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ANTI-BACTERIAL POTENTIAL OF BIDARAUPAS (*Decalobanthus mammosus*) EXTRACT AGAINST LIVER MACROPHAGE CELLS INDICATED BY TUBERCULOSIS

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ABSTRACT

Background: *Tuberculosis (TB) is a serious infection caused by Mycobacterium tuberculosis, mainly affecting the lungs and spreading through the air. Every year, around 10 million new TB cases are reported worldwide, with Indonesia ranking third in the highest number of TB cases. TB treatment faces challenges due to drug resistance, such as MDR-TB and XDR-TB, which is driving research on alternative therapies, one of which is Merremia mammosa extract, which is known for its antibacterial and immunomodulatory potential. This study aimed to evaluate the potential of Merremia mammosa extract in enhancing the immune response, especially through liver macrophages, in mice infected with Mycobacterium tuberculosis.*
Method: *Mice were divided into treatment and control groups, receiving the extract at varying doses after TB bacterial injection.*
Results: *The results showed that most of the groups with lower necrotic cell counts came from the group with low doses, such as P11, P12, P13, P14, and P15. However, groups such as P45, which exhibit a high number of necrotic cells, may suggest that higher doses of Merremia mammosa extract may trigger an excessive inflammatory response.*
Conclusion: *Low-dose administration of Merremia mammosa extract is effective in reducing liver cell necrosis due to Mycobacterium tuberculosis infection. The low-dose group showed better tissue protection than high-doses, which in turn has the potential to trigger excessive inflammation.*

Keywords: Tuberculosis, *Merremia mammosa, Liver Macrophages, Mycobacterium tuberculosis, Drug Resistance*

INTRODUCTION

Bacteria *Mycobacterium tuberculosis*, which mainly infects the lungs, although it can also affect other organs. TB is an infectious disease that spreads through the air when an infected individual coughs or sneezes, releasing bacterial particles into the surrounding air (Organization, 2023). According to the World Health Organization (WHO), about 10 million new cases of TB are reported worldwide each year, with a death toll of around 1.5 million people in 2021. In Indonesia, TB remains one of the main health challenges, with the country ranking third after India and China in terms of the highest number of TB cases (Lestari et al., 2023).

Current treatment for tuberculosis (TB) involves a combination of antibiotics over a period of 6 to 9 months, with primary drugs such as *rifampisin, isoniazid, pyrazinamide*and *ethambutol.* However, the therapy faces several challenges, including patient adherence to long regimens, serious side effects of medications, and the emergence of drug-resistant cases such as multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) (Zumla et al., 2015), (Kim et al., 2020). Drug resistance to TB further complicates the treatment and control of the disease, as patients with MDR-TB and XDR-TB require longer, more complex treatments, generally involving drugs with more severe side effects.

Tuberculosis (TB) is an infectious disease that remains a global health problem, with a high number of cases and deaths in various countries. According to a report from

the World Health Organization (WHO), it is estimated that around 1.7 billion people were infected with TB in 2019 (Organization, 2022). Each year, there are about 10 million new cases of TB, with 1.2 million deaths among people who are not infected with HIV and 251,000 deaths among people with HIV. TB is also one of the main factors that exacerbate poverty and hinder social development (Opperman & Du Preez, 2023). In Vietnam, the WHO estimates that there were 174,000 new TB cases and 13,200 TB-related deaths in 2018. Currently, a serious problem is the increasing number of cases of drug-resistant tuberculosis (MDR-TB). According to a 2019 report from the National TB Program (NTP), the prevalence of MDR-TB among new patients reached 3.6%, while among patients receiving retreatment, it reached 17% (Van et al., 2024).

As drug resistance increases, the need for safer and more effective alternative and complementary therapies in the treatment of TB is becoming more urgent. In recent decades, several studies have focused on the use of traditional medicinal plants that have potential as natural antimicrobial agents and immunomodulators (Shishodia & Schofield, 2020). The use of medicinal plants has the potential not only as an adjunct therapy but also as a source of active compounds that can overcome drug resistance with a lower risk of side effects compared to chemical drugs. One plant that has attracted attention as a complementary therapy for tuberculosis is Merremia mammosa (*Merremia mammosa*), which has long been used in traditional medicine in Indonesia to treat a variety of infections, including respiratory tract infections (Putri & Sakinah, 2020).

