The Effect of Pagoda Flower Extract (*Clerodendrum Paniculatum* L.) on Pancreatic Function and Histopathological Features of the Pancreas of Male Wistar White Rats Infected with Leptospira Bacteria

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ABSTRACT

This study was conducted to test the effect of pagoda flower extract (Clerodendrum paniculatum L.) on pancreatic function and histopathological picture of the pancreas of male Wistar white rats infected with Leptospira interrogans bacteria. Based on the difference in the average lipase levels of treatment group 3, namely rats infected with bacteria and given pagoda flowers at a dose of 200mg/KgBW, had the greatest decrease in lipase levels and approached the control group. P3 group after being infected with bacteria amylase- lipase level 68.45U/L- 42.06U/L and after being given pagoda flower extract with a dose of 200mg/KgBB, the amylase-lipase level became 58.75U/L-22.71U/L. There was no necrosis for the histopathological picture of treatment group 3 (P3). However, there was still a little leukocyte infiltration in the pancreatic cells, so this treatment group got a score of 0 without necrosis of pancreatic cells. Thus, it can be concluded that pagoda flower extract affects the pancreatic function of rats infected with leptospira bacteria. The Kolmogorov-Smirnov data analysis $p>0.05$ is 0.200, so the data is usually distributed.

***Keywords**: Pagoda flower, Pancreas, Leptospira, Amylase, Lipase*

INTRODUCTION

One of the body's organs that can be damaged due to irregular eating patterns and the body being easily attacked by viral and bacterial infections is the weakening of the pancreas function. The function of the pancreas is essential for the digestive system and metabolism. In addition to producing hormones, the pancreas is an important organ that produces enzymes

used to destroy and digest food in the stomach. Bacterial infection is one of the many causes of pancreas inflammation known as pancreatitis. The impact of renal ischemia-reperfusion injury is a significant decrease in pancreatic function and structure as an indicator of acute pancreatitis. Many studies have reported the relationship between pathogenic bacteria and acute pancreatitis caused by Leptospirosis (Leptospira interrogans bacterial infection). Leptospirosis is a disease caused by the bacteria Leptospira interrogans. This bacteria can spread through the urine or blood of infected animals. One of the treatments for infection with this bacteria is medication to relieve symptoms and treat the bacterial infection. Some herbal plants contain antioxidants and antibacterials, including pagoda flower extract (Clerodendrum paniculatum L.). Based on this, researchers are interested in making a research title on the effect of administering pagoda flower extract (Clerodendrum paniculatum L.) on pancreatic function and histopathological description of the pancreas of male white Wistar rats infected with leptospira interrogans bacteria.

LITERATURE REVIEW

The pancreas is an accessory organ in the digestive system that has two main functions: producing digestive enzymes or exocrine functions and several hormones or endocrine functions. The pancreas is in the upper left quadrant of the abdomen or stomach, and its caput/head is attached to the duodenum organ. Enzyme products will be channeled from the pancreas to the duodenum through the central pancreatic duct (Alex, 2024). The function of the pancreas is to produce digestive enzymes (exocrine function) and hormones (endocrine function). The functions of the pancreas include producing digestive enzymes such as amylase, lipase, and trypsin, as well as producing the hormone glucagon to increase blood sugar levels and the hormone insulin to lower it. When we eat, a healthy pancreas will produce enzymes and hormones in the right amount of time. However, if the pancreas is not functioning correctly, it cannot produce digestive enzymes or the hormone insulin properly. This can lead to diseases such as diabetes and food intolerance. Some symptoms, such as decreased appetite, weight loss, fatty stools, nausea, vomiting, and diarrhea, can be caused by pancreatic problems (Rachdaoui, 2020).

Pancreatic damage can lead to insufficiency, which various clinical conditions, such as recurrent acute pancreatitis, chronic pancreatitis, diabetes, autoimmune diseases, or after pancreatectomy, can cause. Malabsorption, malnutrition, vitamin deficiencies, and weight loss (or weight loss in children) are signs of pancreatic insufficiency (Karpinska, 2022).

