

The Acute Toxicity of Ki Hampelas Leaves (*Sterculia rubiginosa* Zoll. Ex Miq)

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ABSTRACT

Background: Ki Hampelas (*Sterculia rubiginosa* Zoll. Ex Miq) is a medicinal plant with antioxidant and nephroprotective activity. **Objective:** This research aims to prove that Ki Hampelas leaves extract through an acute toxicity test. **Materials and Methods:** This study used white male rats of the *Sprague-Dawley* strain divided into four groups, the normal group and the 50 mg/kg, 1000 mg/kg, 2000 mg/kg dose groups. For the acute toxicity test, a single dose with an observation of 14 days. After that, the surgery was done to see changes in the histopathology of the liver and kidneys. **Results:** The administration of Ki Hampelas leaf extract in the acute toxicity test did not cause death in the tested animals. There were no significant liver and kidney changes seen from the SGOT, SGPT, creatinine, urea, and histopathology. **Conclusion:** Ki Hampelas leaves extract did not cause death and toxic effects in the acute toxicity test. **Key words:** Ki Hampelas (*Sterculia rubiginosa* Zoll. Ex Miq), Acute Toxicity, Liver, Kidney.

INTRODUCTION

Sterculia is a genus with many pharmacological activities and is also used as a material in pharmaceutical preparations. Among the genus, *Sterculia*, *Sterculia villosa* Roxb, has antileishmanial activity and a safety level at giving a non-toxic dose of 100 mg/kg body¹. *Sterculia setigera* Del. has the activity of the ethanol extract of *Sterculia setigera* Del. has antioxidant activity with the DPPH method on the fruit of 91.81%. In contrast, ethanol extract on stem bark is 86%². Seeds of *Sterculia foetida* seed have antioxidant and antimicrobial activity³. *Sterculia setigera* Del., has activity as a tyrosinase inhibitory activity. It also has antiproliferative activity against human colon adenocarcinoma HT29⁴. *Sterculia quinqueloba* (Garcke) K. Schum has activity as an antimycobacterial activity⁵. *Sterculia quadrifida* R.br Stem bark also has activity as an anti-hepatitis C⁶. Plants of the genus *Sterculia* are also used in drug delivery applications⁷. Ag nanoparticles using seeds from *Sterculia foetida* L. have activity on mosquito vectors and HeLa cancer cells⁸. Some *Sterculia* genus plants have activities. *Sterculia foetida* for antibacterial and hemolytic¹⁰, apoptosis¹¹, *Sterculia diversifolia* for immunomodulatory and anti-cancer¹², *Sterculia villosa* as fibrinolytic⁵, sedative⁶, *Sterculia tragacantha* as anti-inflammatory and analgesic¹⁵,

One of the plants used as an ingredient in traditional medicine is Ki Hampelas leaves (*Sterculia rubiginosa* Zoll. Ex Miq). These plants are scattered in tropical and subtropical areas, especially in Sumatra. Based on previous research, Ki Hampelas leaves contain tannins, flavonoids, alkaloids, steroids-terpenoids, glycosides, and phenols. The antioxidant activity and total flavonoids equivalent to quercetin¹⁷. So it is interesting to study whether *Sterculia rubiginosa* has antioxidant and nephroprotective activity¹⁶.

To ensure the safety, effectiveness, and quality of a drug must undergo a series of tests. Starting from screening to look for active compounds, then continued with testing the effectiveness or selectivity and its mechanism of action in experimental animals or microbes, after being declared to have certain pharmacological activities by a series of safety tests on experimental animals, the toxicity test¹⁷. In previous studies, Ki Hampelas leaves have activity as a nephroprotective and antioxidant with a minimum dose of 50 mg/kg¹⁶. So it is necessary to do a toxicity test to ensure the safety of Ki Hampelas leaves extract.

The acute toxicity test aims to detect toxic effects that appear quickly and determine the LD₅₀ value in a compound or substance after being given a single dose or repeated doses within 24 hours.

