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The Effect of Administration of Leilem Leaf Extract (Clerodendrum Minahassae) on the Histopathological Features of the Liver in Wistar Rats (Rattus Norvegicus) Induced with Cap Tikus Alcoholic Beverage

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KEYWORDS
Clerodendrum Minahassae;
Leilem Leaf Extract;
rat stamp;
Alcoholic liver Damage;
Histopathology.

ABSTRACT
Excessive alcohol consumption, including traditional alcoholic beverages such as Cap Tikus (alcohol content ±45%) from North Sulawesi, can induce liver damage characterized by steatosis, inflammation, and necrosis. Leilem leaf (Clerodendrum minahassae) extract, rich in phenolic and flavonoid compounds, has potential hepatoprotective effects due to its antioxidant properties. Purpose: To evaluate the effect of Leilem leaf extract on the histopathological features of the liver in Wistar rats (Rattus norvegicus) induced by Cap Tikus alcoholic beverage. This experimental study used a post-test-only control group design with 24 male Wistar rats divided into four groups: normal control, negative control (Cap Tikus 2.16 mL/day), treatment I (Leilem extract 150 mg/kgBW + Cap Tikus), and treatment II (Leilem extract 300 mg/kgBW + Cap Tikus). Treatments were administered orally for 14 days. Liver tissue was processed for histopathological examination using hematoxylin-eosin staining and observed under a light microscope. The negative control group showed significant steatosis and inflammatory cell infiltration. The treatment groups exhibited reduced steatosis and inflammation, along with increased hepatocyte regeneration. The higher dose (300 mg/kgBW) demonstrated greater hepatoprotective effects and more prominent regeneration compared to the lower dose (150 mg/kgBW). No necrosis or fibrosis was observed in any group. Leilem leaf extract exerts a hepatoprotective effect by suppressing inflammatory responses and enhancing hepatocyte regeneration in Wistar rats induced with Cap Tikus. The highest protective efficacy was observed with Leilem leaf extract at 300 mg/kgBW.

INTRODUCTION

The liver is a central organ that plays an important role in xenobiotic metabolism and in processing certain compounds (Esteves et al., 2021; Mohajan, 2025; Vicidomini et al., 2024). Severe liver damage, including cirrhosis, steatohepatitis, and hepatitis, is often associated with alcohol consumption (Sawin et al., 2024). This habit makes liver disease a significant global health threat. According to the World Health Organization (WHO), liver disease accounts for about 2 million deaths globally each year, equivalent to 4% of the total death toll worldwide (World Health Organization, 2024).

Consumption of alcoholic beverages in large quantities—around 80 grams per day—can generally cause mild liver damage that is still reversible, while the consumption of 50–60

grams per day is considered a safe limit to avoid the risk of liver disease (Kumar et al., 2014). Alcohol addiction is now a significant health problem. Data from the World Health Organization (WHO) in 2018 show that 43% of the world's population consumes alcoholic beverages (Hammer et al., 2018). The Health Research and Development Agency (2018) noted that there is excessive alcohol consumption in various regions of Indonesia, with around 3% of the population over 10 years old consuming alcoholic beverages, and 38.7% of them choosing traditional alcoholic beverages (Riskesdas, 2018a). North Sulawesi Province recorded the highest percentage of alcohol drinkers in the same year, reaching 16% among the population over 10 years old (Riskesdas, 2018a). Excessive alcohol consumption not only increases the risk of liver damage but can also lead to impaired functioning of other organs and serious metabolic complications (Rehm et al., 2021).

The main impacts of chronic alcoholism on the liver include fatty liver, alcoholic hepatitis, and cirrhosis (Kumar et al., 2014). By 2024, the World Health Organization (WHO) reported that 42% of deaths from hepatic cirrhosis were related to alcohol consumption, with patients suffering from alcohol use disorders (AUD) having a 35% chance of developing alcoholic liver disease (ALD) (Azizi et al., 2023). Previous studies in Jakarta showed that 16.4% of cirrhosis cases had alcohol-related causes (Lesmana et al., 2020). Behavioral data from Riskesdas in 2018 show that 3.0% of the Indonesian population consumes alcohol, with an uneven geographic distribution (Riskesdas, 2018b). North Sulawesi Province has the third-highest prevalence of alcohol consumption, at 10.9%, making it at higher risk for a greater burden of ALD (Riskesdas, 2018b).

Regional alcoholic beverages can be found in several parts of Indonesia, one of which is Cap Tikus from North Sulawesi. Initially, this drink was consumed by farmers as a body-warming beverage while working or traveling. Today, Cap Tikus is produced using modern methods and is officially sold in stores with an alcohol content of about 45% (Lungan, 2017; Hidayat et al., 2025).

Plant extracts with a high phenolic content have the ability to suppress inflammation and scar tissue formation in the liver caused by alcohol, a condition that characterizes alcoholic liver disease (Zhao et al., 2021). The use of herbal ingredients is one of the alternatives for hepatoprotective therapy, including the use of Leilem leaves. Leilem leaves are rich in polyphenolic compounds with strong antioxidant potential and have a high content of total flavonoids and phenolics, which function to reduce oxidation caused by free radicals (Rachmatiah et al., 2022). Previous research has also shown that Leilem leaf extract can inhibit lipid oxidation, thereby protecting liver tissue from oxidative stress induced by alcohol consumption (Kairupan et al., 2019).

The research by Vania et al. (2024) demonstrated that administration of Leilem leaf extract promotes liver cell regeneration and reduces hepatocellular damage caused by toxic doses of paracetamol. However, its effects on liver injury induced by Cap Tikus alcoholic beverages have not yet been established. Researchers are therefore interested in investigating the effect of Leilem leaf extract on the histopathological characteristics of the liver in Wistar rats (*Rattus norvegicus*) treated with Cap Tikus (Vania et al., 2024).

While the hepatoprotective effects of Leilem leaf extract against paracetamol-induced toxicity have been documented, its effectiveness against liver damage specifically induced by

Cap Tikus—a widely consumed local alcoholic beverage—remains unexplored. This research gap highlights the need for further studies to evaluate the potential of this local plant as a targeted intervention for ALD, particularly in regions such as North Sulawesi where Cap Tikus consumption is prevalent. Therefore, this study is novel in its aim to evaluate the effect of Leilem leaf extract on the histopathological features of the liver in Wistar rats induced with Cap Tikus, building directly upon the methodologies and findings of Rembang et al. (2020) and Vania et al. (2024).