Leptospira bacteria are commensals in the kidneys and liver of mammals, including mice (Karpinska, 2022). Leptospira bacteria are commensals in the kidneys and liver of mammals, including mice (Wening Widjajanti, 2020).

In cases where the infection is quite severe, treatment is aimed at relieving symptoms and preventing complications. There are no symptoms shown by Leptospira infection, as occurs in the maintenance hole rat *Rattus norvegicus* (Arief Mulyono, 2020). The treatment for this bacteria increases the body's resistance through foods containing antioxidants. In addition to counteracting the effects of free radicals, humans must consume foods rich in antioxidants daily, even though the human body naturally produces antioxidants (Syaputri, 2022). Norway rats have a significant impact on our lives. They are one of the most widely used research subjects, producing remarkable progress; thus, there has been a great interest in controlling rat populations since the Middle Ages (Schweinfurth, 2020).

One of the treatments if infected with this bacteria is medication to relieve symptoms and overcome bacterial infections. Some of the drugs that will be given are antibiotic drugs, such as penicillin, amoxicillin, etc. Several herbal plants contain antioxidants and antibacterial, including pagoda leaf extract (Clerodendrum paniculatum L.). In addition to having anti-inflammatory and antioxidant activities, Clerodendrum paniculatum L. has been measured for its pharmacological potential using the Brine shrimp Lethality Toxicity (BSLT) toxicity test, and the result is that the ethanol extract of pagoda flower has a strong activity potential as evidenced by an LC50 value of 45.487 ppm7 (Matsushima, 2011).

METHODS

This research is a laboratory experiment, which is a type of research used in researching the effectiveness of pagoda flower extract (Clerodendrum paniculatum L.) on the pancreatic function of male rats (Rattus norvegicus) Wistar strain infected with leptospira bacteria. The research site is the Department of Pharmacology and Therapeutics Laboratory, Faculty of Medicine, Universitas Sumatera Utara in May – July 2024. Ethical Clearance will be submitted to Universitas Prima Indonesia's Health Research Ethics Commission. The sample in the study used male rats (Rattus norvegicus) Wistar strain. Researchers used the 3R Principle (Replacement, Reduction, and Refinement), namely Reduction, in determining the number of research samples (Kendall *et al*., 2018). All research samples, namely 24 male rats, will be divided into 4 groups. The research procedures include acclimation of test animals for 7 days in the laboratory, making pagoda flower extract with a control group dose

without administration, treatment 1 (P1) 100 gr, treatment 1 (P2) 150 gr, treatment 1 (P3) 200 gr. Then, test the phytochemical content of pagoda flower extract. Before treatment using pagoda flower extract (Clerodendrum paniculatum L.), The mice will be infected with bacteria and wait 24 hours after Leptospira interrogans bacterial infection induction. After 14 days of extract treatment, the examination of pancreatic function was continued by examining the levels of amylase and lipase enzymes, as well as histopathological observations of the function of the pancreas of mice in each experimental group and scoring Debian. The data were then tabulated and presented descriptively. Analysis of the normality of the data used in this study, namely the Kolmogorov-Smirnov normality test. Data is typically distributed if $p > 0.05$. After conducting the data normality test, it was continued. To test the significance between the trial groups, the one-way variance analysis technique or Way ANOVA was used at a confidence level of 95% ($p < 0.05$) (Ghozali, 2018).

