Vol 12 No 1 Year 2027

BULETIN FARMATERA

E-ISSN: 2528-410X

**RESEARCH ARTICLES**

# Giving Bamboo Grass Extract (*Lophatherum gracile) is Effective* as a Hepatoprotector in Male Mice (*Mus musculus)*

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**Abstract:** The use of paracetamol in toxic doses can cause impaired liver function. Bamboo grass is a plant that contains antioxidants, so it can be a hepatoprotector in protecting the liver from damage caused by paracetamol. The dose *of Lopatherum gracile* as a hepatoprotector has been studied in the dose range of 200 mg/kg body weight and 800 mg/kg body weight, with an effective dose result of 800 mg/kg body weight. The purpose of this study was to determine the effective dose of the hepatoprotector of bamboo grass extract against paracetamol-induced liver function in mice. This study is *a true experiment* with *a post-test-only control group design*. 5 groups were given treatment for 7 days, namely the negative control group (C-), positive control (C+), treatment 1 (T I): 400 mg/kg body weight, treatment 2 (T II): 600 mg/kg body weight, and treatment 3 (T III): 800 mg/kg body weight. The SGOT and SGPT levels between groups were analysed by *one-way ANOVA and post hoc Bonferroni.* The results of the ANOVA test showed a significant difference in the level of SGOT and SGPT, namely p=0.001. The *post hoc test* showed no significant difference in SGOT and SGPT levels between T(II) and T(III), with negative controls of p:0.242, and p:0.100, and there was no significant difference in average SGOT between T2 and T3. The effective dose of hepatoprotector of bamboo grass extract in a group of paracetamol-induced mice was 600 mg/kg body weight.

**Keywords:** Extract, liver, male mice, paracetamol, bamboo grass, SGOT, SGPT

## INTRODUCTION

Cirrhosis of the liver is a pathological condition of the liver characterised by the formation of fibrous tissue, changes in normal liver tissue and degenerative nodules. Degenerative changes in liver tissue can cause damage to hepatocyte tissue, so that it is replaced

BULETIN FARMATERA

E-ISSN: 2528-410X

by fibrous tissue.[1] Most of the patients who experience cirrhosis of the liver do not have significant symptoms, but symptoms can also be found in the form of fatigue, weakness, loss of appetite, and discomfort in the upper right abdomen. In addition to that, symptoms of liver function failure, such as *jaundice*, portal hypertension, and hepatic encephalopathy, can also be found.[2]

There are around 1.32 million deaths that occur due to liver disease, with various factors both in developed and developing countries.[3] Cirrhosis of the liver is one of the main diseases that causes death in people with liver disease.

The use of certain drugs over a long period of time can result in the production of reactive metabolites that accumulate excessively so that they are hepatotoxic and can cause apoptosis and necrosis in liver cells.[4]

Acetaminophen, also known as paracetamol, is one of the drugs that has been widely used by the community both as an anti-inflammatory, antipyretic, and analgesic drug.[5]

Based on research that was conducted in 2015, paracetamol is the most widely consumed drug by the general public as the first treatment, with a total percentage (38.2%) followed by NSAID drugs (29.1%), antibiotics (16.9%), herbal drugs (6.7%), and other drugs (9.1%). According to a study that has been conducted in 2018, rats have the same levels of paracetamol hepatotoxicity as humans.[6] Consumption of paracetamol at a dose of ≥ 300 mg/kg body weight can cause injury to liver cells in mice, leading to liver failure due to the accumulation of *N-acetyl-p-benzoquinoneimine* (NAPQI).[7]

Excessive levels of NAPQI in the body will damage cell membranes, mitochondrial dysfunction, and glutathione shrinkage so that hepatocyte cells become more susceptible to damage caused by free radicals.[8]

*Lophatherum gracile* is also one of the herbal plants that has been used as a therapy in various medical conditions. Previous research has shown that *Lophatherum gracile* has anti-inflammatory and antiviral effects that can prevent COVID-19.[9]