The general purpose of this study was to determine the effect of administering Leilem leaf extract (Clerodendrum minahassae) on the histopathological features of the liver in Wistar rats (Rattus norvegicus) induced by Cap Tikus alcoholic beverages. More specifically, this study aimed to evaluate the hepatoprotective effect of Leilem leaf extract (Clerodendrum minahassae) against liver damage induced by Cap Tikus in Wistar rats (Rattus norvegicus). The specific objectives of this research include: first, to evaluate the histopathological changes in the liver, including the degree of steatosis, inflammation, and necrosis, in Wistar rats induced with Cap Tikus; second, to compare the liver histology of Wistar rats between the negative control group and the groups pre-treated with Leilem leaf extract, to assess possible hepatoprotective effects; and third, to analyze the hepatoprotective potential of Leilem leaf extract at doses of 150 mg/kgBW and 300 mg/kgBW on the liver histopathology of Wistar rats induced with Cap Tikus alcoholic beverages.

The benefits of this research can be viewed from several perspectives. Academically, it contributes to expanding knowledge about the hepatoprotective effects of Leilem leaf extract against liver damage induced by Cap Tikus alcoholic beverages. In the field of research and development, the results may serve as a reference for further studies on the potential use of Leilem leaf extract to counteract alcohol-induced liver injury. In terms of community outreach, this study is expected to provide useful information to the public regarding the potential of Leilem leaf extract as a hepatoprotective agent against liver damage caused by alcoholic beverages.

METHOD

Types of Research

This study is an experimental laboratory research in vivo.

Research Time and Location

The research will be carried out in August 2025-January 2026. The extract manufacturing stage was carried out at the UPT Integrated Laboratory of Sam Ratulangi University, while the animal experiment stage and tissue analysis were carried out at the Anatomy Pathology Laboratory, Faculty of Medicine, UNSRAT, Manado.

Research Design

This study is a true experimental research with a post-test only control-trial group design approach.

Research Subject

The research subjects used were male rats (Rattus norvegicus) aged 2-3 months with a weight of 150-200 grams. The research subjects were divided into 4 groups with the number of test animals in each group determined using Federer's formula, namely:

$$(t-1)\ (n-1) \geq 15$$

Description:
t = Treatment group
n = Number of experimental animals per group
In this study, the mice were divided into 4 treatment groups, so that the number of samples required for the study was as follows:

$$(t-1)\ (n-1) \geq 15$$
$$(4-1)\ (n-1) \geq 15$$
$$3(n-1) \geq 15$$
$$3N-3 \geq 15$$
$$3n \geq 18$$
$$n \geq 6$$

Based on the calculation of the formula, it was obtained that the number of samples for each treatment group was greater than or equal to 6, so that the total sample required for the 4 experimental groups was greater than or equal to 24 mice. In this study, 24 male wistar rats were used which were divided into 4 experimental groups, namely:

a. Wistar mice for normal control group: 6
b. Wistar rats for negative groups : 6 Fish
c. Wistar rats for treatment group I : 6 Fish
d. Wistar rats for treatment group II : 6 Fish

Research Variables

1. **Independent Variables**

   The independent variables in the study were leilem leaf extract (Clerodendrum minahassae) and rat stamp alcoholic beverage.

2. **Bound Variables**

   The bound variable in this study is the histopathological picture of the liver of wistar rats (Rattus norvegicus).

Inclusion and Exclusion Criteria

1. **Inclusion Criteria**
   a. Male white rats of the wistar strain (Rattus norvegicus) that have an age of 2-3 months and weigh about 150-200 g.
   b. White rats of the wistar strain (Rattus norvegicus) used in good health, can move actively, and have never been used in previous research activities.

2. Exclusion Criteria

a. White rats of the wistar strain (Rattus norvegicus) that died during the research process.
b. White rats of the wistar strain (Rattus norvegicus) who are in a sick condition, judging from the appearance, namely the hair of the rats falling out or bald, look dull, little active or inactive while the research is ongoing.

Variable Operational Definition

1. Wistar Rats

This study used white rats of the wistar strain (Rattus norvegicus). The wistar rats used are adult male rats aged 2-3 months and weigh about 150-200 g.

2. Rat Cap

Cap Tikus is a traditional alcoholic drink typical of North Sulawesi with an alcohol content of around 45%, which is used as an agent to induce liver damage in test animals. In this study, Cap Tikus was administered orally at a dose of 2.16 mL per rat per day using a gastric probe. This dose is based on previous research that showed that the administration of such doses can cause pathological changes in the liver tissue of the wistar mice, such as steatosis and inflammation of hepatocytes (Hidayat et al., 2025).

3. Leilem Leaf Extract

The leaves of leilem (Clerodendrum minahassae) used in this study were picked directly from a tree in Paal Dua, Manado City, North Sulawesi, then identified by the Biology Section of FMIPA, Sam Ratulangi University. Ethanol extract of leilem leaves is made by maceration method at the UPT Integrated Laboratory of Sam Ratulangi University. In a model of paracetamol-induced liver damage, leilem leaf extract was shown to have a hepatoprotective effect through the mechanism of hepatocyte cell regeneration and inhibition of the inflammatory response at doses of 150 mg/kgBW and 300 mg/kgBW (Vania et al., 2024).
Leilem leaf extract will be administered through a sonde to experimental mice.

4. Histopathological Overview of the Liver of Wistar Rats

The histopathological picture of the liver of wistar rats is a microscopic picture of liver tissue stained with hematoxilin-eosin (HE). The parameters assessed were liver tissue damage in the form of steatosis, ballooning degeneration of hepatocytes, necrosis, inflammatory cell infiltration, and perisinusoidal fibrosis.

Research Instruments

1. Tools

a. For animal cage equipment try
   1) Experimental animal cage
   2) Water bottles

3) Food containers
4) Wire and gauze enclosure cover
5) Husk

b. For test animal treatment equipment
   1) Gastric tube
   2) Gloves
   3) Mask
   4) Disposable 1 and 5 ml

c. For the manufacture of leilem leaf extract

   1) Containers for leilem leaf extract
   2) Blender
   3) Analytical scales
   4) Rotary evaporator
   5) Oven

d. For the collection of liver of experimental animals as well as the observation of histopathological preparations of experimental animal liver

   1) Place of autopsy
   2) Scissors
   3) Needle
   4) Tweezers
   5) Scalpel or scalpel
   6) Glass objects
   7) Containers for fixation and dehydration

2. Ingredients

a. Leilem leaves
b. Ratcap 2.16 ml
c. Wistar rat food
d. Aquades
e. Tissue fixation material (formalin 10%)
f. Leaf maceration material (95% ethanol)
g. Paraffin soaking materials and dyeing (acetone and xylol paraffin)

3. Research Principles

In this study, wistar rats were given leilem leaf extract (*Clerodendrum minahassae*) using an oral sonde with two dose variations (150 mg/kgBW and 300 mg/kgBW) after inducing hepatotoxicity using Cap Tikus alcoholic beverage at a dose of 2.16 mL/day orally. Such doses have been shown to induce acute liver damage in wistar rats, characterized by hepatocellular steatosis, hydropic degeneration, and inflammatory cell infiltration (Hidayat

et al., 2025).The administration of leilem leaf extract is suspected to have a hepatoprotective effect through an antioxidant mechanism that is able to inhibit and prevent liver cell damage due to exposure to free radicals and oxidative stress induced by Cap Rat.

