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Acute Toxicity Test of Lancing Leaf Extract (*Solanum Mauritianum Scop.*) as Well as Determination of Ld50 Values and Histopathology in Male Mice (Wistar Rat)

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Abstract: The purpose of this study is to find out about the acute toxicity test and analysis of its activity on lancing leaves. This research method is an experimental method including sampling and sample processing, extract making, acute toxicity tests, research on toxic symptoms in animals, organ harvesting, organ weighing, organ histopathology examination and data analysis with Statistical Program Service Solution (SPSS). The research was conducted at the Integrated Development and Research Laboratory of Andalas University from September 2024 to December 2024. The tools used in this study are Rotary evaporator (Buchi R-210 Rotavapor), separation funnel, oven (Memmert), furnace, analytical scale (SF-400), decigator, mortar and pestle, porcelain cruce, Moisture Analyzer, Hot plate, Uv-Visible lamp (Camag), dark bottle, funnel, infusion bottle (500 ml and 100 ml), glass beaker (Pyrex), drip plate, rack and test tube, measuring cup (Pyrex), measuring flask, spatels, stirring rods, droppers, ointment pots, object glass, KLT chambers, capillary pipes, syringes, sondes, animal cages, animal feeding and drinking places. The animals that will be used in this study are healthy male white rats aged 2-3 months with a body weight of 200-300 g and have never been used for experiments as many as 25 animalsAn LD50 value was obtained with a mild toxic value (>2000 mg/KgBB – 5000 mg/KgBB) against the acute toxicity test of lancing leaf extract (*Solanum Mauritianum Scop.*) in male rats. There was no significant difference between groups ($p>0.05$) in the body and BOR of male rats compared to the control group after administration of lancing leaf extract (*Solanum Mauritianum Scop.*).

Keywords: Acute toxicity; Lancing leaf extract; Ld50 values

Introduction

The use of herbal medicines derived from various plants has been going on for centuries. Until now, people still utilize knowledge about herbal medicine in medicine. Various health problems and diseases can be overcome through the administration of herbal medicinal herbs. Given its great benefits, the understanding of herbal medicine needs to be maintained and passed on to future generations (Putranto, 2014). Of the approximately 30 thousand to 50 thousand plant species that grow in Indonesia, approximately 7,500 species are recorded that have the potential to be medicinal plants (Ministry of Health, 2017).

Various ways of traditional medicine that develop through empirical learning and are passed down from generation to generation. Herbal medicinal plants from the family group *Rubiaceae* It generally has the characteristics of a stem that grows vines on the ground

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surface. The use of herbal herbs in traditional medicine is often applied as a solution to various health problems. In the use of herbal medicine as a cheap and effective treatment option to maintain health, it is necessary to prove the safety of its use as an aspect that must be prioritized (Mustapa, 2018).

The toxicity test method is a way to analyze the possible impact of toxins derived from the content of extracts or chemical components on leaves and herbal medicines. The implementation of toxicity tests is necessary in estimating the level of damage that can be caused by a compound, both biological and non-biological materials in the body of living things (Sasmito et al., 2017).

Lancing leaves are a type of herbal medicine that has medicinal benefits. The use of this leaf is generally intended as a treatment for several conditions such as gastritis and fever, and can be processed into massage oil. Based on the results of content analysis *phytochemicals*, it was found that lancing leaves contain compounds *terpenoids* (Aththorick & Berutu, 2018). Through this description, the purpose of this study is to find out about the acute toxicity test and analysis of its activity on lancing leaves.

Method

This research method is an experimental method including sampling and sample processing, extract making, acute toxicity tests, research on toxic symptoms in animals, organ harvesting, organ weighing, organ histopathology examination and data analysis with Statistical Program Service Solution (SPSS). The research was conducted at the Integrated Development and Research Laboratory of Andalas University from September 2024 to December 2024. The tools used in this study are Rotary evaporator (Buchi R-210 Rotavapor), separation funnel, oven (Memmert), furnace, analytical scale (SF-400), decigator, mortar and pestle, porcelain cruce, Moisture Analyzer, Hot plate, Uv-Visible lamp (Camag), dark bottle, funnel, infusion bottle (500 ml and 100 ml), glass beaker (Pyrex), drip plate, rack and test tube, measuring cup (Pyrex), measuring flask, spatels, stirring rods, droppers, ointment pots, object glass, KLT chambers, capillary pipes, syringes, sondes, animal cages, animal feeding and drinking places. The animals that will be used in this study are healthy male white rats aged 2-3 months with a body weight of 200-300 g and have never been used for experiments as many as 25 animals. Before the study, the rats were acclimatized first for 7 days. The research materials are in the form of lancing leaves (Peronema canescens Jack.), 70% ethanol, aquades, Na CMC 0.5%, quercetin, filter paper, standard food for rats. The sample used in this study was lancing leaves obtained from Kabanjahe, Tanah Karo, North Sumatra. The mortality of test animals in each group was analyzed using an equation according to the Indonesian Pharmacopoeia Edition III to obtain an LD50 value. Meanwhile, the percentage change in body weight and organ weight was analyzed using the SPSS (Statistical Product and Service Solution) program. The data was analyzed using the One Way Anova test to determine the statistical significance between the test animal groups, then continued with the Duncan follow-up test.