Based on previous research, *Lophatherum gracile* extract has been administered to mice induced with carbon tetrachloride. In the previous study, 2 doses of *Lophatherum gracile extract* of 200 mg/kg body weight and 800 mg/kg body weight were used. Administration of *Lophatherum gracile* extract at a dose of 200 mg/kg body weight showed no significant hepatorpotektor effect on the reduction of SGOT and SGPT levels in these mice compared to the group of mice induced only with carbon tetrachloride, while administration of *Lophatherum gracile* extractwith a dose of 800 mg/kgBB in mice induced with carbon tetrachloride can prevent an increase in the levels of the enzymes SGOT and SGPT compared to the group induced only with carbon tetrachloride so it can be concluded that the administration of *Lophatherum gracile* extract at a dose of 800 mg/kg body weight is proven to have an antioxidant effect that has the potential to protect the liver from damage that can

E-ISSN: 2528-410X

be caused by free radicals, but in the study, doses with intervals that are too far apart, namely between 200 mg/kg body weight and 800 mg/kg body weight, were used, so it is not known whether *Lophatherum gracile* extract with doses such as 400 mg/kg body weight and 600 mg/kg body weight also has a hepatoprotective effect on the liver.[10]

Based on the description above, it can be seen that liver disease is one of the health problems that are often faced in the world. Cirrhosis of the liver can be caused by various factors such as hepatitis B virus, hepatitis C, alcohol consumption, non-alcoholic fatty liver disease, and hepatotoxic compounds. According to *The Global Burden of Disease* (GBD) data, more than 1 million people worldwide died due to cirrhosis of the liver in 2010.[5] In 2017, there was an increase in the prevalence of age standards by 10.4% with the number of cases reaching 1.5 billion people compared to 2007.[4] This study aimed to test the effect of *Lophatherum gracile* administration on the hepatoprotective effect in male mice (*Mus musculus).*

## METHODS

This study is *a true experimental* study with *a post-test* method with random group selection and a control group (*The Randomised Post Test with Control Group Design*), which aims to determine the effect of giving bamboo grass extract (*Lophatherum gracile)* on hepatoprotective effects.

This research was conducted in the integrated laboratory of the Faculty of Medicine, University of Muhammadiyah North Sumatra.

The subjects used in this study were 25 male mice (*Mus musculus)*. The exclusion criteria for taking subjects in this study were sick mice, and during the research period.

The sample in this study was obtained from each group, which was divided using Federer's formula. The experimental group was given a dose of Lophatherum gracile extract (dose T I 400 mg/kg body weight, dose T II 600 mg/kg body weight, dose T III 800 mg/kg body weight), a positive control group (given paracetamol induction at a dose of 300 mg/kg body weight), and a negative control group (given standard food and drink only). The experimental animals were randomly divided into 5 groups, each group consisting of 5 male mice. Furthermore, each group will be given standard feed and drink every day until the 15th day. In treatment group 1, treatment 2, and treatment 3, bamboo grass extract (Lophatherum gracile) will be given on days 1 to 7. On day 15, each of the mice from the negative control group, treatment 1, treatment 2, and treatment 3 will be induced with paracetamol at a dose of 300 mg/kg body weight intraperitoneally. On the 16th day, the mice will be sacrificed and operated on, and blood will be drawn from each treatment group through the heart, then the blood will be collected in a reaction tube. Blood in the centrifuge at 5000 rpm for 5 minutes. After that, there will be a separation of the clear part, namely the serum, and then the serum is taken to

BULETIN FARMATERA
E-ISSN: 2528-410X

determine the levels of SGOT and SGPT using a UV spectrophotometer.

## RESULTS

The results of the average serum measurement of SGOT and SGPT in each group of male mice (*Mus musculus*) are shown in the table below.