RESULTS AND DISCUSSIONS

This study used 24 male wistar rats as samples. The mice were then randomly divided into four groups, namely groups A, B, C, and D. Each group consisted of six mice.

Macroscopic Picture of the Liver of a Wistar Rat.

The results of macroscopic observations of the liver of wistar rats are presented in Figure 18-21. The liver in the normal group, treatment 1, and treatment 2 showed a normal picture, namely the rat liver which was reddish-brown, smooth surface, and divided into four main lobes. In contrast, the liver of the negative control group showed a picture of cirrhosis characterized by a yellowish-white nodule surface and a hardened texture.

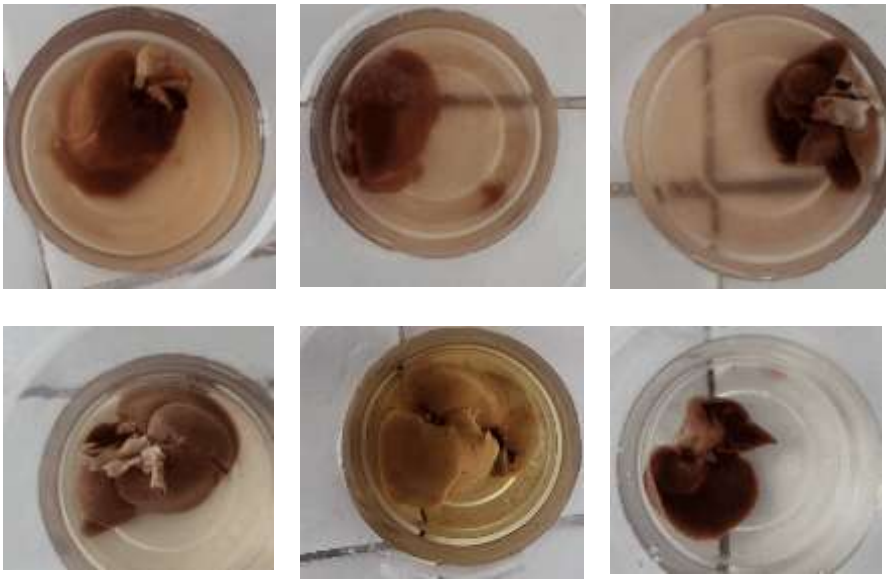


Figure 1. Macroscopic image of 6 hearts of wistar rats of normal control group
Source: Primary data from the study (normal control group), 2026

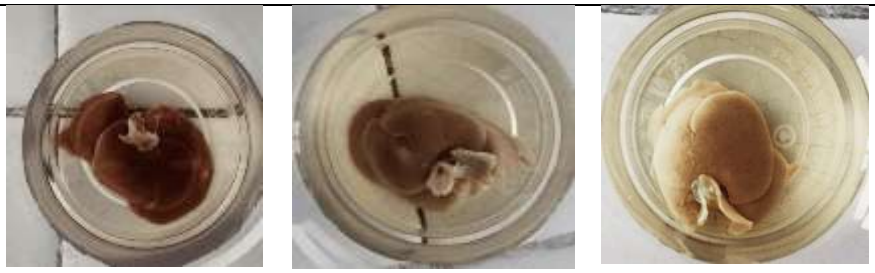


Figure 2. Macroscopic image of 6 hearts of wistar rats of negative control group
Source: Primary data from the study (negative control group), 2026

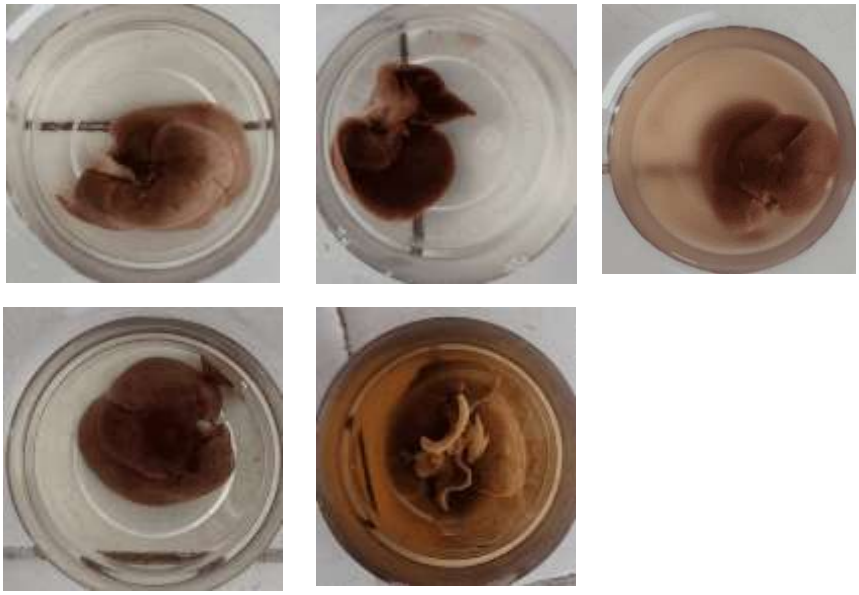


Figure 3. Macroscopic picture of 5 hearts of wistar rats treatment group I
Source: Primary data from the study (treatment group I), 2026