Result and Discussion

Acute Toxicity Test of LD50 Lancing Leaf Extract (Solanum Mauritianum Scop.) against Rats

Assessment of the toxicity level of lancing leaf extract (*Solanum Mauritianum Scop.*) for male rats, the results were obtained on the 12th to 14th day, several treatment groups died, namely in the P1 group (on the 14th day), the P2 and P3 groups (on the 12th and 14th days) and the P4 group (on the 12th and 13th days). The following is further detailed in the table of the development of observation of rat mortality and signs of macroscopic changes in rats through acute toxicity symptoms after oral administration of lancing leaf extract during the 14-day treatment period.

Table 1. Observation of Mortality in Rats after Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*) for 14 Days

Group	Day													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
CMC 0.5% (K-)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300 mg/KgBB (P1)	0	0	0	0	0	0	0	0	0	0	0	0	0	1
900 mg/KgBB (P2)	0	0	0	0	0	0	0	0	0	0	0	1	0	1
2700 mg/KgBB (P3)	0	0	0	0	0	0	0	0	0	0	0	1	0	1
8100 mg/KgBB (P4)	0	0	0	0	0	0	0	0	0	0	0	1	1	0

Table 2. Observation of Symptoms of Acute Toxicity to Rats after Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*) for 14 Days

Observation	Treatment Groups				
	K-	P1	P2	P3	P4
Eyes (watery)	Not	Not	Yes	Yes	Yes
Tremor	Not	Not	Not	Yes	Yes
Diarrhea	Not	Not	Not	Not	Not
Movement (walk)	Usual	Usual	Slow	Slow	Slow
Filtration	Not	Not	Yes	Yes	Yes
Letargi	Not	Yes	Yes	Yes	Yes
Convulsions	Not	Not	Not	Yes	Yes
Salisation	Usual	Usual	Usual	Excess	Excess
Respiratory Rate	Usual	Usual	Usual	Slow	Slow
Urination	Usual	Usual	Usual	Turbid	Turbid

The determination of the LD50 classification that has been calculated using the formula of the Indonesian Pharmacopoeia Edition III, the result was that the LD50 value of lancing leaf extract (*Solanum Mauritianum Scop.*) in rats is 3087 mg/KgBB which belongs to the mild toxic group. The following is shown a table for calculating the LD50 value of lancing leaf extract in rats.

Table 3. Calculation of LD50 Value for Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*) in Mice

Group	Dosage (mg/KgBB)	Dosage Log	Number of Experimental Animals	Number of Deaths	Pi	LD50
P1	300	2.47	5	1	0.2	3087 mg/KgBB
P2	900	2.95	5	2	0.4	
P3	2700	3.43	5	2	0.4	
P4	8100	3.91	5	2	0.4	

Measurement of Blood Glucose Levels of Male Rats Serum after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Measurement of serum blood glucose levels of rats after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was carried out using a spectrophotometry tool after being treated for 14 days. Statistical analysis was carried out after data on blood glucose levels of rats was obtained through the initial stages of normality tests.

Table 4. Results of Normality Test of Serum Blood Glucose Levels of Rats

Group	P value	Information
CMC 0.5% (K-)	0.421	Normal distributed data
Extract 300 mg/KgBB (P1)	0.506	Normal distributed data
Extract 900 mg/KgBB (P2)	0.630	Normal distributed data
Extract 2700 mg/KgBB (P3)	0.107	Normal distributed data
Extract 8100 mg/KgBB (P4)	1.000	Normal distributed data

From table 4, it can be explained that each research group has a *p value* of p>0.05, meaning that each data group is normally distributed. The normality test value in the K- group was 0.421 followed by the P1 treatment group 0.506; P2 treatment group 0.107; the P3 treatment group was valued at 0.107 and the P4 group was valued at 1,000.

The analysis was then continued on the ANOVA one-way parametric bivariate test and it was found that the serum blood glucose levels of rats were significantly related after the administration of lancing leaf extract (*Solanum Mauritianum Scop.*), i.e. p = 0.002 (p<0.05). The average serum blood glucose level in more detail can be seen in the following table.