Merremia mammosa It is known to contain a variety of bioactive compounds, such as flavonoids, alkaloids, saponins, and tannins, which exhibit a wide range of pharmacological activities, including antibacterial, anti-inflammatory, antioxidant, and immunomodulatory effects (Wulandari & Soleha, 2021). This compound is thought to help inhibit growth *Mycobacterium tuberculosis* and improve the immune response in the fight against infection. A study conducted showed that Esktrak *Merremia mammosa* may increase phagocytic activity of macrophages in infected mice *Mycobacterium tuberculosis*, exhibiting significant immunomodulatory effects. In addition, flavonoids in *Merremia mammosa* It is also known to have strong antioxidant activity, which can protect cells from oxidative damage caused by infections (Ani, 2020).

Macrophages are the main immune cells that play an important role in the innate immune response to TB infection. When *Mycobacterium tuberculosis* Entering the body, macrophages try to eliminate bacteria through the process of phagocytosis. But *Mycobacterium tuberculosis* has the ability to survive in macrophages by inhibiting phagolysosomal processes, which allow bacteria to multiply within cells and worsen infections (Kumar et al., 2014). Therefore, increasing macrophage activity in response to TB infection is an important approach in TB therapy. A study suggests that administering Merremia mammosa extract to an animal model infected with TB may increase the phagocytic activity of macrophages, potentially enhancing the immune response to transmission *Mycobacterium tuberculosis*.

The flavonoids found in Merremia mammosa are known to increase the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, which are important enzymes in the body. This antioxidant activity can help reduce oxidative stress caused by TB infection, which often causes damage to immune cells, including macrophages. By increasing antioxidant activity, *Merremia mammosa* can support the maintenance of normal macrophage function, allowing these cells to be more effective in eliminating *Mycobacterium tuberculosis* from the body. In addition, flavonoids are also

known to inhibit the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, which contribute to the chronic inflammation seen in TB.

In addition to flavonoids, the alkaloids contained in Merremia mammosa also have strong antibacterial potential, which can help inhibit growth *Mycobacterium tuberculosis*. Alkaloids work by damaging the structure of bacterial cell walls, which leads to leakage and bacterial death. Research shows that alkaloids can work synergistically with standard antibiotics, improving the effectiveness of TB treatment, potentially reducing the dose of antibiotics needed, and reducing the risk of drug resistance. An in vitro study also showed that the *Merremia mammosa* has significant bactericidal activity against *Mycobacterium tuberculosis*, further strengthening the potential of this plant as a complementary therapy in the treatment of TB (Sutriyawan et al., 2023).

Merremia mammosa has long been used in traditional medicine in Indonesia, particularly by people in Java and Sumatra, to treat various infectious and inflammatory diseases. The plant is usually prepared in the form of a decoction or extract that is consumed orally or used topically to treat open wounds. In traditional medicine, *Merremia mammosa* It is used to treat health problems such as respiratory infections, indigestion, and burns. Some ethnobotanical studies show that *Merremia mammosa* has a good reputation as a safe and effective medicinal plant, with few reports of side effects or toxicity at therapeutic doses (Lisum et al., 2022).

Merremia mammosa in traditional medicine, scientific research on its effectiveness and safety in the treatment of TB is still limited. This study aims to assess the potential of *Merremia mammosa extract* as a pharmacological agent and immunomodulator in the treatment of TB, focusing on its effect on hepatic macrophage activity in mice infected *with Mycobacterium tuberculosis*. The study will also evaluate different doses *of Merremia mammosa extract* to determine the optimal dose that provides the best immunomodulatory effect without causing toxicity. Based on this, this study aims to investigate the application of *Merremia mammosa extract* as a therapy to improve the quality of liver health in pulmonary TB patients. This study will examine the therapeutic effects of Merremia mammosa on the overall condition of the body, especially in increasing the activity of liver macrophages to eliminate *Mycobacterium tuberculosis*, strengthen immunity, and reduce inflammation caused by infection.