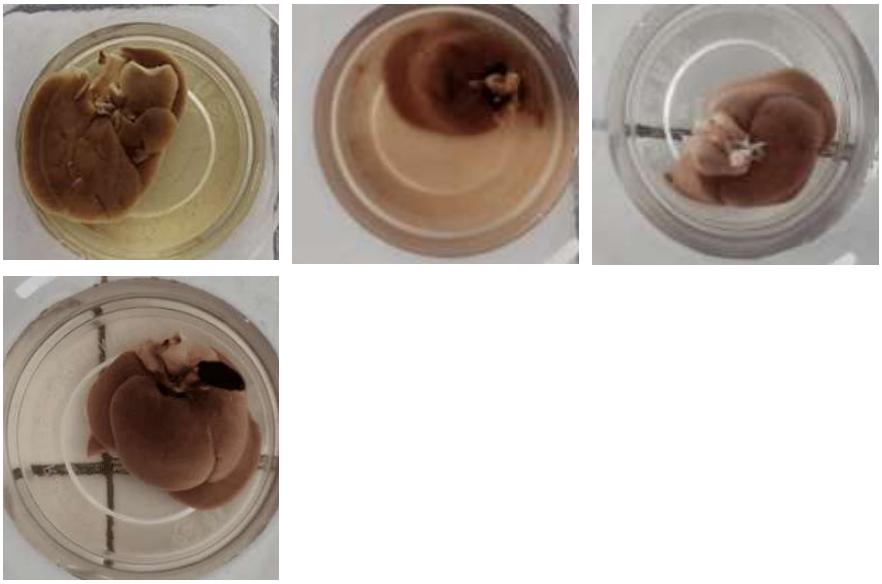


Figure 4. Macroscopic picture of 4 hearts of wistar rats treatment group II
Source: Primary data from the study (treatment group II), 2026

Microscopic Picture of the Liver of Wistar Rats

a. Histopathological Overview of the Liver of Normal Control Group Rats

After acclimatization, the wistar rats were only given pellet food and drinking water for 14 days, then terminated on the 15th day. The liver organs of wistar rats were taken, then processed into histopathological preparations which can be observed in Figure 5 and 6.

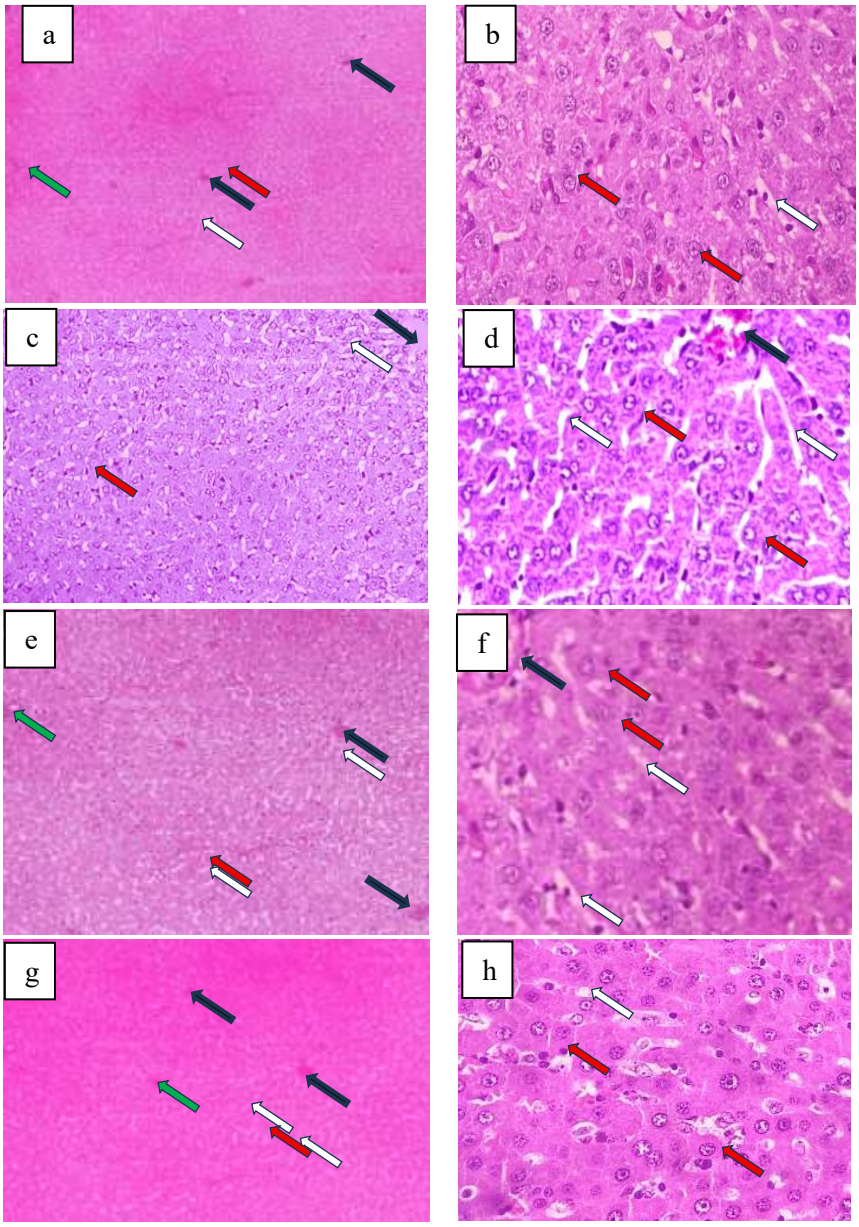


Figure 5. Description of 4 hepatic microscopic preparations of group A wistar rats (normal control).

Source: Primary data from the study (negative control group), 2026

Remarks: Histopathological picture of the hepatic hepatic of normal group wistar mice with hepatocyte cell structure (red arrow), sinusoid (white arrow), central vein (black arrow),

and porta canal (green arrow). Culverts: hematoxilin and eosin. 100x magnification (22a, 22c, 22e, 22g) and 400x magnification (22b, 22d, 22f, 22h).