Table 5. Blood Glucose Levels of Rats after Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*)

Group	Blood Glucose Levels (mg/dL)	P Value
CMC 0.5% (K-)	101.56 ± 28.90	0.002*
Extract 300 mg/KgBB (P1)	56.42 ± 3.36	
Extract 900 mg/KgBB (P2)	50.06 ± 5.09	
Extract 2700 mg/KgBB (P3)	88.93 ± 0.89	
Extract 8100 mg/KgBB (P4)	53.90 ± 0.30	

Remarks: *) p < 0.05 is a significant value

From table 5, it was obtained that serum blood glucose levels experienced an average change in treatment compared to the control group K- (101.56 mg/dL), namely P1 (56.42 mg/dL), P2 (50.06 mg/dL), P3 (88.93 mg/dL) and P4 (53.90 mg/dL). In addition, a significant relationship was also obtained between changes in serum blood glucose levels within normal limits and the administration of lancing leaf extract statistically with a value of p = 0.002 (p<0.05).

Measurement of Serum Creatinine Levels of Male Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Measurement of serum creatinine levels of rats after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was carried out using a spectrophotometry tool after being treated for 14 days. Statistical analysis was carried out after data on serum creatinine levels of rats were obtained through the initial stages of normality tests.

Table 6. Results of Normality Test of Serum Creatinine Levels of Rats

Group	P Value	Information
CMC 0.5% (K-)	0.011	Data is not normally distributed
Extract 300 mg/KgBB (P1)	0.198	Normal distributed data
Extract 900 mg/KgBB (P2)	0.253	Normal distributed data
Extract 2700 mg/KgBB (P3)	0.484	Normal distributed data
Extract 8100 mg/KgBB (P4)	0.637	Normal distributed data

From table 6, it can be explained that the research groups P1, P2, P3 and P4 have a p value of p>0.05 meaning that each data group is normally distributed and K- has a p value of p<0.05 meaning that it is not normally distributed. The normality test value in the K- group was 0.011 followed by the P1 treatment group 0.198; P2 treatment group 0.253; the P3 treatment group was 0.484 and the P4 group was 0.637.

The analysis was then continued on the Kruskal Wallis non-parametric bivariate test and no significant difference was found between the groups, namely p = 0.242 (p>0.05). The average serum creatinine levels in more detail can be seen in the following table.

Table 7. Serum Creatinine Levels of Rats after Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*)

Group	Blood Cratinine Levels (mg/dL)	P Value
CMC 0.5% (K-)	1.46 ± 0.50	
Extract 300 mg/KgBB (P1)	1.18 ± 0.32	
Extract 900 mg/KgBB (P2)	0.96 ± 0.11	0.242
Extract 2700 mg/KgBB (P3)	1.44 ± 0.25	
Extract 8100 mg/KgBB (P4)	0.97 ± 0.07	

From table 7, the results were obtained that serum creatinine levels changed on average compared to the K+ control group (1.46 mg/dL), namely P1 (1.18 mg/dL), P2 (0.96 mg/dL), P3 (1.44 mg/dL) and P4 (0.97 mg/dL). In addition, there was no significant difference in serum creatinine levels between groups of lancing leaf extract statistically with a value of p = 0.242 (p>0.05).

Measurement of Blood Urea Levels of Male Tiku Serum after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Measurement of serum urea levels of rats after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was carried out using a spectrophotometry tool after being treated for 14 days. Statistical analysis was carried out after data on serum urea levels of rats were obtained through the initial stages of normality tests.

Table 8. Results of Normality Test of Serum Urea Levels in Rats

Group	P Value	Information
CMC 0.5% (K-)	0.006	Data is not normally distributed
Extract 300 mg/KgBB (P1)	0.007	Data is not normally distributed
Extract 900 mg/KgBB (P2)	0.052	Normal distributed data
Extract 2700 mg/KgBB (P3)	0.377	Normal distributed data
Extract 8100 mg/KgBB (P4)	0.298	Normal distributed data

From table 7, it can be explained that the research groups P2, P3 and P4 have a p value of p>0.05 meaning that each data group is normally distributed and K- and P1 have a p value of p<0.05 meaning that it is not normally distributed. The normality test value in the K- group was 0.006 followed by the P1 treatment group 0.007; P2 treatment group 0.052; the P3 treatment group was 0.377 and the P4 group was 0.298.

The analysis was then continued on the Kruskal Wallis non-parametric bivariate test and no significant difference was found between the groups, namely p = 0.336 (p>0.05). The average serum urea levels in more detail can be seen in the following table.

Table 9. Serum Urea Levels of Rats after Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*)

Group	Blood urea levels (mg/dL)	P Value
CMC 0.5% (K-)	19.14 ± 4.05	
Extract 300 mg/KgBB (P1)	17.85 ± 1.36	
Extract 900 mg/KgBB (P2)	14.70 ± 3.63	0.336
Extract 2700 mg/KgBB (P3)	19.46 ± 1.53	
Extract 8100 mg/KgBB (P4)	19.03 ± 0.32	

From table 9, it was obtained that serum urea levels experienced an average change in treatment (P1, P2 and P4) compared to the K+ control group (19.14 mg/dL), namely P1 (17.85 mg/dL), P2 (14.70 mg/dL) and P4 (19.03 mg/dL) with an increase in serum urea levels in the P3 group (19.46 mg/dL). In addition, there was no significant difference in creatinine levels between

groups of lancing leaf extract statistically with a value of p = 0.336 (p>0.05).