METHODS

This study is classified as an experimental laboratory, using 5 treatment groups, namely mice infected with *Mycobacterium tuberculosis*, whose liver organs are taken, cut, and stained with paraffin, then observed under a microscope through intraperitoneal injection. Similarly, 35 mice were randomly assigned into 5 groups, with each group containing 7 mice. Groups 1 to 5 are the observation groups, which are further divided into pre-observation (O1 to O5) and post-observation (O6 to O10). The P0 to P4 groups are treatment groups, namely:

a. K+ = Control group, given only *Mycobacterium tuberculosis bacteria*;
b. P1 = Treatment I (injected with *Mycobacterium tuberculosis* and given *Merremia mammosa extract* at 50 ppm);
c. P2 = Treatment 2 (injected with *Mycobacterium tuberculosis* and given *Merremia mammosa extract* at 100 ppm);
d. P3 = Treatment 3 (injected with *Mycobacterium tuberculosis* and given *Merremia mammosa extract* at 150 ppm);
e. K- = Control/comparative group that was not given *Mycobacterium tuberculosis* (P1, P2, P3 received a dose of 2 ml/200 grams of body weight extract orally).

The assessment of cell necrosis in this study used the Manja Roenigk scoring system,

which provides a description of the quality of cell damage based on a scale from 1 to 4. Manja Roennik's score is based on the following criteria:

I. Score 1: Shows normal cell count, with no damage or degeneration;
II. Score 2: Shows parenchymal degeneration, which is a structural change in the cell without any apparent cell death;
III. Score 3: Indicates hydropic degeneration, in which the cells swell due to fluid accumulation;
IV. Score 4: Indicates necrosis, or cell death due to severe damage to the cell structure, which can be caused by infection, inflammation, or other stressors;

RESULTS AND DISCUSSION

TB remains a major global health challenge, despite advances in treatment. In 2022, the WHO reported more than 10 million new TB cases, with high mortality rates, especially in developing countries. Drug resistance is a major problem in the treatment of TB, where *Mycobacterium tuberculosis* resistance to standard drugs further worsens the situation. Therefore, the development of new, more effective, and safer therapies is a priority in the treatment of TB (Farhat et al., 2024). One promising alternative is the use of traditional medicinal plants, such as *Merremia mammosa*, which is known to contain a variety of bioactive compounds with antibacterial and anti-inflammatory activity.

Previous research has shown that *Merremia mammosa* the extract can serve as an immunomodulatory agent that increases the activity of macrophages, which plays an important role in combating *Mycobacterium tuberculosis*. As part of the immune system, macrophages have the ability to ingest and destroy pathogenic bacteria, including *Mycobacterium tuberculosis*. Therefore, an increase in the number and function of macrophages can speed up the recovery of TB patients (Silva, 2022), (Zhou et al., 2022).

This research is particularly relevant because of its use *Merremia mammosa* as a complementary therapy for TB has not been explored in depth. As a traditional medicinal plant with antibacterial potential, *Merremia mammosa* It can be used as an adjunct therapy to reduce dependence on more expensive pharmaceutical drugs with potential side effects. It is also important to improve the effectiveness of TB treatment, especially with the increasing number of drug-resistant cases (Getachew et al., 2022), (Olatunji et al., 2021).

1. Necrosis in Mice Infected with Mycobacterium tuberculosis

Cell necrosis is the process of cell death due to irreversible cell damage, usually caused by factors such as infection, inflammation, or environmental stress. Tissue damage that causes necrosis can occur due to metabolic disorders, failure to maintain cellular homeostasis, or damage to critical organelles such as mitochondria, nucleus, and cell membranes. In the context of infectious diseases, especially tuberculosis (TB), cell necrosis is a major indicator of tissue damage caused by *Mycobacterium tuberculosis infection.* Infection by *Mycobacterium tuberculosis* triggers an inflammatory response that often leads to the formation of necrotic tissue in the liver. This study aimed to evaluate the rate of epithelial cell necrosis in the liver of mice infected with M. tuberculosis and to assess the potential *of Merremia mammosa* extract as a complementary therapy in repairing liver tissue damage caused by this infection.