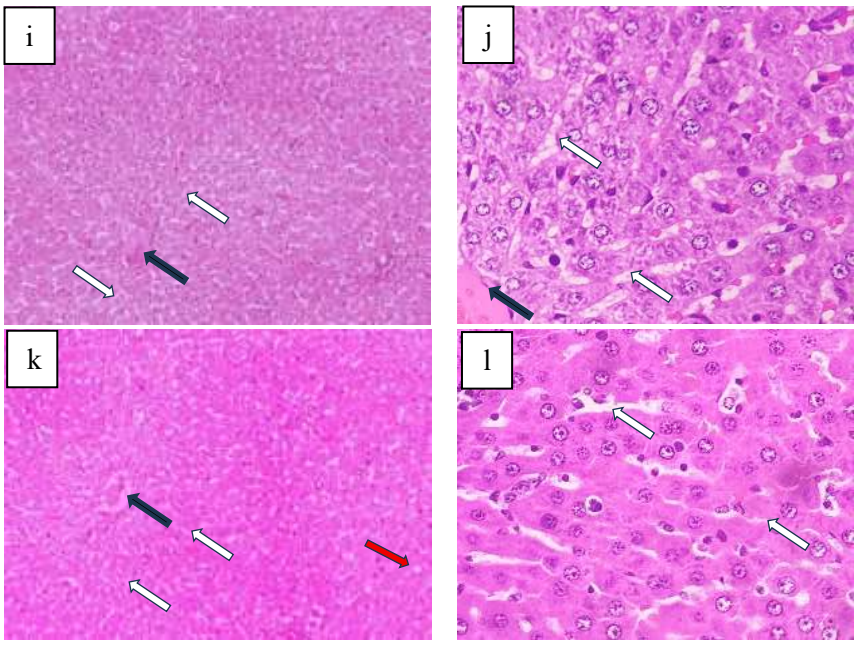


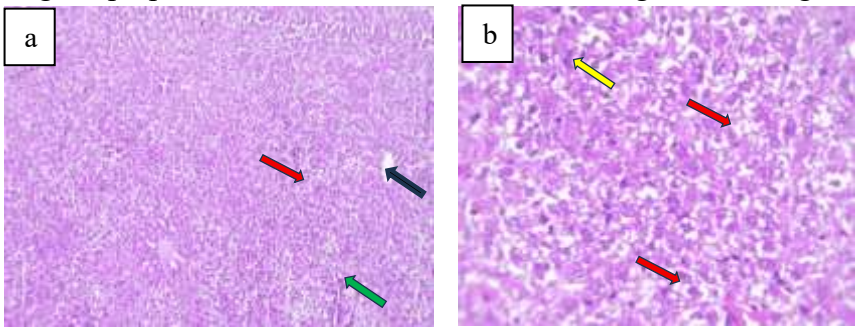
Figure 6. Description 2 of the hepatic microscopic preparations of group A wistar rats (normal control).

Source: Primary data from the study (negative control group), 2026

Remarks: Histopathological picture of the hepatic hepatic of normal group wistar rats with hepatocyte cell structures (red arrow), sinusoid (white arrow), and centralist vein (black arrow). Culverts: hematoxilin and eosin. 100x magnification (22i, 22k) and 400x magnification (22h, 22l).

b. Histopathological Picture of the Liver of Negative Control Group Rats

After acclimatization, the wistar rats were given pellet food and fasted for 6 hours, then induced with an alcoholic beverage with a rat cap dose of 2.16 mL/day orally using a gastric probe. This treatment is given once a day for 14 days. Termination is carried out on the 15th day. The liver organs of wistar rats were taken, then processed into histopathological preparations which can be observed in Figure 7 and figure 8.



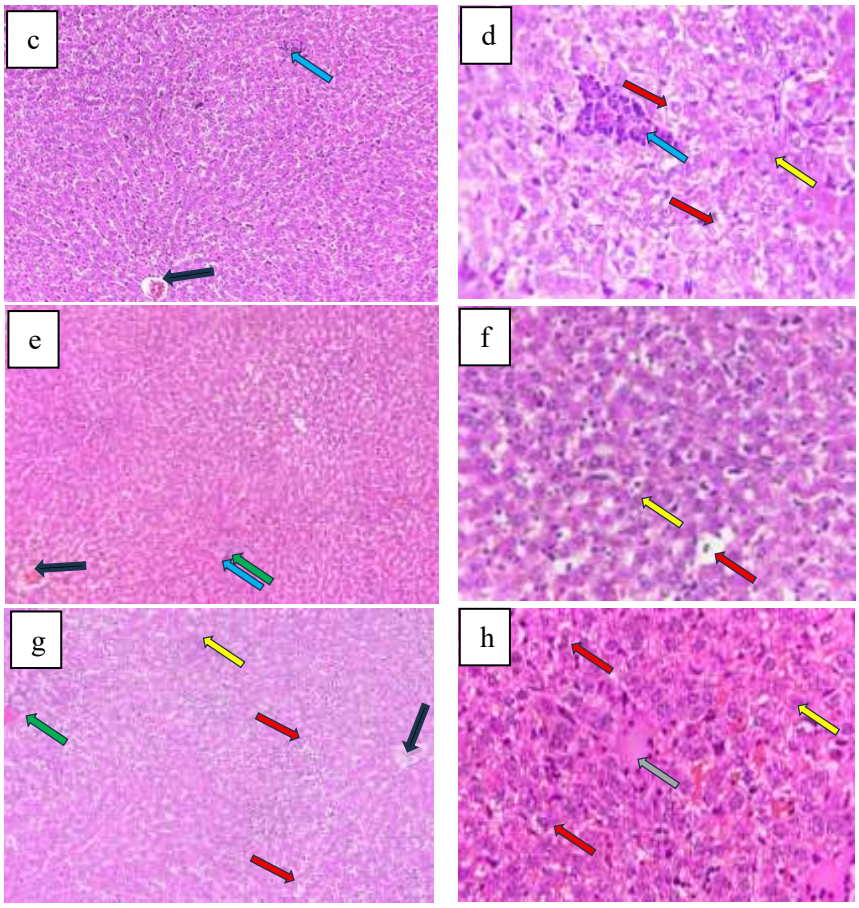
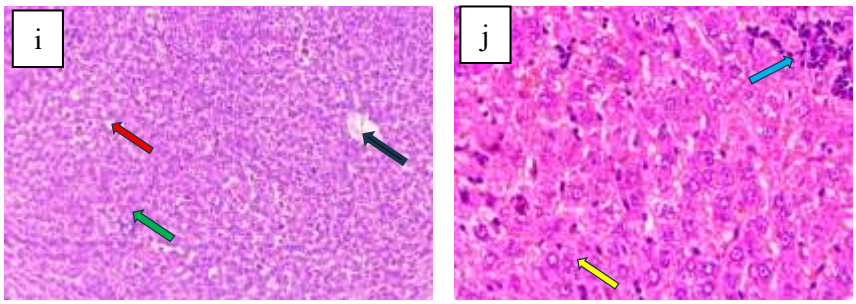


Figure 7. Description of 4 microscopic preparations of the liver of wistar group B rats (negative control).

Source: Primary data from the study (treatment group I, leilem extract 150 mg/kgBW), 2026

Remarks: Histopathological picture of the liver of negative group wistar mice with steatosis cells (red arrow), inflammatory cells (blue arrows) near the porta canal (green arrow), necrosis (gray arrow), hepatocyte cell regeneration (yellow arrow) and central vein (black arrow). Culverts: hematoxilin and eosin. 100x magnification (22a, 22c, 22e, 22g) and 400x magnification (22b, 22d, 22f, 22h).



