conducted from August 2024 to January 2025.

Identification and characterization of phenolic compounds were carried out at the Plant Systematics Laboratory of the Department of Biology, Faculty of Mathematics and Natural Sciences (FMIPA), and the Faculty of Pharmacy, University of North Sumatra. The *in vivo* study was conducted at the Integrated Laboratory of the Faculty of Medicine, University of Muhammadiyah North Sumatra. The population in this study consisted of male Wistar rats (*Rattus norvegicus*) aged 2–3 months in healthy and active condition. The selection of Wistar rats (*Rattus norvegicus*) was based on their genetic similarity to humans, including similarities in anatomical structure and adaptability to the surrounding environment. This study used experimental animal samples of Wistar rats (*Rattus norvegicus*). Sampling was carried out randomly using a simple random sampling method that met the sample criteria. The sample size was calculated using Federer's formula.

Based on the calculation results using Federer's formula, the minimum sample size per group was five rats. Considering a 20% dropout rate and the research design requirements, the sample size used was six Wistar rats (*Rattus norvegicus*) for each group. Therefore, the total number of experimental animals required was 30 rats. Sample selection and grouping were carried out using the simple random sampling method. Each of the 30 samples that met the criteria was numbered, randomly selected by the researcher, and divided into five groups of equal size.

The research groups were divided as follows:

1) K1: Negative control (KN), rats were given only pellets and water.
2) K2: Positive control (KP), rats were given streptozotocin at a dose of 30 mg/kgBW.
3) K3: Treatment 1 (P1), rats were given a single dose of streptozotocin 30 mg/kgBW and oil palm fruit extract (*Elaeis guineensis Jacq.*) at a dose of 100 mg/kgBW for 28 days.
4) K4: Treatment 2 (P2), rats were given a single dose of streptozotocin 30 mg/kgBW and oil palm fruit extract (*Elaeis guineensis Jacq.*) at a dose of 200 mg/kgBW for 28 days.
5) K5: Treatment 3 (P3), rats were given a single dose of streptozotocin 30 mg/kgBW and oil palm fruit extract (*Elaeis guineensis Jacq.*) at a dose of 300 mg/kgBW for 28 days.

The inclusion and exclusion criteria were as follows.

Inclusion criteria:

1) Male Wistar rats (*Rattus norvegicus*)
2) Age 2–3 months
3) Body weight 250–350 g

4) Healthy rats characterized by active movement, no injuries, and no physical deformities.

Exclusion criteria:
1) Anatomical abnormalities in experimental rats
2) Rats that appeared sick during the adaptation period
3) Rats experiencing weight loss of more than 10% during the adaptation process
4) Rats that died during the treatment period.

Research tools used included:
1) Plastic cages measuring 20 × 25 × 15 cm with a wire-mesh lid
2) Digital weighing scale (Ohaus®, Germany)
3) Rat feeding and drinking containers
4) Gloves (Everglove®)
5) Masks (Sensi®)
6) Stationery
7) Experimental work table
8) Blood glucose test meter
9) Scissors
10) Surgical instruments
11) Gastric tube (oral gavage tube)
12) Glass slides and cover slips
13) Pipettes
14) Microtome and microtome blade
15) Tissue cassette
16) Light microscope.

Materials used included:
1) Oil palm fruit (*Elaeis guineensis Jacq.*)
2) Distilled water (aquadest)
3) Feed and husk
4) Streptozotocin (STZ)
5) EDTA
6) Ethanol 70%, 80%, and 96%
7) 10% neutral buffered formalin
8) Hematoxylin–eosin staining reagents.

The oil palm fruit used in the study was obtained from oil palm plantations in Serdang Bedagai Regency, North Sumatra Province. The preparation of oil palm fruit extract (*Elaeis guineensis Jacq.*) was conducted as follows. First, 1 kg of oil palm fruit (*Elaeis guineensis Jacq.*) was cleaned by washing. The fruit was then cut into smaller pieces and placed in an oven at 35°C to reduce its moisture content. The dried oil palm fruit was wrapped in filter paper and placed in a Soxhlet extractor. A 1000 mL round-bottom flask was filled with approximately 350 mL (one-third of the volume) of 70% ethanol and several boiling stones. Extraction was

carried out for approximately 10 hours until the solvent became colorless. The obtained extract was then evaporated using a rotary evaporator at 50°C until a concentrated extract was obtained.