Mycobacterium tuberculosis *infection* in the liver, both in mice and humans, often induces an intense immune response. Bacteria are able to survive inside macrophages and avoid destruction, which leads to chronic inflammation. The immune system responds by forming granulomas made up of immune cells such as

macrophages, T lymphocytes, and dendritic cells, which try to isolate bacteria and prevent their spread. Simultaneously, an excessive inflammatory response can lead to tissue damage, leading to necrosis. Cassatic necrosis is a typical form of necrosis observed in TB infections, in which the necrotic tissue has a soft cheese-like texture. This damage occurs as a result of a combination of cell death caused by bacterial infections, an overactive immune response, and a lack of oxygen in the granuloma area, causing the cells within the affected tissue to die.

2. Liver Cell Necrosis in Mice Infected with Mycobacterium tuberculosis

Necrosis of lung tissue due to *Mycobacterium tuberculosis infection* usually occurs in the form of granulomas, which are characteristic structures that form as part of the immune response to infection. These granulomas are made up of immune cells, such as macrophages, that seek to contain the spread of bacteria but can also cause tissue damage. This damage can progress to necrosis if the infection persists or if the immune response is insufficient to control the infection. In tuberculosis (TB), necrosis can occur in two main forms: cascade necrosis, in which some cells die and damage the surrounding tissue, and caseous necrosis, which occurs in the center of the granuloma, where the tissue becomes hardened and has a cheese-like texture. This necrotic process causes significant impairment of liver cell damage and impaired liver function.

In this study, the number of necrostic epithelial cells was measured in five high-power fields at 400x magnification for each mouse sample infected *with Mycobacterium tuberculosis*. Evaluation was conducted in a group of mice treated with *Merremia mammosa extract* and a control group that did not receive treatment. The data obtained showed significant variability in the number of necrotic cells between the groups receiving treatment of Merremia mammosa extract and those who were not treated. The following table presents the total number of necrotic cells and the average number of necrotic cells per field for each sample:

Table 1. Number of Cells That Undergo Necrosis in 5 Fields of View with 400X Imaging

Code	Total Necrosis Cell Count	Average Necrotic Cells	Group
K-1	30	6	
K-2	22	4,4	
K-3	22	4,4	K-
K-4	25	15	
K-5	27	13,2	
K+1	46	9,2	
K+2	40	8	
K+3	41	4,2	K+
K+4	43	8,6	
K+5	39	7,8	
P 11	9	1,8	
P 12	8	1,6	
P 13	4	0,8	P1
P 14	5	1	
P 15	6	1,2	
P 32	33	6,6	
P 21	35	7	
P 22	32	6,4	P2
P 43	36	9,2	
P 24	30	14,8	
P 26	56	7,2	
P 31	58	11,6	
P 34	65	13	P3
P 36	45	9	
P 45	72	14,4	

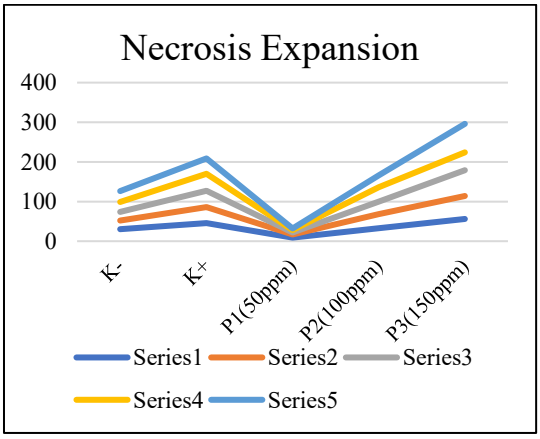

Figure 1. Necrosis Expansion Curve

2.1 Variability in the number of necrotic cells

In this study, the groups treated with

Merremia mammosa extract, such as P26, P31, P34, P36 and P45, showed a higher number of necrotic cells compared to the negative control (K-) group and the positive control group. The P26 group, which recorded 56 necrotic cells with an average of 7.2 necrotic cells per field of view, showed significant damage. This value was much higher than that of the negative control group (K-), which did not receive any treatment or infection and showed 56 necrotic cells in the observed field. This can be attributed to two main factors. First, more severe *Mycobacterium tuberculosis* infections in the P26 group may cause a more intense immune response, ultimately leading to more severe tissue damage.