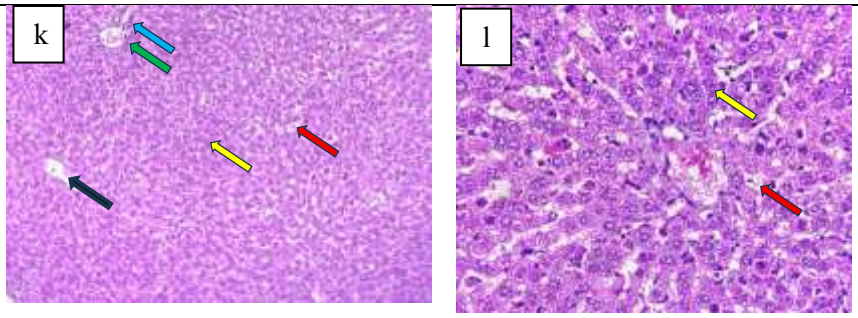


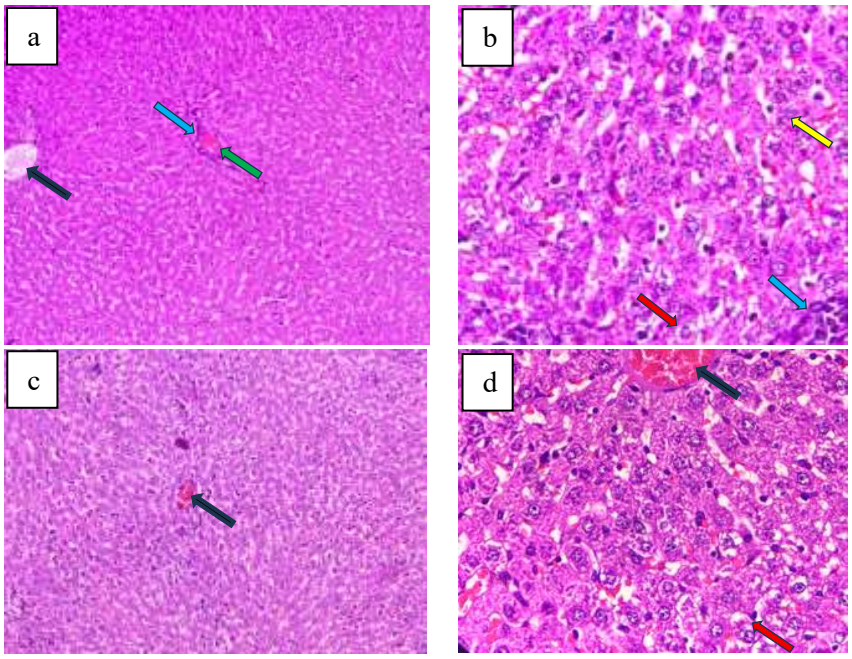
Figure 8. Description of 2 hepatic microscopic preparations of wistar group B rats (negative control).

Source: Primary data from the study (treatment group I, leilem extract 150 mg/kgBW), 2026

Remarks: Histopathological picture of the hepatic liver of negative group wistar mice with steatosis cells (red arrow), inflammatory cells (blue arrows) near the porta canal (green arrow), hepatocyte cell regeneration (yellow arrow) and centralist vein (black arrow). Culverts: hematoxilin and eosin. 100x magnification (22i, 22k) and 400x magnification (22h, 22l).

c. Histopathological Picture of Rats in Treatment Group I

After acclimatization, the wistar rats were given pellet food and fasted for 6 hours, then given leilem leaf extract at a dose of 30 mg/head/day orally. One hour after the administration of the extract, the rats were induced with a rat cap alcoholic drink at a dose of 2.16 mL/day orally using a gastric sonde. This treatment is given once a day for 14 days. Termination is carried out on the 15th day. The liver organs of wistar rats were taken, then processed into histopathological preparations which can be observed in Figure 9 and Figure 10.



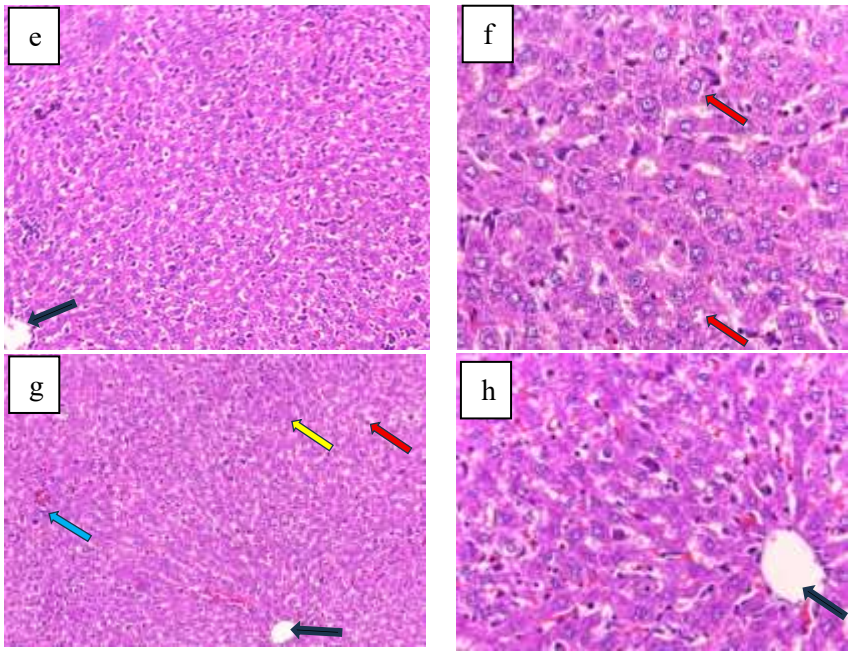


Figure 9. Description of 4 hepatic microscopic preparations of wistar rats group C (treatment I).
Source: Primary data from the study (treatment group II, leilem extract 300 mg/kgBW), 2026

Remarks: Histopathological picture of the liver of negative group wistar mice with centralist veins (black arrows), steatosis cells (red arrows), inflammatory cells (blue arrows) especially near the porta canal (green arrow). In addition, there is a regeneration of hepatocyte cells (yellow arrow). Culverts: hematoxilin and eosin. 100x magnification (22a, 22c, 22e, 22g) and 400x magnification (22b, 22d, 22f, 22h).