RESULTS

The research sample, namely 24 male rats, will be divided into 4 groups, each comprising 6 rats. In this study, mice will be infected with bacteria and wait 24 hours after Leptospira interrogans bacterial infection induction. Treatment P0 as a control group was not given pagoda flower extract. Treatment groups P1, P2, and P3 were each given pagoda flower extract of 100 mg/kg BW, 150 mg/kg BW, and 200 mg/kg BW orally using a gastric tube. After ensuring that all mouse samples had been infected with bacteria, the results of the calculation of the mouse's body temperature were seen where all in group P3 reached an average temperature of 40.7 ˚C from the average original temperature of the mice before being infected with bacteria, which was 37.6 ˚C. This proves that there was a change in the body temperature of mice before and after being infected with leptospira bacteria. Then, the active substances contained in the pagoda flower extract (Clerodendrum paniculatum L.), which were tested through phytochemical testing, were testing the content of secondary metabolites such as alkaloids, flavonoids, saponins, and tannins which were positive for pagoda flowers.

Based on the observations made, the researchers' average lipase levels concluded that treatment group 3, namely mice infected with bacteria and given pagoda flowers (Clerodendrum paniculatum L.) at a dose of 200mg/KgBB, had the most significant decrease in lipase levels and approached the control group. Treatment group 1, mice infected with

bacteria and given pagoda flower extract (Clerodendrum paniculatum L.) at a dose of 100mg/KgBB, experienced the least decrease or improvement in lipase levels.

Moreover, the average value of amylase levels, the researcher concluded that treatment group 3, namely mice infected with bacteria and given pagoda flower extract (Clerodendrum paniculatum L.) at a dose of 200mg/KgBB, had the most significant decrease in amylase levels and obtained results below the control group. Treatment group 1, mice infected with bacteria and given pagoda flower extract (Clerodendrum paniculatum L.) at a dose of 100mg/KgBB, experienced the most minor decrease or improvement in amylase levels.

In the observation of the histopathology of treatment 3 (P3) infected with leptospira bacteria and given pagoda flower extract treatment with a dose of 200mg/KgBW, there was no necrosis, but there was still a slight leukocyte infiltration in the pancreatic cells, so that this treatment group got a score of 0, namely without pancreatic cell necrosis. So, administering pagoda flower extract (Clerodendrum paniculatum L.) effectively healing pancreatic cells infected with leptospira bacteria.

Reporting Research Results

The Conceptual Framework can be seen in Figure 1 below. The following is the conceptual framework in this study:

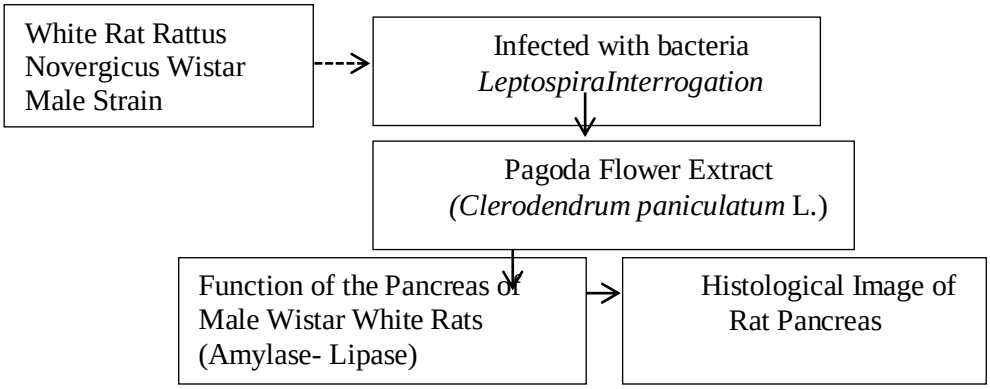


Figure 1. Conceptual Framework

This study hypothesizes that administering pagoda flower extract (Clerodendrum paniculatum L.) affects pancreatic function and the histopathological picture of the pancreas of male Wistar strain white rats infected with the bacteria Leptospira Interrogation.

The research results prove that the extract pagoda flower (Clerodendrum paniculatum L.) has pharmacological properties such as anti-aging, antioxidant, anticancer, anti-inflammatory,

and bacterial properties because the content in it contains alkaloids, flavonoids, saponins, and tannins where the content is good and can be categorized as medicinal plants.