MATERIALS AND METHODS

Material

The leaves of Ki Hampelas obtained from the Bogor Botanical Gardens, Indonesia. Determination at the Botanical Garden Plant Conservation Center, Botany Division, Biology Research Center-LIPI, Indonesia. Ethanol obtained from local suppliers. Urea reagent kit, Creatinine kit, SGOT kit, SGPT kit from PT. Human, Indonesia. Na CMC (PT. Brataco), aqua destillata, obtained from local suppliers.

Extraction

Ki Hampelas leaves powder was extracted by maceration method with 70% ethanol. Two hundred (200) grams of *Simplicia* powder by immersing 70% ethanol. Then concentrated using a vacuum rotary evaporator at a temperature of 50°C to obtain a thick extract, evaporated on a water bath with a temperature of 50°C until a viscous extract¹⁸.

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Extract characteristics

The extract was indentified with organoleptic, the yield, moisture content, ash content and phytochemical screening.

Acute toxicity test

Acute toxicity test used white male rats *Sprague Dawley* strain. The tested animals used in this study were 24 animals divided into four groups consisting of 6 animals for each group. The normal control group was given standard feed and 0.5% Na CMC, extract dose of 50 mg/kg, 1000 mg/kg, 2000 mg/kg. The test animals acclimatized for seven days. During acclimatization, the rats were fed and drunk and controlled the health and weight. Before taking blood, the animal test has fasted for \pm 12 hours. The animals anesthetized using ketamine intramuscularly, then blood serum samples taken from white rats. The liver's acute toxicity parameters determined by SGOT, SGPT, and histopathology of the central vein and pyknotic nucleus size. The kidneys' observation done by determining creatinine, urea, and histopathology by looking at the cast on the tubules and the percentage of tubules with close and glomerular swelling. Glomerular calculated by measuring the distance from the Bowman's capsule's edge to the glomerular rim¹⁹. Tubular damage calculated using the formula = $(n / m \times 100\%)$, where n= is the number of proximal tubules covered in one field of view and m= is the number of all proximal tubules in one field of view. Then the results were averaged to get the percentage of kidney damage in each mouse²⁰. This research was permitted by the Ethics Committee KEPK-UHAMKA No. 02 / 20.03 / 0358.

Data analysis

The Kolmogorov-Smirnov and Levene's test determined the homogeneity and normal distribution of the data. The analytical continuous with the Tukey Test.

RESULTS AND DISCUSSION

Phytochemical screening

Flavonoids, glycosides, alkaloids, tannins, saponins, triterpenoids and steroids, are present in the extract. The test results show in Table 2.

Table 1: Quality Characteristics of extract *S. rubiginosa*.

No.	Characteristics	Result
1.	Organoleptic	
	a.) Form	Thick extract
	b.) Color	Brownish green
	c.) Smell	Typical
2.	d.) Taste	A bit bitter
	Rendement	13.19 %
3.	Water content	7.95%
4.	Ash content	8.54%

Table 2: Phytochemical Screening of extract *S. rubiginosa*.

Chemical Ingredients	Result
Alkaloids	+
Flavonoids	+
Tannins	+
Phenol	+
Saponins	-
Triterpenoi d & Steroids	+

Description : (+) = Presence; (-) = Absence

Acute toxicity of Ki hampelas leaf extract

The results Ki Hampelas leaf extract with the highest dose of 2000 mg/kg did not cause death in the test animals, the value of LD₅₀ extract of Ki Hampelas leaves for test animals male white rats Sprague-Dawley is more than 2000 mg/kg.

Heart

At SGOT levels, SGPT showed an increase between the normal group and the extract group. However, this increase is still in the normal range, so it concluded that Ki Hampelas leaves extract's giving does not influence it. From the results of examining SGOT and SGPT levels, the value obtained ($p > 0.05$) indicated no significant difference in each treatment group. The results show in Figures 1 and 2.