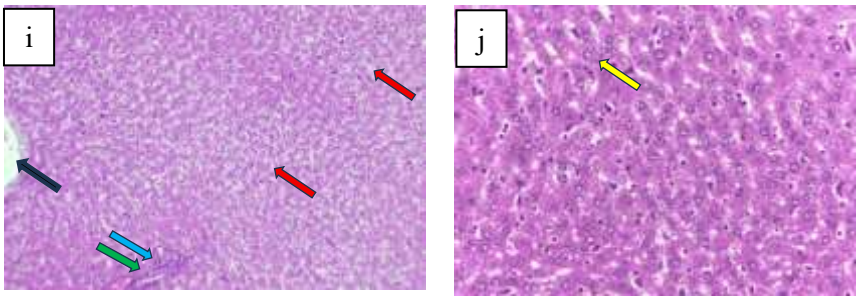


Figure 10. Description 1 of microscopic preparations of the liver of wistar group C rats (treatment I).
Source: Primary data from the study (treatment group II, leilem extract 300 mg/kgBW), 2026

Remarks: Histopathological picture of the liver of negative group wistar mice with centralist veins (black arrows), steatosis cells (red arrows), inflammatory cells (blue arrows) especially near the porta canal (green arrow). In addition, there is a regeneration of hepatocyte cells (yellow arrow). Culverts: hematoxilin and eosin. 100x magnification (22i) and 400x magnification (22h).

d. Histopathological Picture of the Liver of Treatment Group II Rats

After acclimatization, the wistar rats were given pellet food and fasted for 6 hours, then given leilem leaf extract at a dose of 60 mg/head/day orally. One hour after the administration of the extract, the rats were induced with a rat cap alcoholic drink at a dose of 2.16 mL/day orally using a gastric sonde. This treatment is given once a day for 14 days. Termination is carried out on the 15th day. The liver organs of wistar rats were taken, then processed into histopathological preparations which can be observed in Figure 11.

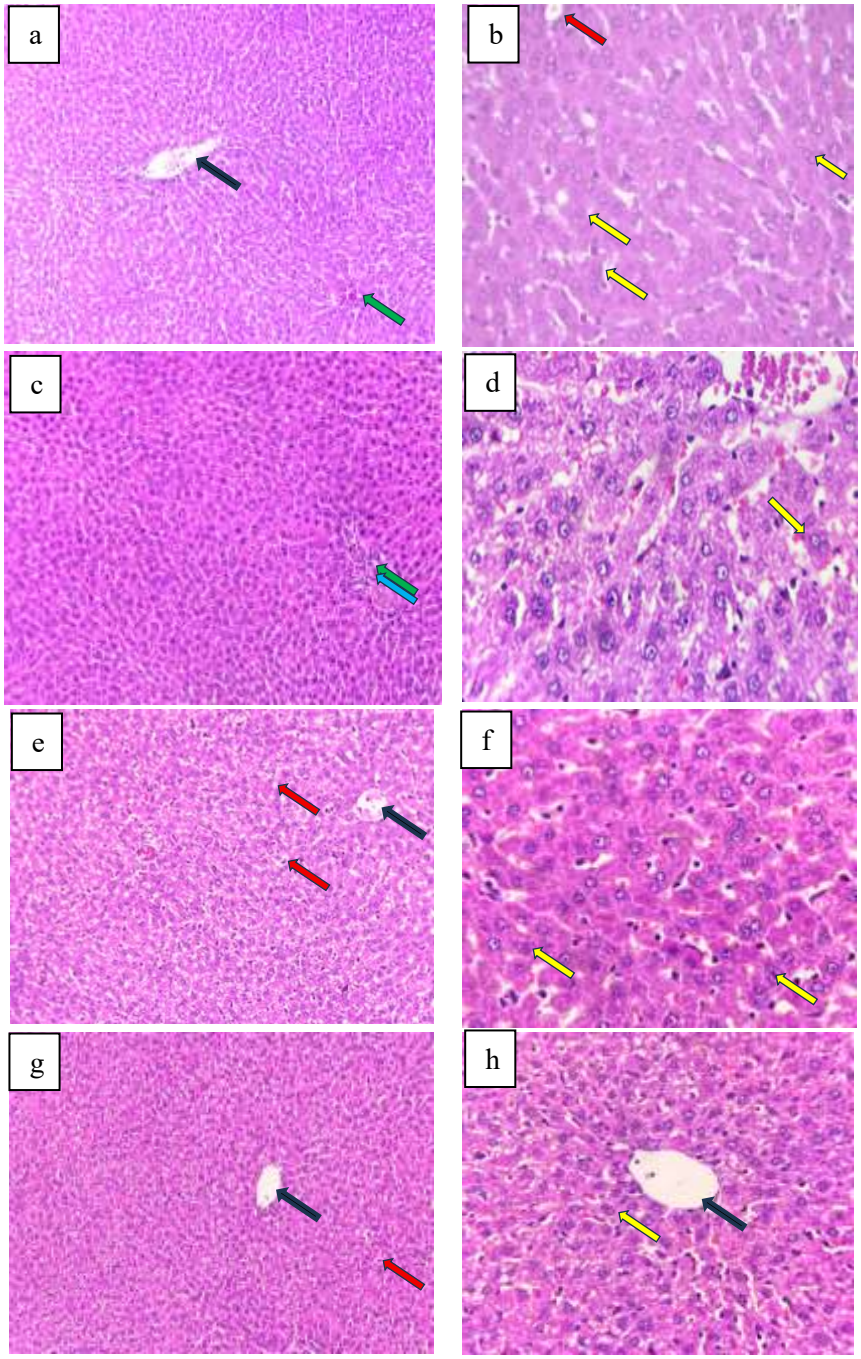


Figure 11. Description of 4 hepatic microscopic preparations of wistar rats group D (treatment II).

Source: Primary data, 2026

Remarks: Histopathological picture of the liver of negative group wistar mice with centralist veins (black arrows), steatosis cells (red arrows), inflammatory cells (blue arrows) especially near the porta canal (green arrow). In addition, there is a regeneration of hepatocyte cells (yellow arrow). Culverts: hematoxilin and eosin. 100x magnification (22a, 22c, 22e, 22g) and 400x magnification (22b, 22d, 22f, 22h).

Table 1 displays the data of the qualitative assessment of histopathological images in each treatment group. The table shows that there were many inflammatory cells in the negative group, a few in treatment group 1 and very few in treatment 2. Steatosis cells in the negative group were large in number, few in treatment group 1 and very few in treatment group 2. Very little cell regeneration occurs naturally in the negative group, in treatment group 1 there is little cell regeneration and in treatment 2 there is a lot of cell regeneration. In addition, no necrosis and fibrosis were found in the four trial groups.