Mycobacterium tuberculosis Infection can lead to the formation of granulomas, which serve to isolate bacteria from healthy tissues. However, in some cases, excessive inflammation can lead to caseous necrosis, a type of necrosis that occurs in the granuloma area due to tissue damage caused by inflammatory cytokines and oxidative stress (Ahmad, 2011). This condition often worsens liver tissue damage and hinders the healing process. In this study, higher doses of Merremia mammosa extract in some groups showed an impact on the rate of tissue damage. Although the compounds in Merremia mammosa extract have anti-inflammatory and antibacterial properties, giving too high a dose can affect the balance of the immune response, potentially worsening tissue damage (Collin et al., 2018).

In the treatment group (P1), the area of necrosis was only around ± 6.4 mm, meaning that bidara upas extract could reduce necrosis, but the P2 group averaged ± 33.2 mm and P3 ±59.2, this shows that *Merremia mammosa* extract cannot reduce liver cell necrosis. These results show that *Merremia mammosa* extract at a dose of 50mg/ml is able to provide a therapeutic effect in reducing liver tissue damage in mice infected *with Mycobacterium tuberculosis.*

2.2 Roennik's Spoiled Score and Necrotic Cell Count

The results of the study on the rate of lung cell necrosis in mice infected with Mycobacterium tuberculosis showed variation in the number of necrotic cells across treatment groups. The assessment of cell necrosis in this study was carried out using the Manja Roenigk assessment system, which provides an overview of the quality of cell damage based on a scale from 1 to 4. Using these scoring criteria, we were able to analyze the results of the study based on the average necrotic cell score for each treatment group, including the control group and *the smeared* Merremia mammosa extract.

From Table 1, significant differences in the mean number of necrotic cells between the group treated with Merremia mammosa extract and the control group can be observed. The following is a discussion of the results of the study, starting from the K-1 to P45 group, based on necrotic cell data calculated per field of view and the Manja Roenigk assessment system. This discussion aimed to delve deeper into the effects of treatment of Merremia mammosa extract on cell necrosis in the liver organs *of mice infected* with Mycobacterium tuberculosis.

Group P11

Total necrotic cells : 9

Average Necrotic Cells :1.8

The P11 group showed a total of 9 necrotic cells, with an average of 1.8 necrotic cells per field of view. This value indicates that the P11 group tends to be close to a score of 2, indicating the presence of parenchymal degeneration of lung cells, although necrosis is not as widespread in other groups. This score reflects significant cell damage in some lung cells, but there are still some normal cells. It is possible that *the treatment of Merremia mammosa* extract in this group still has a therapeutic effect, although not

completely.

Group P12

Total necrotic cells : 8

Average Necrotic Cells :1.6

The P12 group showed a total of 8 necrotic cells, with an average of 1.6 necrotic cells per field of view. This value indicates that the P12 group tends to be close to a score of 2, indicating the presence of parenchymal degeneration of lung cells, although necrosis is not as widespread in other groups. This score reflects significant cell damage in some lung cells, but there are still some normal cells. It is possible that *the treatment of Merremia mammosa* extract in this group still has a therapeutic effect, although not completely.

Group P13

Total necrotic cells : 4

Average Necrotic Cells :0.8

The P13 group showed a total of 4 necrotic cells, with an average of 0.8 necrotic cells per field of view. This value indicates that the P13 group tends to be close to a score of 1, which indicates that more cells are normal than those that are degenerated or necrosis. In this case, treatment with Merremia mammosa extract showed quite positive results in repairing lung tissue damage caused by Mycobacterium tuberculosis infection. The P13 group can be considered a group that undergoes significant tissue repair, with minimal cell damage.