Liver histopathology

Histopathological observations of the liver include measuring the central vein's diameter and the number of pyknotic nuclei. The central vein's diameter is used in the measurement because the central venous area is the center of the hepatic lobule and part of the reservoir of blood originating from the hepatic artery and portal vein²¹. The results of liver histopathological preparations show in Figure 5.

The parameter of liver organ, the central vein's diameter, between normal and the test group, shows no difference between groups. This result show in figure 6. The pyknotic nuclei show the differences between the normal and the test groups. Besides, the number of pyknotic nuclei which a sign of the occurrence of cell necrosis. This result show in Figure 7.

Kidney

The creatinine and urea levels of rats given the extract showed that treatment with different doses had increased creatinine and urea levels in rats. However, the increase in levels was still within normal limits. The results showed that creatinine and urea levels found that acute toxicity Ki Hampelas ki leaf extract had no significant effect on creatinine and urea levels $p > 0.05$. The results show in figures 3 and 4.

Kidney histopathology

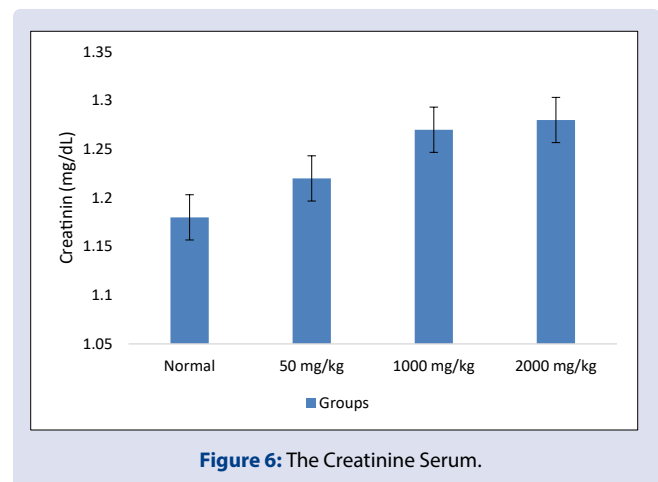
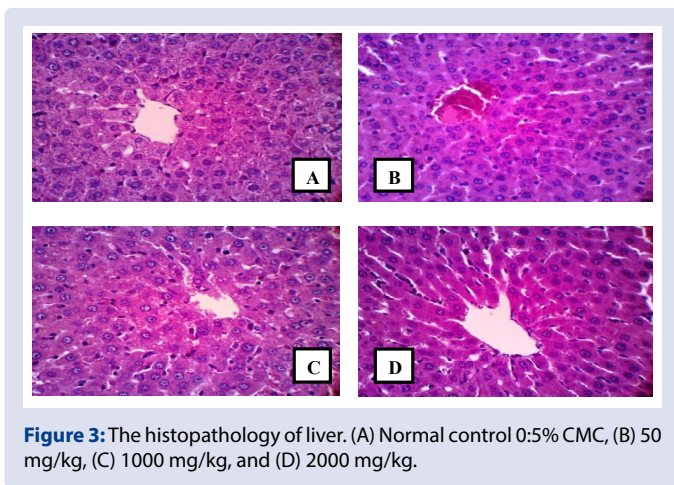
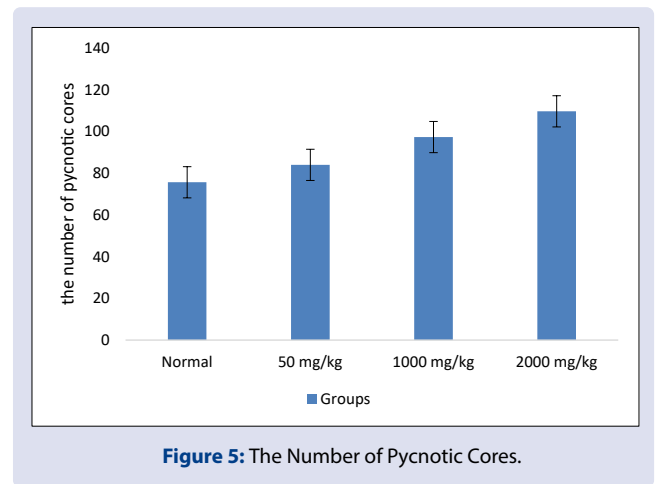
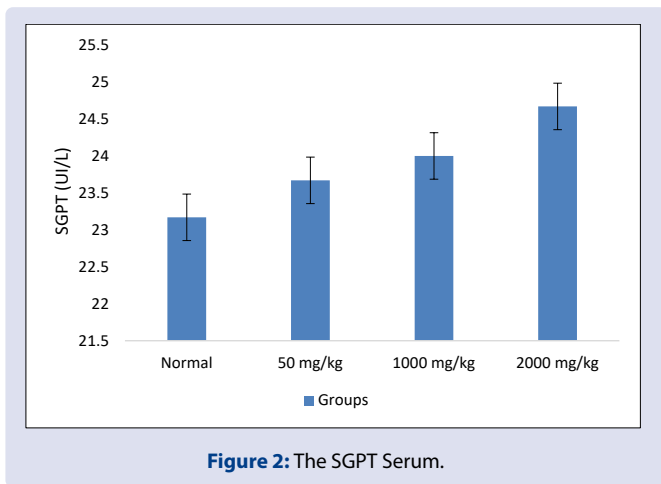
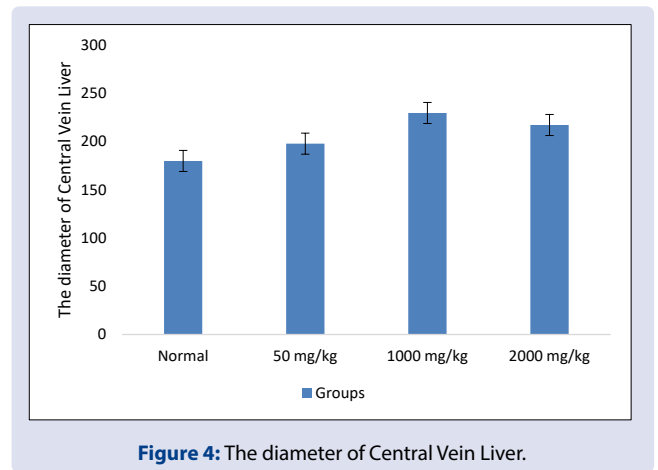
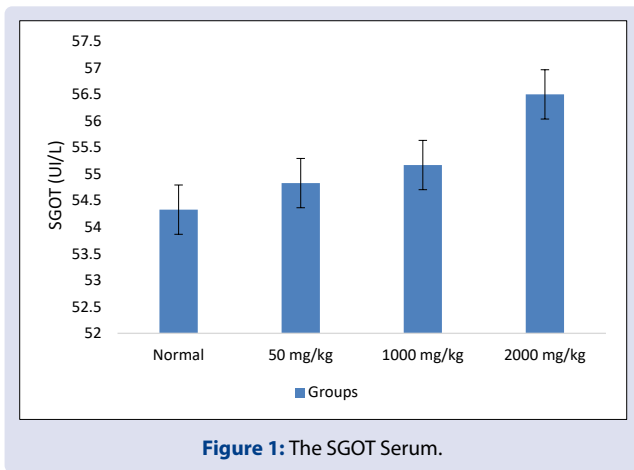
Observations on the structure of the kidney structure include the distance between the glomerulus and Bowman's capsule, the percentage of tubules that close in one view and the cast on the tubules, can be seen in Figure 8. Casts are a collection of proteins that result in channeling through the tubular renal hampered, also stimulate the occurrence of necrosis

of the tubules. While necrosis is death Jarin gan due to the absence of metabolites²².