Phytochemical testing of oil palm fruit extract (*Elaeis guineensis Jacq.*)

For the flavonoid test, 1 mg of oil palm fruit extract was placed into a test tube and dissolved in 2 mL of ethanol. Magnesium powder was added, followed by 4–5 drops of concentrated HCl solution. For the phenolic test, the extract solution was placed in a test tube and mixed with three drops of 3% $FeCl_3$ solution dissolved in ethanol to observe color changes. A color change to black, red, purple, green, or blue indicated a positive result.

Preparation of liver histological specimens

1) Fixation stage: Liver tissue was fixed in 10% formalin solution for 12–18 hours.
2) Dehydration stage: Tissue was dehydrated using 70%, 96%, and absolute alcohol twice for one hour each.
3) Clearing stage: The tissue was cleared using xylene for one hour to remove alcohol.
4) Embedding stage: Liver tissue was infiltrated with paraffin and placed in a freezer for two hours.
5) Sectioning stage: Tissue sections were cut using a manual microtome at a thickness of 3–5 µm and placed on glass slides.
6) Deparaffinization stage: Slides were soaked in xylene followed by absolute alcohol, 95%, and 70% alcohol for three minutes each.
7) Staining stage:
    a) Slides were immersed in xylene twice for two minutes.
    b) Slides were soaked in 95% alcohol for one minute.
    c) Slides were rinsed in running tap water for five minutes.
    d) Slides were stained with hematoxylin for two minutes and eosin 1% for two minutes, then placed in 95% alcohol for two minutes followed by absolute alcohol for two minutes.
    e) Slides were immersed in xylene for two minutes.
8) Mounting stage:
    a) Slides were allowed to dry at room temperature.
    b) After drying, the slides were ready for observation under a microscope for histopathological analysis.

Microscopic observation was performed using a light microscope in five fields of view at magnifications of 40×, 100×, 200×, and 400×.

Histopathological assessment of rat liver tissue

Histological preparations were examined under a microscope by observing multiple fields of view at magnifications of 40×, 100×, 200×, and 400×. The percentage of rat liver tissue damage was assessed histopathologically using the following criteria.

1) Steatosis: Macrovesicular steatosis with some microvesicular features characterized by large and small vacuoles. In macrovesicular steatosis, lipid droplets filled the cytoplasm of hepatocytes and displaced the nucleus to the cell periphery. Microvesicular steatosis

showed a foamy cytoplasmic appearance and was typically identified in single hepatocytes, often initially appearing in zone 3 of the hepatic acinus. Assessment score: None = 0.

2) Inflammation: Identified mainly by lobular inflammatory infiltrates. Portal inflammation was rare and generally associated with fibrosis stages. Lobular infiltrates included lymphocytes and Kupffer cell aggregates. Polymorphonuclear leukocytes (PMNs) and eosinophils could also be observed. Assessment score: None = no foci; Mild = up to 4 foci.
3) Fibrosis: Characterized by the formation of fibrous connective tissue in liver tissue with varying severity levels. Fibrosis typically presented a "chicken wire" pattern and initially appeared in zone 3 of the liver. Severity levels:
    a) 0 = No fibrosis
    b) 1 = Perisinusoidal fibrosis in zone 3
    c) 2 = Perisinusoidal and portal/periportal fibrosis in zone 3
    d) 3 = Bridging fibrosis or lobular septal fibrosis.
4) Necrosis: Irreversible hepatocyte damage or cell death resulting from severe liver injury. Necrosis patterns included apoptosis (programmed cell death), spotty necrosis involving small groups of hepatocytes, zonal necrosis involving specific hepatic zones such as centrilobular zone 3, and confluent necrosis affecting multiple liver lobules.

Ethical considerations

Ethical approval for the study was obtained from the Health Research Ethics Commission of the University of Muhammadiyah North Sumatra.