**Table 1. Average Values of SGOT and SGPT Levels in the Group of Male Mice (Mus musculus)**

| Groups | Average SGOT ± SD | Average SGPT ± SD |
|---|---|---|
| C (-) | 32,82 ± 2,52 | 14,5 ± 1,59 |
| C (+) | 89,64 ± 1,15 | 50,78 ± 1,05 |
| T (I) | 49,88 ± 1,69 | 28,12 ± 0,96 |
| T (II) | 39,52 ± 1,57 | 19,14 ± 1,84 |
| T (III) | 31,02 ± 1,84 | 15,18 ± 1,04 |

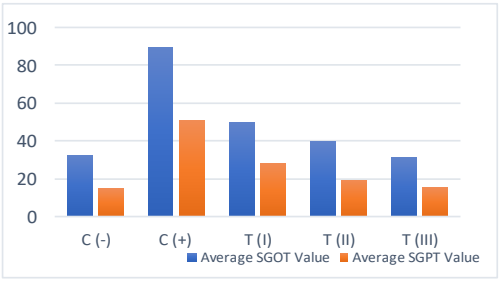


**Figure 1. Chart of Average Values of SGOT and SGPT Levels in Each Group of Male Mice (*Mus musculus*)**

Table 1 above shows that the induction carried out using paracetamol was successful, as evidenced by the results of the average levels of SGOT and SGPT in the C (+) group, which increased approximately 3 times the average levels of SGOT and SGPT from the C (-) group. In the T(I) group, the administration of bamboo grass extract at a dose of 400 mg/KgBB showed a decrease in the average levels of SGOT and SGPT compared to the C (+) group. On the other hand, in groups T (II) and T (III), bamboo grass extract was administered at a dose of 600 mg/kg body weight and 800 mg/kg body weight, and the administration showed a decrease in the average levels of SGOT and SGPT from the liver of mice that had entered the normal limit range.

**Table 2. Anova One-Way Test Results on Average Results of SGOT and SGPT Levels**

| Groups | Sig | P Value | Significancy |
|---|---|---|---|
| Average of SGOT level | 0,001 | < 0,05 | Significant |
| Average of SGPT level | 0,001 | < 0,05 | Significant |

Based on table 2 above, it is found that the results of *the One Way Anova* test on average SGOT levels show results of p=0.001 with significant significance, this shows that the data from the results of the average SGOT levels in each group has significant differences, as well as the test results on the average SGPT levels, the test results show a value of p = 0.001 with significant significance, This also shows that the data from the results of the average SGPT level in each group has a significant difference.

**Table 3. Bonferroni Test Results of SGOT Levels Group C (-), C (+), T (I), T (II), and T (III)**

| Groups | Sig | P | Significancy |
|---|---|---|---|
| C (-) vs C (+) | 0,001 | < 0,05 | Significant |

E-ISSN: 2528-410X

| | | | |
|---|---|---|---|
| C (-) vs T (I) | 0,001 | < 0,05 | Significant |
| C (-) vs T (II) | 0,167 | > 0,05 | Not Significant |
| C (-) vs T (III) | 1,001 | > 0,05 | Not Significant |
| C (+) vs T (I) | 0,001 | < 0,05 | Significant |
| C (+) vs T (II) | 0,001 | < 0,05 | Significant |
| C (+) vs T (III) | 0,001 | < 0,05 | Significant |
| T (I) vs T (II) | 0,006 | < 0,05 | Significant |
| T (I) vs T (III) | 0,000 | < 0,05 | Significant |
| T (II) vs T (III) | 0,035 | < 0,05 | Significant |

Table 3 above shows that, if it is associated with pharmacological principles, it can be concluded that bamboo grass extract with a dose of 600 mg/KgBB is the most effective dose because it can cause a hepatoprotective effect when viewed statistically. This is also proven by the results of the comparison test between groups T (II) and T (III) and group C (-), which showed that there was no significant difference. The insignificant difference indicates that the administration of bamboo grass extract at a dose of 600 mg/kg body weight and 800 mg/kg body weight has a hepatoprotective effect because the average SGOT level value is similar to the average SGOT level in the C group (-), who are only given standard food and drink.