To determine the success of the infection, serum will be taken. Serum collection is intended to diagnose leptospirosis, and a serological examination is carried out. If particle agglutination occurs on the Leptospira antigen, blood serum is declared positive for containing Leptospira bacteria. The following table shows mice's average body weight and body temperature before and after infection with Leptospira interrogans bacteria. The average Body Temperature of Mice Before and After Infection with Leptospira interrogans bacteria can be seen in Table 2.

Table 1. Average Body Temperature of Mice Before and After Infection Leptospira interrogans bacteria

Group	**Body Temperature Measurement Results**	
	BeforeC)	**AfterC)**
Control (P0)	35.6	40.16
Treatment 1 (P1)	37.6	39.56
Treatment 2 (P2)	37.9	40.7
Treatment 3 (P3)	37.6	39.3

It can be seen that the group that experienced the most drastic increase was group P3 with an average temperature of 40.7˚C from the average original temperature of the mice before being infected with bacteria. This indicates a reaction to the increase in body temperature of mice that have been infected with the bacteria. After ensuring that all mouse samples have been infected with bacteria, the next step in this study is to see the function of the mouse pancreas through amylase and lipase levels. The results of observations of the lipase levels of test animals during the treatment process can be seen in Table 3 below.

Table 2. Lipase Levels

No	Group	Repetition	Lipase Level After High Fat Diet (U/L)	Lipase Levels After Treatment (U/L)
1	Control	1	21.1	21.7
2		2	22.3	22.8
3		3	21.6	22.9
4		4	23.2	24.4
5		5	23.6	24.9
6		6	22.7	23.6
		Average	**22.4**	**23.4**
7	Treatment I (100mg/KgBW)	1	41.9	33.2
8		2	44.7	31.9
9		3	43.3	32.9
10		4	40.1	30.8
11		5	41.7	31.7
12		6	43.2	32.1
		Average	**42.48**	**37.5**
13	Treatment II (150mg/KgBW)	1	42.9	28.7
14		2	41.7	29.3
15		3	43.9	26.3
16		4	40.4	28.5
17		5	41.6	26.3
18		6	40.8	27.1
		Average	**41.8**	**27.7**

19	Treatment III (200mg/KgBW)	1	42.4	20.5
20		2	43.1	23.1
21		3	41.5	22.3
22		4	40.7	23.8
23		5	41.2	24.3
24		6	43.5	22.3
		Average	**42.06**	**22.71**

Based on the average lipase levels, it can be seen that the control group had an average value of 22.4U/L before treatment and 23.4U/L after being given distilled water for 14 days. The lipase levels of mice in the control group are a reference for the high and low levels in the treatment group. Treatment group 1, after being infected with bacteria Leptospira interrogans, has a lipase level of 42.48U/L, and after being given pagoda flower extract (Clerodendrum paniculatum L.), at a dose of 100mg/KgBB, it became 37.5U/L. Treatment group 2 after 1 after being infected with bacteria Leptospira interrogans 41.8 U/L, and after being given pagoda extract at a dose of 150 mg/KgBB, it became 27.7U/L. Finally, in treatment group 3, after being infected with bacteria 42.06U/L and after being given pagoda flower extract at a dose of 200mg/KgBB, it became 22.71U/L.

Then, observations were made on changes in amylase levels by inducing leptospira bacterial infection and after administering pagoda flowers (Clerodendrum paniculatum L.). The following are the results of observations on the lipase levels of test animals during the treatment process:

Table 3. Average Amylase Levels (U/L)