Acclimatization of experimental animals

Rats that met the inclusion criteria were acclimatized in the laboratory for one week to ensure uniform physiological conditions prior to the experiment. During this period, the rats were provided with pellet feed and drinking water *ad libitum*.

Induction of hyperglycemia

Hyperglycemia in male Wistar rats (*Rattus norvegicus*) was induced by intraperitoneal injection of streptozotocin (STZ) at a dose of 30 mg/kgBW after a 16-hour fasting period. Hyperglycemia was confirmed 72 hours after STZ injection by measuring fasting blood glucose levels. Rats with blood glucose levels greater than 140 mg/dL were considered diabetic and included in the experiment.

Blood glucose levels were measured using a glucometer by cutting approximately 1 mm from the tip of the rat's tail using scissors. Blood droplets were applied to the glucometer test strip, and the displayed value was recorded. Blood glucose measurements were performed on day 0 and day 3 after STZ induction. Following a 7-day acclimatization period and STZ induction on day 11, the rats received oil palm fruit extract (*Elaeis guineensis Jacq.*) treatment for 28 days.

Data processing

After data collection, the data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS) program. The data were tabulated and entered into a computer for analysis using SPSS. Data processing was conducted through the following steps:

1) Editing: Checking the completeness of data on observation sheets.
2) Coding: Classifying data into appropriate categories.
3) Data entry and processing: Entering collected data into the SPSS program for analysis and tabulation.
4) Cleaning: Rechecking data for possible entry errors.
5) Saving: Storing the finalized dataset for analysis.

Data analysis

The results of this study were analyzed using non-parametric statistical tests. The Kruskal–Wallis test was used to determine overall differences among groups, followed by the Mann–Whitney test to compare differences between individual groups. All statistical analyses were performed using SPSS Statistics for Windows Release 25.0.

RESULTS AND DISCUSSIONS

Table 1. Results of Phytochemical Test of Oil Palm Fruit Extract (Elais guineensis Jacq.)

Parameter	Reaction	Observations
Flavonoid	+	Reddish-orange color formed
Alkaloid	+	Formed white (Meyer) Formed red brick (Dragendorf)
Saponins	+	Foam formed
Tannins	+	Formed a blackish-green color

Source: Adapted from Faramayuda et al., 2024

Based on Table 1. It is proven that there is oil palm fruit extract (*Elais guinennsis jacq*) that has bioactive compounds in the form of flavonoids, alkaloids, saponins, tannins, triterpenoids.

Overview of Histopathology of Liver Tissue and Hepatic Histopathology Scoring for Each Group Hepatic histopathology examination was carried out at the Histology Laboratory of the University of Muhammadiyah North Sumatra using an Olympus light microscope with TrueChrome III software with 40x, 100x magnification. From the results of research that has been carried out on the histopathology of the liver of male rats of the wistar strain (*Rattus norvegicus*) at the University of Muhammadiyah North Sumatra after the administration of oil palm fruit extract (*Elais guinennsis jacq*.), the following histopathological picture was obtained:

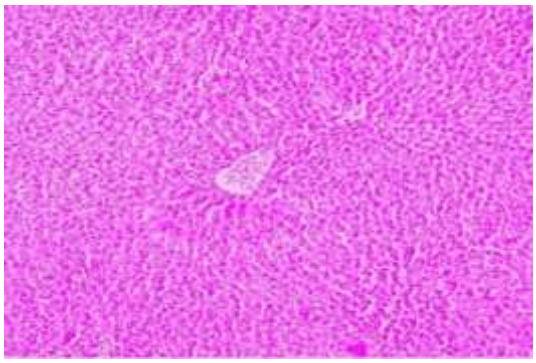

Figure 1. The histopathological picture of the KN group was magnified 100x with 0 degrees, the cell boundaries were firm, and the nucleus of hepatocyte cells was clearly visible, there was no picture of steatosis in the negative control group.
Source: Primary data, 2026