**Table 4. Bonferroni Test Results of SGPT Levels Group C (-), C (+), T (I), T (II), and T (III)**

| Groups | Sig | P | Significancy |
|---|---|---|---|
| C (-) vs C (+) | 0,000 | < 0,05 | Significant |
| C (-) vs T (I) | 0,000 | < 0,05 | Significant |
| C (-) vs T (II) | 0,242 | > 0,05 | Not Significant |
| C (-) vs T (III) | 1,000 | > 0,05 | Not Significant |
| C (+) vs T (I) | 0,000 | < 0,05 | Significant |
| C (+) vs T (II) | 0,000 | < 0,05 | Significant |
| C (+) vs T (III) | 0,000 | < 0,05 | Significant |
| T (I) vs T (II) | 0,001 | < 0,05 | Significant |
| T (I) vs T (III) | 0,000 | < 0,05 | Significant |
| T (II) vs T (III) | 0,504 | > 0,05 | Not Significant |

Table 4 above shows that in the comparison of groups T (II) and T (III) with group C (+), there is a significant difference. The difference was obtained from the difference in the average level of SGPT in the T (II) and T (III) treatment groups with the C (+) group, so that it had a significant difference. This significant difference indicates that the administration of bamboo grass extract at a dose of 600 mg/kg body weight and 800 mg/kg body weight has a hepatoprotective effect that can protect the liver from damage caused by the toxic substance paracetamol, so from these results it can be concluded that bamboo grass extract with a dose of 600 mg/kg body weight is the most effective dose in causing hepatoprotective effects in mice induced using paracetamol.

E-ISSN: 2528-410X

## DISCUSSION

Paracetamol in high doses has a role in causing liver cell damage in mice. When decomposed by the processes of glucuronidation and sulfation, paracetamol turns into a non-toxic metabolite and is excreted through the urine. However, in the case of paracetamol poisoning, the production of NAPQI metabolites could exceed the ability of liver cells to replenish glutathione supplies. Glutathione deficiency causes NAPQI to bind to proteins in cysteine groups covalently, especially in mitochondrial proteins, which interferes with ATP production and results in mitochondrial dysfunction and the formation of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS), resulting in oxidative stress and hepatotoxicity.[11]

Based on previous research, liver damage due to paracetamol overdose can cause liver cell necrosis, characterised by swelling, plasma leakage, disintegration, and infiltration of inflammatory cells. Studies in male mice given paracetamol at a dose of 300 mg/kg body weight for 1 day showed a decrease in antioxidant enzymes. This is evidenced by the results of SGOT and SGPT levels in the positive control group, who were given treatment in the form of paracetamol induction for 1 day with a dose of 300 mg/kg body weight, which showed a 3-fold increase from the normal value in the SGOT and SGPT tests. [12,13]

Based on the results of the average SGOT and SGPT levels in mice, it indicates that there are metabolite compounds produced from paracetamol in the form of NAPQI which can cause damage to hepatocyte cells so that there is an increase in serum SGOT in the blood, while the administration of bamboo grass extract (Lophatherum gracile) with a dose of 600 mg/kg body weight and 800 mg/kg body weight in groups T (II) and T (III) can reduce serum SGOT levels by approximately 3 times so that the results The average serum level of SGOT in mice had almost the same value as the group of mice that were only fed and drank. In the results of the SGPT serum examination, group C (+) there was an increase in serum SGPT levels due to induction with the administration of paracetamol at a dose of 300 mg/kg body weight, this also indicates that the administration of paracetamol can also increase serum SGPT in the blood of mice due to damage that occurs to mouse hepatocyte cells, when compared to group C (-), group T (II), and group T (III), the three groups had significantly lower average scores compared to the C (+) group. In the T (I) group, there was a significant change in the mean serum levels of SGOT and SGPT in mice that were not significant in the mean serum levels of SGOT and SGPT in mice compared to the C (-) group. These changes give the impression that the administration of extract (Lophatherum gracile) at a dose of 400 mg/kg body weight can reduce SGOT and SGPT levels even though it has not reached the normal level of liver function. Based on the table, it can be concluded that the administration of Lophatherum gracile extract can reduce SGOT levels