Measurement of Serum SGOT Levels of Male Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Measurement of SGOT (*Serum Glutamic Oxaloacetic Transaminase*) levels of rat serum after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was carried out using a spectrophotometry tool after being treated for 14 days. Statistical analysis was carried out after obtaining data on serum SGOT levels of rats through the initial stages of normality tests.

Table 10. Results of Normality Test of Serum SGOT Levels of Rats

Group	P Value	Information
CMC 0.5% (K-)	0.069	Normal distributed data
Extract 300 mg/KgBB (P1)	0.038	Data is not normally distributed
Extract 900 mg/KgBB (P2)	0.038	Data is not normally distributed
Extract 2700 mg/KgBB (P3)	0.264	Normal distributed data
Extract 8100 mg/KgBB (P4)	0.567	Normal distributed data

From table 10, it can be explained that the research groups K-, P3 and P4 have a *p value* of p>0.05 meaning that each data group is normally distributed and P1 and P2 have a *p value* which is p<0.05 meaning that it is not normally distributed. The normality test value in the K- group was 0.069 followed by the P1 treatment group 0.038; P2 treatment group 0.038; the P3 treatment group was valued at 0.264 and the P4 group was valued at 0.567.

The analysis was then continued on the non-parametric bivariate test *of Kruskal Wallis* and no significant differences were found between groups of lancing leaf extract (*Solanum Mauritianum Scop.*), i.e. p = 0.088 (p>0.05). The average serum SGOT levels in more detail can be seen in the following table.

Table 11. Serum SGOT Levels of Rats after Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*)

Group	Blood SGOT Levels (U/L)	P Value
CMC 0.5% (K-)	21.04 ± 9.16	0.088
Extract 300 mg/KgBB (P1)	23.07 ± 2.27	
Extract 900 mg/KgBB (P2)	17.40 ± 2.51	
Extract 2700 mg/KgBB (P3)	24.70 ± 2.53	
Extract 8100 mg/KgBB (P4)	25.46 ± 0.51	

From table 11, it was obtained that serum SGOT levels increased on average in the treatment (P1, P3 and P4) compared to the K+ control group (21.04 U/L), namely P1 (23.07 U/L), P3 (24.70 U/L) and P4 (25.46 U/L) with changes in serum urea levels in the P2 group (17.40 U/L). In addition, there was no significant difference in serum SGOT levels between groups of lancing leaf extract statistically with a value of p = 0.088 (p>0.05).

Measurement of SGPT Levels in Male Rat Serum after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Measurement of SGPT (*Serum Glutamic Pyruvic Transaminase*) levels of rat serum after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was carried out using a spectrophotometry tool after being treated for 14 days. Statistical analysis was carried out after obtaining data on serum SGPT levels of rats through the initial stages of normality tests.

Table 12. Results of Normality Test of Serum SGPT Levels of Rats

Group	P Value	Information
CMC 0.5% (K-)	0.058	Normal distributed data
Extract 300 mg/KgBB (P1)	0.051	Normal distributed data
Extract 900 mg/KgBB (P2)	0.024	Data is not normally distributed
Extract 2700 mg/KgBB (P3)	0.521	Normal distributed data
Extract 8100 mg/KgBB (P4)	0.537	Normal distributed data

From table 12, it can be explained that the research groups K-, P1, P3 and P4 have a p value of p>0.05 meaning that each data group is normally distributed and P2 has a p value of p<0.05 meaning that it is not normally distributed. The normality test value in the K- group was 0.058 followed by the P1 treatment group 0.051; P2 treatment group 0.024; the P3 treatment group was 0.521 and the P4 group was 0.537.

The analysis was then continued on the non-parametric bivariate test *of Kruskal Wallis* and no significant differences were found between groups of lancing leaf extract (*Solanum Mauritianum Scop.*), i.e. p = 0.087 (p>0.05). More detailed average serum SGPT levels can be seen in the table 13.

From table 13, the results were obtained that serum SGPT levels experienced an average change in treatment (P1, P2 and P3) compared to the control group K+ (26.86 U/L), namely P1 (26.81 U/L), P2 (19.38 U/L) and P3 (26.82 U/L) with an increase in serum urea levels in the P4 group (35.00 U/L). In addition, there was no statistically significant difference in SGOT levels

between lancing leaf extract groups with a value of p = 0.088 (p>0.05).

Table 13. Serum SGPT Levels of Rats after Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*)

Group	Blood SGPT Level (U/L)	P Value
CMC 0.5% (K-)	26.86 ± 12.31	
Extract 300 mg/KgBB (P1)	26.81 ± 3.85	
Extract 900 mg/KgBB (P2)	19.38 ± 5.92	
Extract 2700 mg/KgBB (P3)	26.82 ± 2.87	0.088
Extract 8100 mg/KgBB (P4)	35.00 ± 0.72	

Measurement of Body Weight and BOR of Male Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Weight Calculation in rats after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was carried out after 14 days of treatment. The measured weight was then followed by a statistical analysis test in the form of analysis of the normal distribution of data as the initial stage of parametric and non-parametric statistical tests.