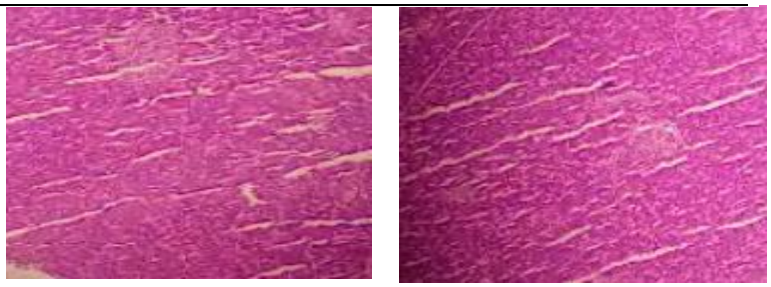
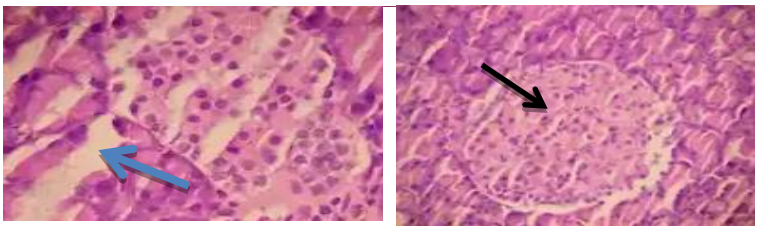
No	**Group**	**Repetition**	**Amylase Level After High Fat Diet (U/L)**	**Amylase Level after Treatment (U/L)**
1	Control	1	60.8	58.9
2		2	61.6	60.3

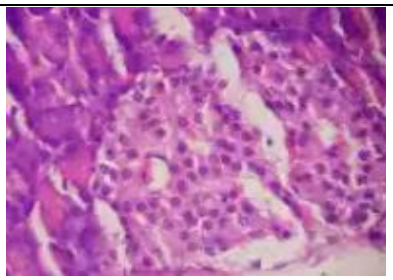
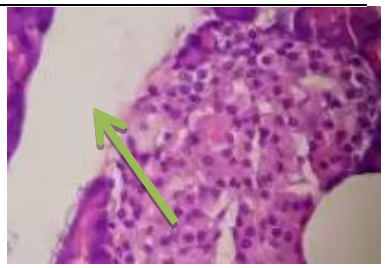
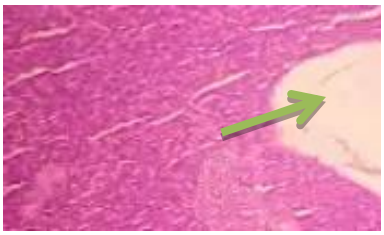
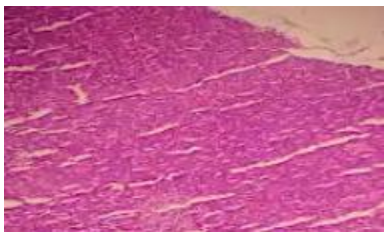
3		3		59.6	59.3
4		4		60.7	59.5
5		5		61.5	60.4
6		6		60.6	59.4
			Average	**60.8**	**59.6**
7	Treatment I	1		68.8	67.1
8	(100mg/KgBW)	2		68.2	67.1
9		3		68.7	67.7
10		4		69.4	68.4
11		5		69.6	67.8
12		6		68.2	67.3
			Average	**68.81**	**67.57**
13	Treatment II	1		67.8	62.6
14	(150mg/KgBW)	2		69.2	62.3
15		3		66.1	63.6
16		4		67.3	62.4
17		5		69.2	64.2
18		6		66.2	64.3
			Average	**67.63**	**63.23**
19	Treatment III	1		68.9	59.1
20	(200mg/KgBW)	2		69.3	58.1
21		3		69.1	59.5
22		4		67.3	58.4
23		5		67.4	60.2
24		6		68.7	57.2
			Average	**68.45**	**58.75**

The results of observations made on all groups showed that there was a change in amylase levels in the treatment group. Based on the average amylase levels, it can be seen that the control group had an average value of 60.8 U/L before treatment and 59.6 U/L after being given distilled water for 14 days. The amylase levels of mice in the control group are used as a reference for the high and low levels in the treatment group. Treatment group 1, after being infected with leptospira bacteria, had an amylase level of 68.81U/L, and after being given pagoda flower extract at a dose of 100mg/KgBB, it became 67.57U/L. Treatment group 2, after being infected with bacteria 67.63U/L and pagoda flower extract at a dose of 150mg/KgBB, became 63.23U/L. Finally, in treatment group 3, after being infected with bacteria 68.45U/L and given pagoda flower extract at 200mg/KgBB, it became 58.75U/L.