E-ISSN: 2528-410X

and provide a hepatoprotective effect in mice induced using paracetamol. This result is in line with previous research, which stated that the administration of bamboo grass extract with a dose of 800 mg/kg body weight can reduce SGOT levels and cause a hepatoprotective effect, but in this study, it was found that 2 doses can lower SGOT levels to normal values of 600 mg/kg body weight and 800 mg/kg body weight.[10,14]

In tables 2 and 3, it was found that there was a significant change between the C group (-) and the C (+) group. This indicates that the induction carried out using paracetamol 300 mg/kg body weight showed a result of (+). Administration of pasatemol at a dose of 300 mg/kg body weight to male mice intraperitoneally may cause damage to the liver of mice. Normally, paracetamol consumption will be metabolized by the digestive organs within 2 hours after oral consumption. In this study, induction of paracetamol through intraperitoneal injection was used, which caused the metabolic process of the drug to become faster. Most of the paracetamol will be metabolised through the process of gluconization and sulfation, while the remaining small amount of paracetamol (10-15%) will be metabolised by cytochrome P450 in hepatocytes into N-acetyl-p-benzoquinone imine, also known as NAPQI, which is highly toxic. These toxic metabolites will be converted by endogenous antioxidants in the form of glutathione into a non-toxic form and excreted through the gallbladder. In this study, a toxic dose of paracetamol was used so that the amount of glutathione contained in mice was not able to convert all remaining NAPQI metabolites, which bound to mitochondrial proteins, which would form cytotoxic proteins, resulting in necrosis in liver cells, so that there was an increase in SGOT and SGPT levels in mice.[7,15,16]

In tables 2 and 3, it was also found that there was a significant difference between the C group (-) and the C (+) group, which shows that the induction carried out using paracetamol showed positive results due to the significant difference in SGOT and SGPT values. Furthermore, in the T (I) and C (+) groups, there was a significant difference; this shows that the administration of bamboo grass extract at a dose of 400 mg/KgBB also has a hepatoprotective effect that can reduce SGOT and SGPT levels, even though it has not been able to reach normal values of liver function. On the other hand, in the T (I) and T (II) groups, when compared to K (+) the two groups also have quite significant differences, this shows that the administration of bamboo grass extract with a dose of 600 mg/kg body weight and 800 mg/kg body weight can provide a hepatoprotective effect that can be seen through the levels of SGOT and SGPT that have reached normal values of liver function and have the average value of SGOT and SGPT levels similar to the C group (-). The results of this study are strong evidence that supports the conclusion of previous research conducted by Qingfe et al., where the administration of bamboo grass extract at

E-ISSN: 2528-410X

a dose of 800 mg/kg body weight can provide a hepatoprotective effect on mice induced using carbon tetrachloride. In the study, the results showed that the average levels of SGOT and SGPT in the group of mice given an extract with a dose of 800 mg/kg body weight were similar to the average levels of SGOT and SGPT in the group of mice that were only given standard feed.[8,10,14]

This study shows that the administration of bamboo grass extract in male mice induced by paracetamol can affect liver function, as observed through measurements of SGOT and SGPT levels. This is in line with research conducted by Qingfe et al. In the study, carbon tetrachloride with a dose of 0.1 ml/10 g was used to trigger liver damage in mice. The results of the study found that the average value of SGOT and SGPT levels in the group of mice given bamboo grass extract with a dose of 800 mg/kg body weight was in the form of 26 U/L and 17 U/L, respectively. An examination of the average levels of SGOT and SGPT in the group of mice that were only given standard feed was also carried out and showed results of around 27 U/L and 14 U/L. The results of the study have similar results to the study where the results of the examination of SGOT and SGPT levels in the group of mice was given bamboo grass extract with a dose of 800 mg/KgBB in the form of 31.02 U/L and 15.18 U/L. In the examination of the average levels of SGOT and SGPT in the group of mice that were only given standard feed, this study also had results close to the research conducted by Qingfe et al, namely in the form of 32.82 U/L and 14.5 U/L. The results of this study are in line with the research that has been conducted by Qingfe et al., where the administration of bamboo grass extract at a dose of 800 mg/kg body weight has a hepatoprotective effect on the liver of mice. However, in this study, it was found that the average level values of SGOT and SGPT were higher compared to previous studies, both in the group that was only given standard feed and the group that was given bamboo grass extract with a dose of 800 mg/kg body weight. This may be due to environmental factors, differences in the induction method carried out, and the length of time it takes to apply the bamboo grass extract.[10]