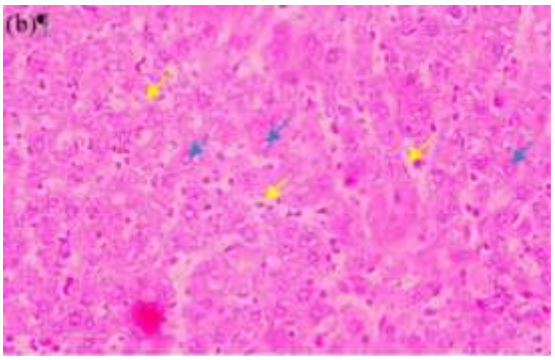

Figure 2. Histopathological picture of the KP group with 100x magnification with Assessment of steatosis of the 3rd degree, the yellow arrow indicates the boundary between the cells is not firm, and the blue arrow indicates steatosis with this being pushed to the edge on hepatocyte cells.
Source: Primary data, 2026

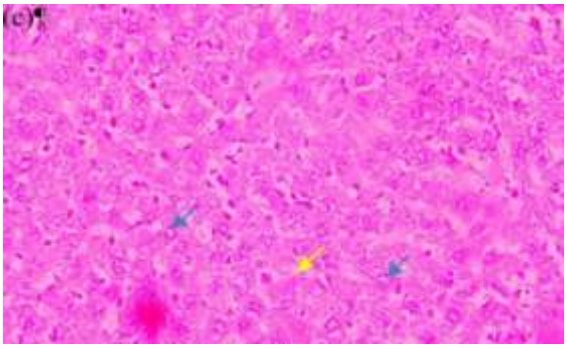

Figure 3. Histopathological picture of the P1 group magnified 100x with Assessment of 2nd degree steatosis, the yellow arrow indicates the formation of tissue repair at the hepatocyte cell boundary, in the blue arrow there is an improvement in the form of a reduction in the number of hepatocyte cells that experience steatosis
Source: Primary data, 2026

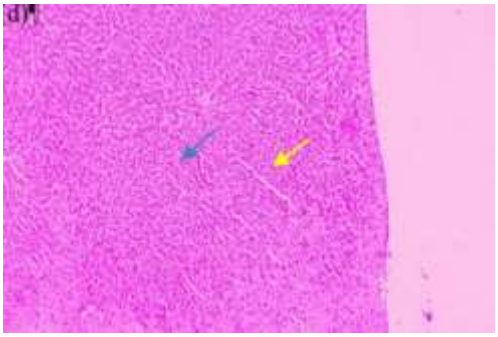

Figure 4. Histopathological picture of the P2 group magnified 100x with an assessment of steatosis of degree 1, on the yellow arrow the cell boundary is visible, the blue arrow indicates almost no cells are found hepatocytes that undergo steatosis.
Source: Primary data, 2026

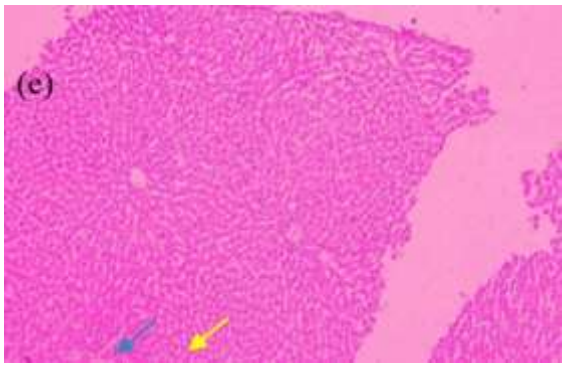

Figure 5. Histopathological picture of the P3 group magnified 100x with 0 degrees, the cell boundaries were firm, no hepatocyte cells were found that underwent steatosis
Source: Primary data, 2026

Tabel 2. Histopathology Scoring Results

Steatosis	Groups				
No.	**KN**	**KP**	**P1**	**P2**	**P3**
1	0	3	2	1	0
2	0	3	2	1	0
3	0	2	1	1	0
4	0	3	2	2	1
5	0	3	2	1	0

Source: Primary data, 2026

Remarks : K- : Negative control was given pellet feed and drinking K+: Positive control was given STZ 30 mg/kgBB to each rat P1 : Treatment group 1 was given STZ injection and induction of oil palm fruit extract (*Elais guinennsis jacq*) at a dose of 100 mg/kgBB. P2: Treatment group 2 was given STZ injection and induction of oil palm fruit extract (*Elais guinennsis jacq*) at a dose of 200mg/kgBB. P3 : Treatment group 3 was given STZ injection and induction of oil palm fruit extract (*Elais guinennsis jacq*) at a dose of 300mg/kgBB.