Then, histopathological observations were made on the pancreas organs of mice. Pancreatic tissue in the control and treatment groups were given pagoda flower extract at doses of 100mg/KgBB, 150mg/KgBB, and 200mg/KgBB. Administration of the extract pagoda flower (Clerodendrum paniculatum L.) was performed every day in the morning for 14 days. Table 5 shows the histological picture of pancreatic tissue in each treatment group:

Table 4. Histopathological Description of Pancreatic Tissue

No	Group	Histopathological Image of Pancreatic Tissue
1	Control (Aquades)	
2	Treatment 1 (100mg/KgBW)	

3	Treatment 2 (150mg/KgBW)		
4	Treatment 3 (200mg/KgBW)		

Based on the data of the cell morphology results above, there are differences in each group. The control group (K) got a score of 0, namely without pancreatic cell necrosis, because this group was not infected with leptospira bacteria. Treatment group 1 (P1), which was infected with leptospira bacteria and given pagoda flower extract treatment at a dose of 100 mg/KgBB, had a histological picture of the pancreas in the form of interstitial edema found between the serous acini, leukocyte infiltration, mild vacuolization, and pancreatic necrosis so that this group got a score of 3, namely there was ¾ total pancreatic cell necrosis. Treatment group 2 (P2) In treatment group 2, which was infected with leptospira bacteria and given pagoda flower extract treatment at a dose of 150 mg/KgBB, a difference was seen because there was moderate leukocyte infiltration and necrosis in the pancreatic cells with a score of 2, namely ½ total Pancreatic Cell necrosis. There was no necrosis in treatment group 3 (P3), which was infected with leptospira bacteria and given pagoda flower extract treatment at a dose of 200 mg/KgBW. However, there was still a slight leukocyte infiltration in the pancreatic cells, so this treatment group received a score of 0, namely, no pancreatic cell necrosis.

Next, to analyze the data, the normality test in this study used the Kolmogorov-Smirnov test, with the results that can be seen in Table 6 below.

Table 5. Normality Test Results

Variables	**Group**			
	K	**P1**	**P2**	**P3**

	n=6	n=6	n=6	n=6
		Sig		
Lipase	.200	.200	.200	.200
Amylase	.200	.200	.200	.200

The result of the test is p> 0.05 which is 0.200 then the data has been normally distributed. Furthermore, homogeneity testing is carried out using the Levene test with a significance level of 5%, the following table:

Table 6. Homogeneity Test

	Levene static	**df1**	**df2**	**Sig.**
Amylase	2,524	3	20	.087
Lipase	.813	3	20	.502

The probability value of significance obtained is greater than 0.05, so it can be concluded that the control group, treatment group 1, treatment group 2, and treatment group 3 come from a population that has the same variance, or is homogeneous. Furthermore, testing the significant effectiveness between the trial groups with one way anova.

Table 7. One Way Anova Test Results

		Amount	**df**	**Mean square**	**F**	**Sig**
Amylase	Inter Group	289,935	3	96,645	149,432	.000
	In Group	12,935	20	.647		
	Total	302,870	23			
Lipase	Inter Group	340,948	3	113,649	80,899	.000
	In Group	28,097	20	1.405		

	Total	369,045	23

The results of the One-Way Anova test in the table above show that the significance value produced on amylase is 0.000 or <0.05 and lipase is 0.000 or <0.05. Based on these data, it can be concluded that there is a significant difference between the control group and the treatment group.