Group P14

Total necrotic cells : 5

Average Necrotic Cells :1

The P14 group showed a total of 5 necrotic cells, with an average of 1 necrotic cell per field of view. This value indicates that the P14 group is included in the score of 1, which indicates that more cells are normal than those that are degenerated or necrosis. In this case, treatment with Merremia mammosa extract showed quite positive results in repairing lung tissue damage caused by Mycobacterium tuberculosis infection. The P14 group can be considered a group that undergoes significant tissue repair, with minimal cell damage.

Group P15

Total necrotic cells : 6

Average Necrotic Cells :1,2

The P15 group showed a total of 6 necrotic cells, with an average of 1.2 necrotic cells per field of view. This value suggests that the P15 group tends to be close to a score of 2, which indicates the presence of parenchymal degeneration of lung cells, although necrosis is not as widespread in other groups. This score reflects significant cell damage in some lung cells, but there are still some normal cells. It is possible that *the treatment of Merremia mammosa* extract in this group still has a therapeutic effect, although not completely.

Group P32, P21, P22, P24, P26, P31, P34, P36, P45

In this group, there were P21 (35 necrotic cells) with an average of 7 necrotic cells per field of view. P22 (32 necrotic cells) with an average of 6.4 necrotic cells per field of view, P32 (33 necrotic cells) with an average of 6.6 necrotic cells per field of view, P34 (65 necrotic cells) with an average of 13, P36 (45 necrotic cells) with an average of 9, P45 (72 necrotic cells) with an average of 14.4, and P31 (58 necrotic cells) with an average of 11.6 necrotic cells per field of view. This value indicates that the group tends to be close to a score of 4, as well as other groups that have an average score of 4 or greater than 4. This indicates that there is severe necrosis in the liver. This could be caused by *a more severe* Mycobacterium tuberculosis infection or *a higher dose of Merremia mammosa* extract, which may lead to more intense inflammation of liver tissue. Increased necrosis scores in this group require further attention, including a review of doses or mechanisms that may contribute

to increased necrosis.

Group K+ and Group K-

In all K+ groups and K- groups have an average of 4 or more necrotic cells. This indicates that there is severe necrosis in the liver. This could be caused by *a more severe* Mycobacterium tuberculosis infection or *a higher dose of Merremia mammosa* extract, which may lead to more intense inflammation of liver tissue. Increased necrosis scores in this group require further attention, including a review of doses or mechanisms that may contribute to increased necrosis.