Table 14. Results of the Rat Weight Normality Test

Group	P Value	Information
CMC 0.5% (K-)	0.886	Normal distributed data
Extract 300 mg/KgBB (P1)	0.003	Data is not normally distributed
Extract 900 mg/KgBB (P2)	0.089	Normal distributed data
Extract 2700 mg/KgBB (P3)	0.380	Normal distributed data
Extract 8100 mg/KgBB (P4)	0.161	Normal distributed data

From table 14, it can be explained that the research groups K-, P2, P3 and P4 have a p value of p>0.05 meaning that each data group is normally distributed and the P1 group has a p value of p<0.05 meaning that each data group is not normally distributed. The normality test value in the K- group was 0.886 followed by the P1 treatment group 0.003; P2 treatment group 0.089; the P3 treatment group was 0.380 and the P4 group was 0.161.

The analysis was then continued on the non-parametric bivariate test *of Kruskal Wallis* and no significant differences were found between groups of lancing leaf extract (*Solanum Mauritianum Scop.*), i.e. p = 0.173 (p>0.05). The average weight level of rat badab in more detail can be seen in the table 15.

Table 15. Weight Levels of Rats after Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*)

Group	Weight Rate (grams)	P Value
CMC 0.5% (K-)	131.20 ± 17.31	
Extract 300 mg/KgBB (P1)	172.75 ± 39.52	
Extract 900 mg/KgBB (P2)	160.66 ± 74.84	0.173
Extract 2700 mg/KgBB (P3)	211.33 ± 50.64	
Extract 8100 mg/KgBB (P4)	149.33 ± 23.75	

From table 15, it was obtained that the weight level increased on average in all treatment groups (P1, P2, P3 and P4) compared to the K+ control group (131.20 grams), namely P1 (172.75 grams), P2 (160.66 grams), P3 (211.33 grams) and P4 (149.33 grams). In addition, it was also found that there was an insignificant relationship between weight gain within normal limits and the administration of lancing leaf extract statistically with a value of p = 0.173 (p>0.05).

Calculation of BOR in rats after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was carried out after 14 days of treatment. The BOR measured includes the liver, kidneys and pancreas. Statistical analysis was carried out after organ weighing in the form of analysis of normal distribution of data as the initial stage of parametric and non-parametric statistical tests.

Table 16. Results of the Normality Test of BOR Liver of Rats

Group	P Value	Information
CMC 0.5% (K-)	0.192	Normal distributed data
Extract 300 mg/KgBB (P1)	0.210	Normal distributed data
Extract 900 mg/KgBB (P2)	0.199	Normal distributed data
Extract 2700 mg/KgBB (P3)	0.764	Normal distributed data
Extract 8100 mg/KgBB (P4)	0.680	Normal distributed data

From table 16, it can be explained that all research groups have a p> 0.05 value meaning that each data group is normally distributed. The normality test value in the K- group was 0.192 followed by the P1 treatment group 0.210; P2 treatment group 0.199; the P3 treatment group was valued at 0.764 and the P4 group was valued at 0.680.

Table 17. Results of the Normality Test of Rat Kidney BOR

Group	P Value	Information
CMC 0.5% (K-)	0.403	Normal distributed data
Extract 300 mg/KgBB (P1)	0.267	Normal distributed data
Extract 900 mg/KgBB (P2)	0.094	Normal distributed data
Extract 2700 mg/KgBB (P3)	0.300	Normal distributed data
Extract 8100 mg/KgBB (P4)	0.609	Normal distributed data

From table 17, it can be explained that all research groups have *a p*> 0.05 value meaning that each data group is normally distributed. The normality test value

in the K- group was 0.403 followed by the P1 treatment group 0.267; P2 treatment group 0.094; the P3 treatment group was valued at 0.300 and the P4 group was valued at 0.609.

From table 18, it can be explained that all research groups have *a p*> 0.05 value which means that each group of data is normally distributed. The normality test value in the K- group was 0.778 followed by the P1 treatment group 0.519; P2 treatment group 0.567; the P3 treatment group was 0.281 and the P4 group was 0.637.