Table 1. Qualitative Data on the Histopathological Picture of the Liver of Each Treatment Group in Wistar Rats

Group Name	Inflammatory Cells	Steatosis Cells	Cell Regeneration	Necrosis	Fibrosis
Normal Group	-	+	-	-	-
Negative Group	+++	+++	+	+	-
Treatment Group 1	++	++	++	-	-
Treatment Group 2	+	+	+++	-	-

Source: Primary data, 2026

Description:
- = None
+ = Very few
++ = A little
+++ = Lots

The study was conducted on male Wistar rats weighing 150–200 grams, given Leilem leaf extract as a hepatoprotective agent and induced with Cap Tikus alcoholic beverage to observe morphological changes in the liver. The observations in this study focused on histopathological changes in the liver, including inflammation, steatosis, necrosis, and regeneration. During the study period, three rats died, which were suspected to be related to confounding bias: one in treatment group I and two in treatment group II.

The normal control group of rats (Figure 23), which received only feed and water without alcoholic induction or Leilem leaf extract administration, showed normal liver architecture characterized by hexagonal lobules and normal histopathology with minimal steatosis. No pathological changes such as inflammation, necrosis, or signs of hepatocyte regeneration were observed.

The group of rats induced with 2.16 mL of Cap Tikus alcoholic beverage alone displayed normal liver architecture with distinguishable hexagonal lobules, but signs of steatosis caused by fat accumulation in hepatocytes were visible, indicating fat degeneration. Fat degeneration manifested as clusters of fat droplets, most prominent in the centrilobular region (perivenular/zone 3) around the central vein and extending toward the portal tract (portal triad) (Kumar et al., 2014). Lymphocytic inflammatory cells and a few necrotic cells were also observed, caused by oxidative stress due to Cap Tikus induction in the negative control group. This finding aligns with Rembang et al. (2020), who reported the presence of fatty liver cells, particularly around the central vein, necrosis, and limited regeneration in liver tissue of rats exposed to Cap Tikus alcoholic beverages.

Signs of degeneration can be attributed to primary alcohol metabolism, which occurs through the cytosolic alcohol dehydrogenase (ADH) pathway that oxidizes ethanol into acetaldehyde primarily in the liver. This process involves the transfer of hydrogen ions from ethanol to NAD^+, producing excess NADH that leads to metabolic disturbances such as lactic acidosis and hypoglycemia in acute poisoning, as well as complications in chronic alcoholism. Acetaldehyde is further oxidized by mitochondrial aldehyde dehydrogenase (ALDH) into acetate, which can be metabolized into CO_2 and water or converted into acetyl-CoA for fatty acid synthesis. In addition to the ADH–ALDH pathway, ethanol metabolism can proceed through the cytochrome P450 system (particularly CYP2E1), which increases NADPH consumption and generates reactive oxygen species (ROS)—including hydroxyl radicals, superoxide anions, and hydrogen peroxide—thereby amplifying oxidative stress and hepatocyte damage in chronic alcohol exposure (Hidayati et al., 2022).

In addition to signs of degeneration, evidence of hepatocyte regeneration was observed, characterized by enlarged nuclei, often binucleated, and expanded cytoplasm. This occurs due to the rapid regenerative capacity of the liver in rats, with recovery typically taking 5–7 days, during which hepatocytes undergo one or two replication cycles during the regeneration phase.

The ethanol extract of Leilem leaves contains antioxidant compounds that function to neutralize oxidative stress caused by free radicals (Indonesia, 2023). Flavonoid and phenolic compounds are the primary antioxidant constituents of this plant. Flavonoids counteract free radicals through three main mechanisms: inhibiting ROS formation, directly scavenging existing ROS, and protecting cells via antioxidant activity. Meanwhile, polyphenols inactivate free radicals to reduce oxidative stress (Rahmi, 2017).

Excess ROS can cause lipid peroxidation of cell membranes, mitochondrial damage, inflammation, and hepatocyte necrosis. This process plays an important role in liver damage pathogenesis. ROS accumulation further aggravates tissue conditions by increasing oxidative stress and triggering histopathological changes such as hydropic degeneration and hepatocellular necrosis (Salsabila et al., 2025; Indonesia, 2023).

Leilem leaf extract can inhibit liver damage through several mechanisms. One key mechanism is its flavonoid and phenolic content, which acts as ROS scavengers by donating electrons to stabilize free radicals. In addition, the extract enhances the endogenous antioxidant system. Similar mechanisms have been reported in other species of the *Clerodendrum* genus, which increase the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase. The resulting anti-inflammatory and antihyperlipidemic

effects also help prevent fat accumulation in the liver (fatty liver) and reduce inflammatory cell infiltration (Salsabila et al., 2025; Indonesia, 2023).

Administration of Leilem leaf extract at a dose of 150 mg/kgBW in alcohol-induced rats showed improved liver conditions. The rats' livers retained normal hexagonal architecture with reduced steatosis and inflammatory cell infiltration. Hepatocyte regeneration was also more pronounced than in the control group that received only alcohol. These findings are consistent with Vania et al. (2024), who reported that Leilem leaf extract (*Clerodendrum minahassae*) at doses of 150 mg/kgBW and 300 mg/kgBW exerts hepatoprotective effects by promoting hepatocyte regeneration and inhibiting inflammatory processes.

Rats given Leilem leaf extract at a dose of 300 mg/kgBW and induced with 2.16 mL of Cap Tikus alcoholic beverage exhibited nearly normal liver architecture. Hepatic lobules appeared hexagonal with a marked reduction in steatosis. Inflammatory cells decreased, while hepatocyte regeneration increased compared to rats given only 150 mg/kgBW of Leilem leaf extract.

Leilem leaf extract at higher doses (300 mg/kgBW) produced faster and more extensive hepatocyte regeneration than lower doses (150 mg/kgBW). This effect is due to the higher antioxidant content at these doses, providing more effective protection against liver damage caused by oxidative stress from alcohol consumption.

The results of this study may have been influenced by confounding factors. Variables such as stress, feed type, environmental conditions, and individual physiological variations among rats may have contributed to differences in the observed liver histopathology.

CONCLUSION

From the results of this research, it can be concluded that the administration of Leilem leaf extract has a hepatoprotective effect on the liver of Wistar rats induced with Cap Tikus alcoholic beverages. This effect is evidenced by the reduction in the number of inflammatory cells, necrotic cells, and steatotic cells.

A comparison between Leilem leaf extract doses of 150 mg/kgBW and 300 mg/kgBW showed a significant difference in the rate of hepatocyte regeneration, where the higher dose (300 mg/kgBW) demonstrated better protective effects and greater overall liver cell regeneration.

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