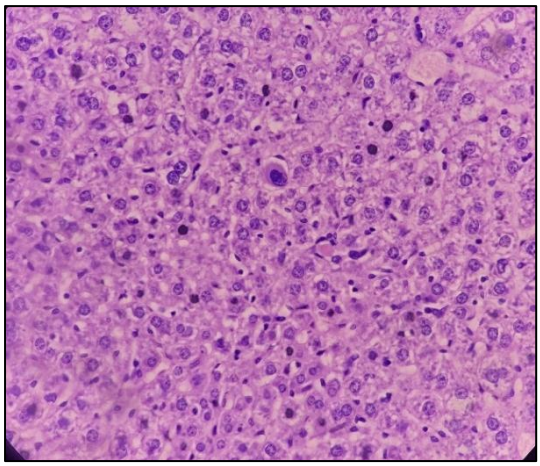

Figure 2. Histopathological Images Group 1.4

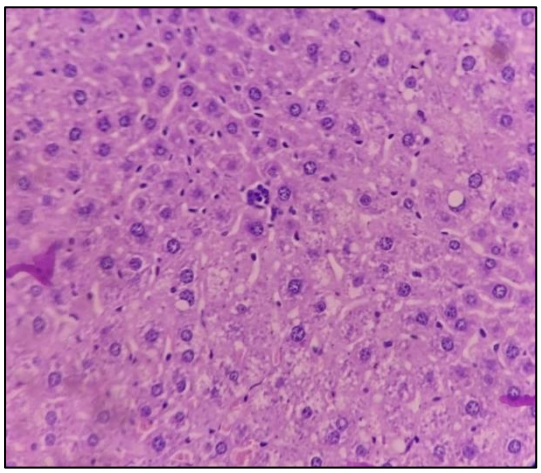

Figure 3. Histopathological Images Group 23

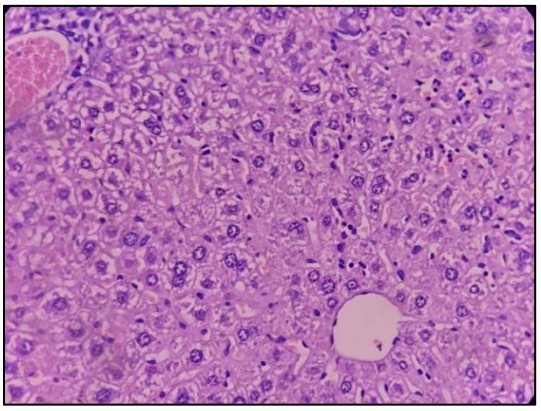

Figure 4. Histopathological Images Group 34

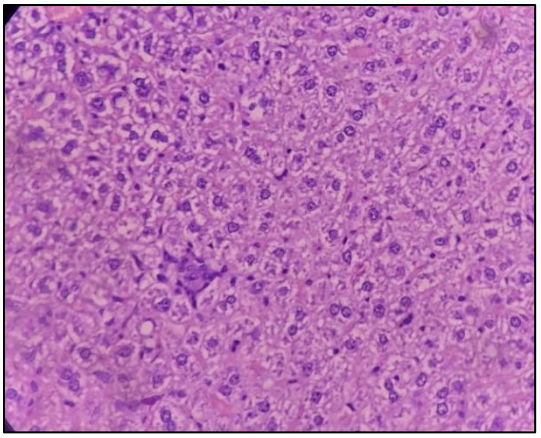

Figure 5. Histopathological Images Group 45

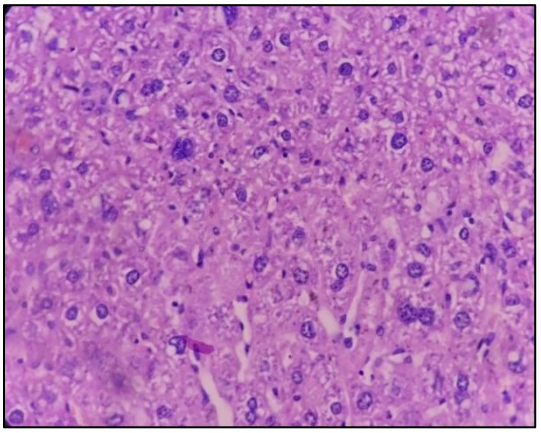

Figure 6. Histopathological Images of Group K+1

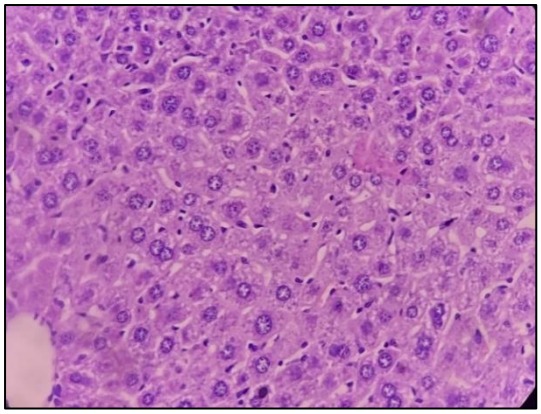

Figure 7. Histopathological Images of Group K-1

2.3 Dosage Response of Merremia mammosa Extract

The results showed that most of the groups with lower necrotic cell counts came from the group with low doses, such as P11, P12, P13, P14, and P15. Lower doses may be more effective in preventing further damage to liver tissue without causing side effects or an over-immune response. A significant reduction in cell necrosis in these groups suggests that proper dosing regulation can lead to substantial improvements in tissues damaged by bacterial infections. However, groups such as P45, which exhibit a high number of necrotic cells, may indicate that higher doses of *Merremia mammosa* the extract can trigger an excessive inflammatory response. It highlights the importance of dosage regulation in herbal therapy to ensure that optimal therapeutic effects are achieved without causing harmful side effects. The exact dosage of Merremia mammosa extract needs to be determined through further research to establish safe and effective tolerance limits for infected lung tissue (Kitagawa et al., 1997).