Table 18. Pancreatic BOR Normality Test Results

Group	P Value	Information
CMC 0.5% (K-)	0.778	Normal distributed data
Extract 300 mg/KgBB (P1)	0.519	Normal distributed data
Extract 900 mg/KgBB (P2)	0.567	Normal distributed data
Extract 2700 mg/KgBB (P3)	0.281	Normal distributed data
Extract 8100 mg/KgBB (P4)	0.637	Normal distributed data

The analysis was then continued on the parametric bivariate test *of One Way ANOVA* and obtained BOR of the liver and kidneys of rats showing that there was no effect of the dose variant of lancing leaf extract (*Solanum Mauritianum Scop.*) which is meaningful, namely p = 0.496 and p = 0.334 (p>0.05) and the pancreatic BOR shows that there is a significant difference in lancing leaf extract (*Solanum Mauritianum Scop.*) between groups, i.e. p = 0.000 (p<0.05). A more detailed average BOR of rats can be seen in the table 18.

Table 19. BOR of Liver, Kidney and Pancreas of Rats after Administration of Lancing Leaf Extract (*Solanum Mauritianum Scop.*)

Group	Rat BOR (%)	P Value
Liver		
CMC 0.5% (K-)	3.34 ± 0.45	
Extract 300 mg/KgBB (P1)	3.44 ± 0.31	
Extract 900 mg/KgBB (P2)	3.76 ± 0.93	0.496
Extract 2700 mg/KgBB (P3)	3.06 ± 0.38	
Extract 8100 mg/KgBB (P4)	3.61 ± 0.08	
Kidney		
CMC 0.5% (K-)	0.82 ± 0.04	
Extract 300 mg/KgBB (P1)	0.78 ± 0.12	
Extract 900 mg/KgBB (P2)	0.82 ± 0.28	0.334
Extract 2700 mg/KgBB (P3)	0.59 ± 0.17	
Extract 8100 mg/KgBB (P4)	0.87 ± 0.23	
Pancreas		
CMC 0.5% (K-)	0.28 ± 0.01	
Extract 300 mg/KgBB (P1)	0.16 ± 0.03	
Extract 900 mg/KgBB (P2)	0.18 ± 0.05	0.000
Extract 2700 mg/KgBB (P3)	0.17 ± 0.03	
Extract 8100 mg/KgBB (P4)	0.17 ± 0.18	

Histopathology of Rat Liver after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Testing the effect of toxicity effects of lancing leaf extract (*Solanum Mauritianum Scop.*) is carried out on the liver through HE staining. The assessment was carried out using a 200X microscope magnification. The histopathological results of the rat liver can be seen in the figure 1.

Results obtained from the histopathology of the liver of rats after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) that is, fat degeneration occurred in each treatment group, mainly increased in the P4 group with a concentration of 8100 mg/KgBB. In addition, it was also found that bleeding affected the sinusoid hepatocytes with an increase, especially in the P3 and P4 groups with concentrations of 2700 mg/KgBB and 8100 mg/KgBB.

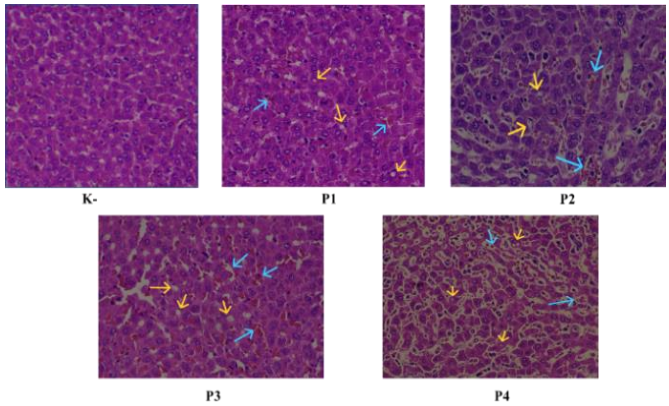

Figure 1. Histopathology of rat liver. The yellow arrow indicates fat degeneration and the blue arrow indicates bleeding inside the sinusoid

Histopathology of Rat Kidneys after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Testing the effect of toxicity effects of lancing leaf extract (*Solanum Mauritianum Scop.*) is carried out on the kidney organ through HE staining. The assessment was carried out using a 200X microscope magnification. The histopathological results of the rat kidneys can be seen in the following figure.

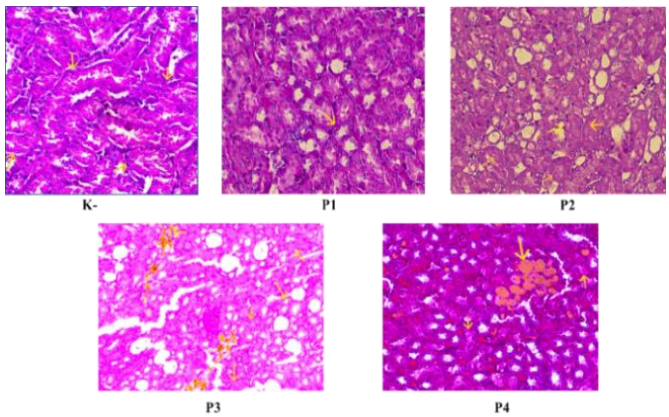

Figure 2. Histopathology of rat kidneys. The yellow arrow indicates cloudy swollen degeneration

Results obtained from the histopathology of rat kidneys after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) in the control group and treatment, turbid swelling degeneration was found in cuboid epithelial cells in the renal tubules, especially increased most in the P4 group with a concentration of 8100 mg/KgBB.