DISCUSSION

The function of the pancreas is to produce digestive enzymes (exocrine function) and hormones (endocrine function). The function of the pancreas includes producing digestive enzymes such as amylase, lipase, and trypsin, as well as producing the hormone glucagon to increase blood sugar levels and the hormone insulin to lower them (Karpińska, 2022). Bacterial infection is one of the many causes of pancreas inflammation known as pancreatitis. One treatment if infected with this bacteria is drugs to relieve symptoms and treat bacterial infections. Some drugs that will be given are antibiotics, such as penicillin and amoxicillin. Some herbal plants contain antioxidants and antibacterials, including pagoda leaf extract (Clerodendrum paniculatum L.). In this study, the extract pagoda flower positive contains active compounds such as alkaloids, flavonoids, saponins, and tannins. So, pagoda flower extract has good antioxidant benefits for the body.

After examining the entire mice group that had been infected with the bacteria, the measurement of the body temperature of the mice was carried out as a comparison before and after the mice were infected with the bacteria. From the observation of the body temperature of the mice in the table above, it can be seen that the average body temperature in the mice increased after 14 days of being induced by the bacterial infection. Leptospira interrogans, it can be seen that the group that experienced the most drastic increase was group P3, with an average temperature of 40.7˚C from the average original weight of the mice before being infected with the bacteria. This shows a reaction to the increase in body temperature of mice infected with the bacteria.

Based on the difference in the average lipase levels, the researchers concluded that treatment group 3, namely mice infected with bacteria and given pagoda flowers (Clerodendrum paniculatum L.) at a dose of 200mg/KgBW had the most significant decrease in lipase levels and approached the control group. In treatment group 1, mice infected with bacteria and

given pagoda flower extract (Clerodendrum paniculatum L.) at 100mg/KgBW dose experienced the least decrease or improvement in lipase levels.

Amylase levels for treatment group 3, namely mice infected with bacteria and given pagoda flower extract (Clerodendrum paniculatum L.) at a dose of 200mg/KgBB, had the most significant decrease and obtained results below the control group. Treatment group 1, mice that experienced bacterial infections and were given pagoda flower extract (Clerodendrum paniculatum L.) at a dose of 100mg/KgBB, experienced the least decrease or improvement in amylase levels.

In the histopathological examination of the pancreas of mice, it was seen that treatment groups 1, 2, and 3 experienced improvement, and in treatment group 3 (P3), which was infected with leptospira bacteria and given pagoda flower extract treatment with a dose of 200mg/KgBW, there was no necrosis. However, there was still a little leukocyte infiltration in the pancreatic cells, so this treatment group got a score of 0 without pancreatic cell necrosis. So, administering pagoda flower extract (Clerodendrum paniculatum L.) effectively healing pancreatic cells infected with leptospira bacteria.

This is in line with research on the effectiveness of pagoda flowers (Banne et al., 2023). Research related to the content of pagoda flower extract has pharmacological activities such as anti-aging, antioxidant, anticancer, anti-inflammatory, and antibacterial activities. Thus, based on the research, pagoda flower extract (Clerodendrum paniculatum L.) is effective against the pancreas function of male white Wistar rats infected with Leptospira interrogans bacteria.

CONCLUSION

1. In this study, it was found that there was an effect of administering pagoda flower extract (*Clerodendrum paniculatum* L.) on the function of the pancreas of male Wistar white rats infected with Leptospira interrogans bacteria, as seen from the results of amylase and lipase levels and histopathological examination of the pancreas of rats which improved after being administered pagoda flower extract.
2. The content of secondary metabolites in pagoda flower extract (*Clerodendrum paniculatum* L.) through phytochemical tests shows that pagoda flowers are positive for containing active compounds such as alkaloids, flavonoids, saponins, and tannins.

3. By examining serum amylase and lipase levels, we found that pagoda flower extract is effective in healing the pancreatic function of mice infected with leptospira bacteria.
4. Likewise, the histopathological examination of the pancreas of mice infected with bacteria showed improvement after treatment with pagoda flower extract.

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