To determine the significant scoring difference for each group, the Kruskal Wallis test was carried out, which is a non-parametric test that functions to determine that there is a significant difference between two or more groups of independent variables and categorically scale dependent variables.

Table 3. Kruskal Wallis Test

Groups	N	P-Value
KN	5	
KP	5	
P1	5	0,000
P2	5	
P3	5	

Source: Primary data, 2026

Based on the results of the Kruskal-Wallis test in table 3, the values of $p = 0.000 < 0.005$ were obtained, so it can be concluded that there is a significant difference between the control variables and the results of the histopathological improvement of liver tissue improvement in

Wistar strain rats (*Rattus norvegicus*) diabetes mellitus. Furthermore, the Mann-Whitney post-hoc test was used to test the significance of the difference in scoring between groups.

Tabel 4. Mann-Whitney Test

Scoring Comparison	P-Value	P	Meaning
KP and KN	p : 0,004	< 0.05	Significant
KP and P1	p : 0,015	< 0.05	Significant
KP and P2	p : 0,007	< 0.05	Significant
KP and P3	p : 0,005	< 0.05	Significant
KN and P1	p : 0,004	< 0.05	Significant
KN and P2	p : 0.004	< 0.05	Significant
KN and P3	p : 0.317	> 0.05	Insignificant
P1 and P2	p : 0.072	> 0.05	Insignificant
P1 and P3	p : 0.007	< 0.05	Significant
P2 and P3	p : 0.015	< 0.05	Significant

Source: Primary data, 2026

Based on the results of the Mann-Whitney test in table 4 of the Man-Whitney test, the results were obtained that there was an effect of administering oil palm fruit extract on the histopathological picture of the liver of male rats of the Wistar strain (*Rattus norvegicus*) that had been induced by diabetes mellitus.

The results of the analysis of the table above show that the positive group (KP) has a significant difference with the negative group (KN) as well as the treatment group 2 (P2) and treatment 3 (P3). This shows that in P2 and P3 there is a change effect on the histopathological picture of the liver of rats that have been induced by streptozotocin (STZ), while in the positive group (KP) with treatment 1 (P1) there are significant results of this showed that oil palm fruit extract (*Elais guinennsis jacq*) already had an effect on histopathological changes in rat liver tissue.

In the negative group (KN) there was a significant difference in njlai with P1 and P2, indicating the effect of the administration of oil palm fruit extract (*Elais guinennsis jacq*) on the histopathological picture of rat liver tissue but not optimal. Meanwhile, P3 has insignificant changes to KN, which means that the administration of oil palm fruit extract (*Elais guinennsis jacq*) to P3 has a good effect on the repair of liver tissue of male rats of the wistar strain (*Rattus norvegicus*).

In the treatment group, significant differences were found between P1 to P3 and P2 to P3. However, there was a non-significant difference between P1 and P2, which means that the group had the same effect in repairing damage to the histological picture of liver tissue in male rats of the wistar strain (*Rattus norvegicus*).

This study observed the antioxidant effect of oil palm fruit (*Elais guinennsis jacq*) on the histopathological picture of the liver of male rats of the wistar strain (*Rattus norvegicus*) that were damaged by the administration of streptozotocin (STZ). Changes in the histopathology of rat herpaste in the form of steatosis, inflammation, fibrosis, necrosis are a score for damage to hepatocyte cells of liver tissue.

In the operational definition, the parameters to be seen from the improvement of histopathological liver tissue in male rats (*Rattus norvegicus*) consist of several things, namely: steatosis, inflammation, fibrosis, and necrosis. After assessing the liver tissue preparations of the rats, only the scoring of improvement from liver tissue damage for the steatosis parameters

was found, and for other parameters such as inflammation, fibrosis, and necrosis could not be identified in the preparations, because the STZ dose applied to the test mice was low enough that there was less impact on liver organ damage and the parameters were not identified. The score scale for hepatocyte cells that experience steatosis is: 0 degrees : 60% (Severe).