Histopathology of Rat Pancreas after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Testing the effect of toxicity effects of lancing leaf extract (*Solanum Mauritianum Scop.*) is performed on the pancreatic organs through HE staining. The assessment was carried out using a 200X microscope magnification. The histopathology results of the rat pancreas can be seen in the following figure.

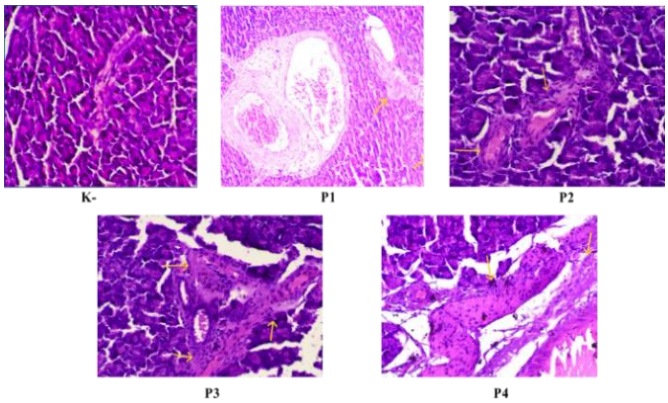

Figure 3. Histopathology of the rat pancreas. The yellow arrow indicates fibrosis of the ascetic gland

Results obtained from the histopathology of the rat pancreas after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) is the formation of fibrosis in pancreatic asinic cells and continues to develop, especially in the P2, P3 and P4 groups with concentrations of 900 mg/kgBB, 2700 mg/KgBB and 8100 mg/KgBB. The increase in fibrosis area was seen most in the P4 group with the administration of extracts with a concentration of 8100 mg/KgBB.

Discussion

Assessment of LD50 Acute Toxicity in Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

LD50 toxicity test that has been carried out on rats against the administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was obtained that the extract was mildly toxic with an LD50 value in the toxic category at a dose of >2000-5000 mg/KgBB (Morris-Schaffer & McCoy, 2021). This assessment is based on the number of deaths of experimental animals in the form of rats during the study. In the research that has been carried out, several signs of animals experiencing symptoms of acute toxicity were also obtained, including watery eyes, tremors, diarrhea, pilcorrection (standing feathers), lethargy (weakness and lethargy), convulsion (squirming and convulsions), salivation (mouth releasing excess saliva), irregular breathing and increased urinary levels (Syahroni et al., 2023).

From several studies, it is concluded that the use of extracts Lancing Leaf (*Solanum Mauritianum Scop.*) is still classified as safe with the concentration of extract below 2000mg/KgBB (Aydin et al., 2016).

Serum Blood Glucose Levels in Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Measurement of blood sugar levels after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was found that there was a significant relationship between changes in blood sugar levels and the administration of the extract ($p = 0.002$). The results obtained can be interpreted as changes in blood sugar levels within the normal limit, namely 50-135 mg/dL (Oktafiano et al., 2016). In addition, it was concluded that lancing leaf extract did not exert a toxicity effect in the mechanism of action of blood glucose.

Effects of changes in blood sugar levels after administration of the extract Lancing Leaf (*Solanum Mauritianum Scop.*) caused by the presence of phytochemical compounds in plants, especially saponins and phenolics which is abundant in lancing (Smakosz et al., 2024). Saponins have a role in reducing the increase in blood glucose by inhibiting enzymes that break down disaccharides into monosaccharides (El Barky et al., 2017). In addition, saponns also affect the oxidative stress changes of pancreatic beta cells along with phenolic through electron transfer and hydroxyl bonds in the group *Reactive Oxygen Species* (ROS) (Hoda et al., 2019).

Serum Creatinine Levels in Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Serum creatinine levels in rats after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) was obtained that no significant relationship was found with the value of $p = 0.242$ ($p>0.05$). The results obtained mean that there is no significant change or increase in creatinine levels, with values close to control. The creatinine levels obtained were normal values in the range of 0.57-1.12 mg/dL (Dewi et al., 2016).

From the results obtained and other research results, it can be concluded that the use of plant extracts, especially lancing leaf extracts (*Solanum Mauritianum Scop.*) does not have a toxic effect on kidney function through creatinine levels are still within normal limits, but at the highest dose creatinine levels also increase

which indicates a change in early kidney function (Kellum et al., 2021).

Serum Urea Levels in Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Measurement of serum urea levels after administration of lancing leaf extract (*Solanum Mauritianum Scop.*) in male Wistar rats, no significant difference was found between groups with a value of p = 0.336 (p>0.05). The results obtained mean that there was no significant change or increase in serum urea levels, with values close to control. The serum urea values found in each treatment group were normal with a value range of 15.0 – 21.0 mg/dL (Perdanawati et al., 2022). So it can be concluded that the acute toxicity test carried out does not provide a toxic reaction that can damage the kidneys with a decrease in urea value (Ballesteros-Ramírez et al., 2024).