Active compounds in *Merremia mammosa* Extracts, such as flavonoids and saponins, are known to have antioxidant activity that can reduce oxidative stress caused by infection (Purwitasari & Agil, 2022). In addition, the antibacterial compounds in *Merremia mammosa* extracts can help inhibit growth *Mycobacterium tuberculosis*, thus directly reducing infection and tissue damage. *Merremia mammosa* It is recognized in traditional medicine for its therapeutic benefits, including wound healing, anti-inflammatory, and infection treatment. This plant is found in many tropical regions and has been widely used in traditional healing. Modern research has shown that *Merremia mammosa* contains active compounds with anti-inflammatory, antibacterial, and antioxidant properties, which have the potential to reduce tissue damage caused by infections, especially in tuberculosis (TB) caused by *Mycobacterium tuberculosis*. Several mechanisms may explain how Merremia mammosa extract works: First, it has anti-inflammatory potential that can reduce excessive inflammation. Chronic inflammation often causes damage to healthy tissues and worsens necrosis, especially in *Mycobacterium tuberculosis infection*. Anti-inflammatory compounds in *Merremia mammosa* It works by inhibiting the production of pro-inflammatory cytokines such as TNF-α and IL-1β, which contribute to inflammatory processes and tissue damage.

Second, Merremia mammosa extract functions as an antioxidant. The inflammatory process triggered by *M. tuberculosis* infection produces high oxidative stress, which damages healthy cells. The antioxidants in *Merremia mammosa* can reduce this oxidative damage, thus helping to protect liver cells from further damage and speeding up the healing process. In addition, the antibacterial compounds in Merremia mammosa extract can help suppress the growth of *Mycobacterium tuberculosis*. Although not as potent as conventional drugs such as rifampicin in killing bacteria, this extract can help inhibit the growth of bacteria, thereby reducing infection and further tissue damage. *Merremia mammosa* has been used in

traditional medicine, particularly in Indonesia, to treat a variety of health problems, including infectious diseases and inflammation. The roots, leaves, and stems *of Merremia mammosa* are often used to alleviate symptoms of respiratory illnesses, such as coughs, colds, and even tuberculosis. With its anti-inflammatory, antibacterial, and antioxidant properties, this plant can accelerate healing and repair liver tissue damaged by *Mycobacterium tuberculosis infection*.

To evaluate the effectiveness of herbal remedies, scoring systems such as the Manja Roenigk score are used to measure changes in infected tissues, especially in cases of cell necrosis caused by bacterial infections. Based on this study, *Merremia mammosa* extract showed varied results in reducing cell necrosis in liver tissue. Some groups treated with *Merremia mammosa extract* showed a reduction in cell necrosis, while others experienced a greater increase in necrosis, likely due to higher doses or more severe infectious conditions. Groups that did not show cell necrosis, such as P11, P12, P13, P14 and P15 showed better protection against liver tissue damage. This provides evidence that *Merremia mammosa extract* may help protect liver tissue from further damage, although results vary depending on the dose and individual body conditions.

CONCLUSION

The administration of *low-dose Merremia mammosa* extract is effective in reducing liver cell necrosis due to *Mycobacterium tuberculosis infection*. The low-dose group showed better tissue protection than high-doses, which in turn has the potential to trigger excessive inflammation. The active compounds in the extract, such as flavonoids and saponins, play a role through anti-inflammatory, antioxidant, and antibacterial mechanisms. These results confirm the potential of *Merremia mammosa* as an adjunct therapy in treating liver damage due to TB infection, with the need for further research to determine safe and effective doses.

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CONFLICT OF INTEREST

The author states that there is no conflict of interest.

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