The results of histopathological observations in the negative control group (KN) who were only given pellet feed and drinking were not found to be damaged and hepatocyte cells appeared normal with a steatosis assessment degree of 0. The positive group (KP) who were given pellet feed, drinking and streptozotocin at a dose of 30 mg/kgBB were found to have hepatocyte cell damage in the form of steatosis of degrees 3 and 2 or as much as 30->60% of the field of view.

In this study, the results of histopathological observations of the liver of positive group rats (KP) given streptozotocin showed a picture of hepatocyte cells in the form of steatosis (degeneration). This is in line with the research of Silvana et al, which found a histopathological picture in the liver of streptozotocin-induced rats (STZ) in the form of damage to the histological structure of the liver including degeneration in hepatocyte cells of the liver tissue of male rats of the Wistar strain (*Rattus norvegicus*). The diabetogenic effects are toxic to liver tissue, the induction of streptozotocin in Wistar rats (*Rattus norvegicus*) which causes hyperglycemia due to oxidative stress occurs through the mechanism of NO donors which causes destruction in cells.

beta pancreas through DNA alkylation thus causing DNA fragmentation that alters the DNA of cells β pancreas. Inhibited activity of the krebs cycle can reduce oxygen consumption by mitochondria so that there is a decrease in ATP β pancreatic cells resulting in hyperglycemia, Increased expression of GLUT-2 in mouse hepatocyte cells that due to oxidative stress. High blood glucose levels due to STZ induction cause β cell failure, thus allowing a response to increase the expression of GLUT-2 stimulated by the presence of glucose in hepatocyte cells on gene transcription. Increased expression of GLUT-2 will have an impact on the number of glucose transporters (GLUT-2) in the pancreatic organ which decreases but increases in number in the liver.

The results of histopathological picture analysis in KN and KP showed a significant difference ($p = 0.004<0.05$) which means that the damage to the hepatic histopathological picture was greater in KP given streptozotocin (STZ) at a dose of 30 mg/kgBB compared to KN who was only given pellet feed, and drinking. Research by Nengah et al (2018) showed that with an injection dose of streptozotocin (STZ) at a dose of 40 mg/kgBB, it can make white male mice diabetes mellitus. This statement is in accordance with the research of Silvana et al. (2024) which states that the administration of streptozotocin 40 mg/kgBB can cause damage to the histology of rat liver tissue through a decrease in the activity of antioxidant enzymes such as glutathione peroxidase, superoperoxide, dismutase, catalase, and significantly increase malondialdehyde and ROS.

The P1 group given streptozotocin (STZ) at a dose of 30 mg/kgBB and oil palm fruit extract (*Elais guinennsis jacq*) at a dose of 100 mg/kgBB showed a significant difference ($p = 0.015<0.05$) with KP given streptozotocin at a dose of 30 mg/kgBB. The damage that occurred in the P1 group obtained a score of 3-2 (steatosis occurred in hepatocyte cells with a tissue damage area of 30->60%). This proves that the administration of oil palm fruit extract (*Elais guinennsis jacq*) at a dose of 100 mg/kgBB has minimal effect on the improvement of the

histological structure of the liver of rats that have been damaged, and in KN that has a histological picture of the liver with degree 0 (normal) the P1 group has a significant difference ($p = 0.004<0.05$) and this means that the administration of oil palm fruit extract (*Elais guinennsis jacq*) protects maximally the damage to the liver of rats Exposure to toxic streptozotocin. P1 also had an insignificant value ($p = 0.072>0.05$) to the P2 group, which means that P1 had the same effect on the histopathological picture of streptozotocin-induced rats. In contrast to the P1 group compared to P3 which had a significant value ($p = 0.007<0.05$) which meant a smaller dose of palm oil extract (*Elais Guiennsis jacq*) in the treatment group had a minimal effect on the histopathological picture of streptozotocin-induced rats.