In this study, 3 different doses of bamboo grass extract were used, and each dose showed different results of SGOT and SGPT levels as well. In the use of a dose of 400 mg/kg body weight, there was a change in SGOT and SGPT levels compared to the negative group. These changes showed a decrease in the value of SGOT and SGPT levels in mice, even though these values did not reach the threshold of normal values of liver function. On the other hand, in the administration of bamboo grass extract with a dose of 600 mg/kg body weight and 800 mg/kg body weight, there was a decrease in SGOT and SGPT levels, which reached the normal threshold of mouse liver function values, namely 23.2 – 48.8 U/L and 2.1 – 23.8 U/L.17 If viewed from tables 4.3 and 4.4, the administration of bamboo grass extract with a dose of 600 mg/kg body weight

E-ISSN: 2528-410X

and 800 mg/kg body weight in the T (II) and T (III) groups showed quite significant differences, this indicates the effect of the hepatoprotective effect on bamboo grass extract in accordance with the research of Qingfe et al, in the study 2 doses of bamboo grass extract were used, namely 200 mg/kg body weight and 800 mg/kg body weight where the administration of bamboo grass extract with a dose of 800 mg/kg body weight is a dose that can cause a hepatoprotective effect, but in this study, a new dose was obtained that can cause a hepatoprotective effect and reduce the average level of SGOT and SGPT to the normal limit, which is 600 mg/kg body weight so that it can be concluded that the administration of bamboo grass extract at a dose of 600 mg/kg body weight is the most effective dose in causing a hepatoprotective effect on mice induced by paracetamol.[10,14]

In bamboo grass extracts, there are compounds rich in flavonoids and flavonoids, but the flavonoids that play the most significant role in this hepatoprotective effect are luteolin, apigenin, and isoorientin. The presence of these compounds can suppress free radical activity and help increase endogenous antioxidant activity, such as glutathione, in metabolising excessive NAPQI levels caused by overdose from paracetamol consumption. Thus, preventing the damage to hepatocyte cells and changes in liver function.[18–20]

In this study, it can be concluded that the administration of bamboo grass extract at a dose of 600 mg/kg body weight for a week is the most effective dose that can provide a hepatoprotective effect on mice induced by paracetamol. To be more convincing, the results of this study need to be confirmed with liver damage by histopathological examination or MDA examination, which is a shortcoming of this study. In addition, SGOT and SGPT levels should be checked in mice before the administration of extracts to prevent bias.

## CONCLUSION

1. The average level of SGOT enzyme in male mice given bamboo grass extract at a dose of 400 mg/kg body weight was 49.88 U/L, 600 mg/kg body weight of 39.52, and 800 mg/kg body weight of 31.02. The average level of SGPT enzyme in male mice given bamboo grass extract at a dose of 400mg/kg body weight was 28.12, 600 mg/kg body weight was 19.14 U/L, and 800 mg/kg body weight was 15.18 U/L.
2. The administration of bamboo grass extract (Lophatherum gracile) at a dose of 600 mg/kg body weight for 7 days is the most effective dose that can reduce the levels of SGOT and SGPT enzymes and cause hepatoprotective effects in male mice (Mus musculus).
3. Giving bamboo grass (Lophtaherum gracile) extract affects the hepatoprotective effect on male mice (Mus musculus).

## ACKNOWLEDGMENTS

The author would like to express his deepest gratitude to Universitas

E-ISSN: 2528-410X

Muhammadiyah Sumatera Utara for the facilities that have been provided to carry out and complete this research, especially to the pharmacology laboratory.

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