Serum SGOT/SGPT Levels in Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

Assessment of SGOT/SGPT levels in acute toxicity test of lancing leaf extract (*Solanum Mauritianum Scop.*) was obtained that there was no significant difference between the control group and the treatment with the values p = 0.088 (SGOT) and p = 0.087 (SGPT). The results obtained mean that there was no significant change or increase in serum urea levels, with values close to control. The SGOT/SGPT values obtained in this study are included in the normal value range, namely 5-40 U/L for SGOT and 5-35 U/L for SGPT (Nofita et al., 2020).

From the results of the research that has been carried out, it can be concluded that the administration of plant extracts, especially lancing leaf extracts (*Solanum Mauritianum Scop.*) does not have a significant toxic effect on the liver through the assessment of SGOT/SGPT levels.

Effect of Body Weight and BOR in Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

The results showed that the administration of lancing leaf extract (*Solanum Mauritianum Scop.*) did not have a significant effect on body weight (p = 0.173) and the relative organ weight of the liver (p = 0.496) and kidneys (p = 0.334). However, significant changes were found in the relative organ weight of the pancreas (p = 0.000), which is likely related to the effects of bioactive compounds such as saponins and phenolics contained in lancing leaf extracts. Saponins are known to reduce oxidative stress and protect organ cells through membrane stabilization, while phenolic compounds act as anti-inflammatory agents that support tissue repair (Hussain et al., 2021).

The significant effects on the pancreas seen in this study suggest the potential of tissue adaptation to the extract treatment, which requires further research to understand its specific mechanisms.

Assessment of Organ Histopathology in Rats after Administration of Lancing Leaf Extract (Solanum Mauritianum Scop.)

The histopathological results of the liver organ show that the higher the dose of the extract given, the more severe the degree of liver damage. In the control group (CMC 0.5%), the liver was in good condition without fat degeneration or sinusoidal hemorrhage. However, in the treatment group, there was little fat degeneration and sinusoid hemorrhage at the dose of 300 mg/KgBB, which increased significantly at the dose of 2700 mg/KgBB and reached a very severe condition at the dose of 8100 mg/KgBB. This indicates the existence of a dose-reaction relationship, reflecting the potential toxicity of the extract in the liver at high doses.

Renal histopathology showed changes in cloudy swelling degeneration in the treatment group with low doses (300 mg/KgBB and 900 mg/KgBB). However, at high doses (2700 mg/KgBB and 8100 mg/KgBB), an increase in cloudy swelling degeneration was found. This may reflect the extract's ability to protect the kidneys at low doses, but trigger toxicity at high doses. In the pancreatic organs, healthy pancreatic tissue was found in the control group and treated at low doses (300 mg/KgBB). However, at a dose of 900 mg/KgBB, mild fibrosis began to be seen in the ascites gland, which increased to moderate and severe at doses of 2700 mg/KgBB and 8100 mg/KgBB.

Effects of Saponin Content and those contained in lancing leaf extract are known to have a biphasic effect, i.e. protection at low doses through the reduction of free radicals, but can cause lipid peroxidation and cell membrane damage at high doses. The phenolic compounds in this extract also act as effective antioxidants, but at high doses, it can cause excessive oxidative stress that triggers inflammation and damage to liver, kidney, and pancreatic tissues (Eseberri et al., 2022; Jodynis-liebert & Kujawska, 2020).

Conclusion

LD50 value was obtained with a mild toxic value (>2000 mg/KgBB – 5000 mg/KgBB) against the acute toxicity test of lancing leaf extract (*Solanum Mauritianum Scop.*) in male rats. There was no significant difference between groups (p>0.05) in the body and BOR of male rats compared to the control group after administration of lancing leaf extract (*Solanum Mauritianum Scop.*). Several structural changes were obtained in the

histological organs of the liver (sinusoid hemorrhage and hemorrhage), kidneys (degeneration, swelling, cloudiness, cuboid cells) and pancreas (asini-cell fibrosis) which were toxicity reactions of lancing leaf extract (*Solanum Mauritianum Scop).*). There was no significant difference between the clinical chemical groups of liver function and kidney function, but there was a significant difference between groups in blood glucose, so it was recommended to use a lower dose.

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Conceptualization: A.I, R.I, E.T, A.N.N; data curation: A.I, R.I, E.T., A.N.N funding acquisition: A.I, R.I, E.T., A.N.N methodology: A.I, R.I, E.T., A.N.N visualization: A.I, R.I, E.T., A.N.N – original draft: A.I, R.I, E.T., A.N.N writing: A.I, R.I, E.T., A.N.N – review & editing A.I, R.I, E.T., A.N.N

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