P2 was the group that was given streptozotocin at a dose of 30 mg/kgBB and oil palm fruit extract (*Elais Guiennsis jacq*) at a dose of 200 mg/kgBB showed a significant difference ($p = 0.007<0.05$) with KP given streptozotocin at a dose of 30 mg/kgBB. The P2 group had a score of 1 to 2 (histopathological picture in the form of steatosis with a damage area of 10-60%), P2 also had a significant value on KN ($p = 0.004<0.05$) which means that the administration of oil palm fruit extract (*Elais Guiennsis jacq*) to the group did not have maximum results in correcting the damage to the histopathological picture of liver tissue of male rats of the wistar strain (*Rattus norvegicus*).

P3 was the group that was given streptozotocin 30 mg/kgBB and palm oil extract (*Elais Guiennsis jacq*) at a dose of 300 mg/kgBB showed a significant difference ($p = 0.005<0.05$) with KP given streptozotocin at a dose of 30 mg/kgBB. P3 has an assessment of 0-1 degrees (histopathological picture in the form of steatosis with an area of <10-30%). Meanwhile, when compared to KN, P3 has an insignificant difference ($p = 0.317>0.05$) so, from the results analyzed from the histopathological results of the liver in the P3 group given a dose of palm oil extract (*Elais Guiennsis jacq*) of 300 mg/kgBB has maximum effectiveness in repairing liver tissue damage in male rats of the Wistar strain (*Rattus norvegicus*).

This is related to the antioxidant content contained in palm oil such as flavanoids, alkaloids, saponins, tannins which can cause a decrease in oxidative stress as a result of which the body's need for natural antioxidant defense in the early stages is reduced, so that lower antioxidant enzyme activity is enough to maintain MDA levels within normal physiological limits.

Flavanoids are compounds that have the potential to be antidiabetic and provide a protective effect against damage to this DNA (nDNA) and mitochondrial DNA (mtDNA) due to the reactivity of oxygen compounds (ROS), in the process of recovering from degenerative diseases, flavanoids work as antioxidants that can repair damaged pancreatic beta cells. In addition, flavanoids also function to delay, prolong and, prevent lipid oxidation that contributes to the formation of MDA, as well as increase the sensitivity of insulin receptors so that they can overcome insulin deficiency.

Alkaloids are phytochemical compounds that have significant potential in the management of diabetes mellitus through various stages of mechanisms, such as inhibiting the activity of glucosidase enzymes in the intestine to slow down the glucose absorption process, increasing insulin secretion from pancreatic beta cells, and also modulating metabolic pathways through the activation of AMP-activated protein kinase AMPK which increases insulin sensitivity and reduces glucose production by the liver. In addition, alkaloids act as antioxidants that protect cells, including, including pancreatic beta cells, from damage due to oxidative stress

and have anti-inflammatory effects that can reduce the risk of complications in diabetes cases. Saponins act as blood sugar levels controllers and prevent diabetic complications, the hypoglycemic ability of saponins works through various stages of mechanisms, such as stimulating glycogen synthesis, inhibiting the activity of disaccharide enzymes, regulating release of insulin from pancreatic beta cells, as well as inhibiting the activity of the enzyme alpa-glucosidase

CONCLUSION

There was an improvement in the histopathological picture of streptozotocin-induced rat liver tissue in treatment group 1 which was given 100 mg/kgBB and treatment group 2 which was given 200 mg/kgBB of oil palm fruit extract (*Elais Guiennsis jacq*) for 28 days, namely a minimal reduction in steatosis in hepatocyte cell tissue in the liver of male rats of the wistar strain (*Rattus norvegicus*). There was a histopathological picture of streptozotocin-induced rats in treatment group 3 who were given 300 mg/kgBB of oil palm fruit extract (*Elais Guiennsis jacq*) for 28 days, namely a maximum reduction in staetosis in hepatocyte cell tissue in the liver of male rats of the wistar strain (*Rattus norvegicus*). The administration of palm oil extract (*Elais guinennsis jacq*) at a dose of 300 mg/kgBB is better than the administration of palm oil extract (*Elais guinennsis jacq*) at a dose of 100 mg/kgBB and 200 mg/kgBB. Further studies should explore the long-term effects of palm fruit extract on liver function in diabetic models and assess the potential for combining this treatment with other therapeutic strategies for enhanced efficacy. Additionally, future research could investigate the molecular mechanisms behind the extract's antioxidant and anti-inflammatory properties to better understand its therapeutic potential.

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