The result of the study showed no presence of cast in control normal and the test groups. The percentage of tubules that closed in one field of view showed that there was no significant difference between the normal group and the 50 mg/kg dose group $p > 0.05$, and the results between the 1000 mg/kg dose group and the 2000 mg/kg dose test group not seen. The significant difference with $p > 0.05$ shown in Figure 9. Meanwhile, the bowman room distance shows a significant difference between the normal control and test groups. The result show in Figure 10.

CONCLUSION

The ethanol extract of 70% Ki Hampelas leaves in the acute toxicity test did not cause death and toxic effects. The examination of SGOT and SGPT levels showed no significant difference between the dose treatment group and the normal group ($p > 0.05$).



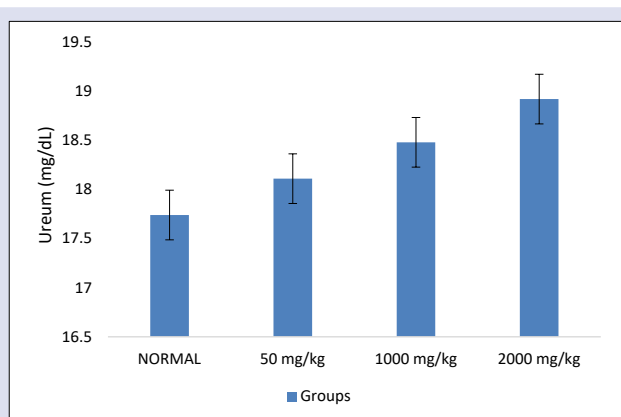


Figure 7: Ureum levels.

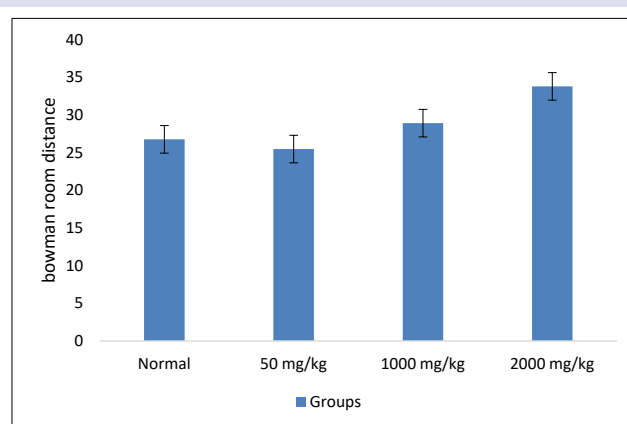


Figure 10: Kidney Bowman's Space Distance.

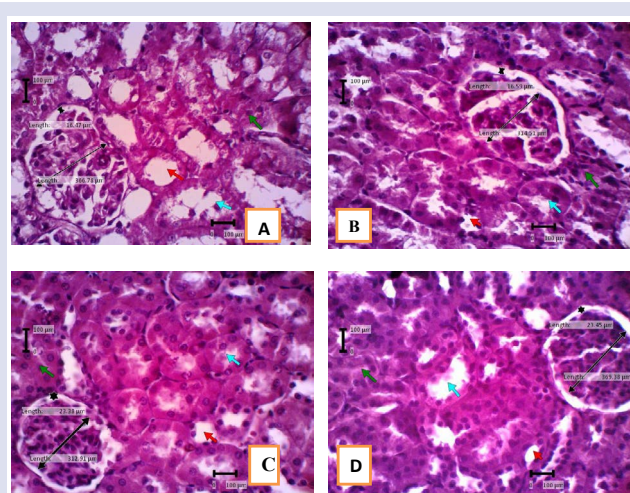


Figure 8: The Histopatology of Kidney. (A) Normal CMC 0,5%, (B) 50 mg/kg, (C)1000 mg/kg, dan (D) 2000 mg/kg.

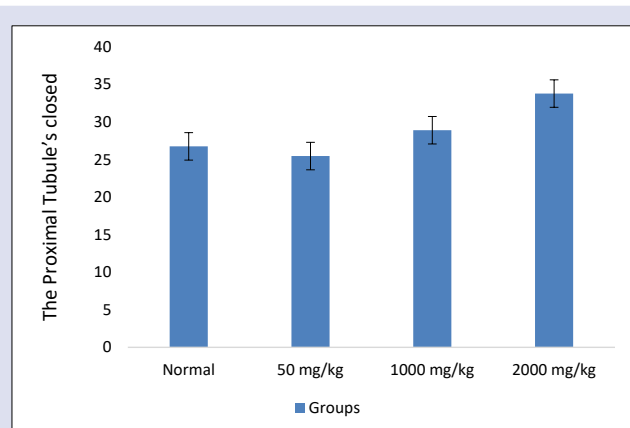


Figure 9: The Proximal Tubule's closed.

ETHICAL ISSUES

The Ethics Committee permitted this research with the number KEPK-UHAMKA No. 02 / 20.03 / 0358.

CONFLICTS OF INTEREST

All authors state there is no conflicts of interest.

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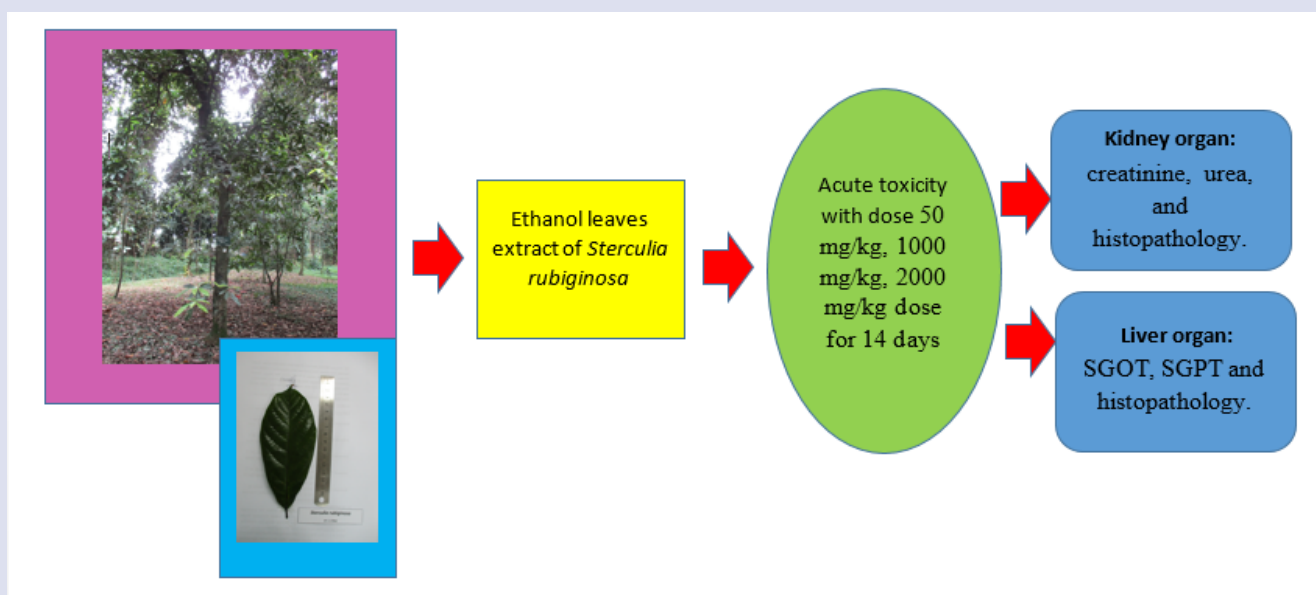
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GRAPHICAL ABSTRACT



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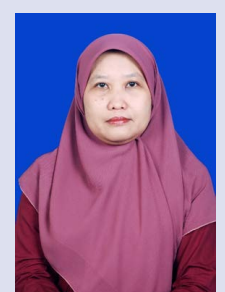
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