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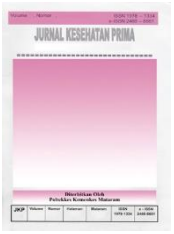

# Effect of Bajakah *(Spatholobus littoralis* Hassk.*)* Extract on Malondialdehyde Serum of Wistar Rats Induced by Streptozotocin

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**Abstract**
Bajakah extract has antioxidant and antidiabetic compounds including phenols, flavonoids, saponins, and tannins. These compounds delay glucose absorption, bind free radicals, and stabilize hydroxides that can suppress oxidative stress conditions. The aim of this study is determined the effect of bajakah extract on serum malondialdehyde in wistar rats induced by streptozotocin. This research is an experimental study using a randomized post-test only control group design. The research sample was 25 male wistar rats ages 2-3 months, grouped into two control groups (K) which were given standard feed (K1) and those given standard feed and induced by streptozotocin (K2) and three treatment groups (P) with bajakah extract intervention as much as 50mg/kgBB (P1), 100mg/kgBB (P2), and 150mg/kgBB (P3). Statistical test using Manova test and Tukey HSD post hoc test. The antioxidant content of the pirated extract is 4.64% phenol, 2.48% flavonoid, 1.06% saponin, and 0.028% tannin. After being given the intervention of bajakah extract for 14 days, the mean serum malondialdehyde levels in groups P1 (2.43±0.33 nmol/L), P2 (1.98±0.50 nmol/L), and P3 (1.79±0.29 nmol/L) were control groups K1 (1.25±0.09 nmol/L) and K2 (3.87±0.70 nmol/L). Based on statistical tests, there were differences in serum malondialdehyde between the control and treatment groups after being given the pirated extract for 2 weeks ($p<0.05$). The conclusion was obtained that the provision of bajakah extract had antidiabetic and antioxidant activity, was able to reduce serum malondialdehyde in wistar rats with hyperglycemia.

**Keywords:Bajakah Extract; Malondialdehyde; Hyperglycemia**

## INTRODUCTION

Chronic non-communicable diseases are a global health problem. One of them is diabetes mellitus and is the leading cause of premature death in the world (WHO, 2020). The prevalence of DM has also increased, DM sufferers in 2019 reached 463 million people and are expected to increase by 578 million people in 2030 and 700 million people in 2045. Indonesia ranks seventh out of the ten highest countries with DM sufferers in the world with 10.7 million people (IDF, 2019). Based on data from Basic Health Research, the prevalence of DM in Indonesia has increased from 1.5% in 2013 to 2% in 2018 (Kementerian Kesehatan RI, 2018). One of the causes of T2DM is an increase in free radicals in the body that cause damage or changes in pancreatic cells due to obesity, improper diet, and etc. (PERKENI, 2019). In general, people with DM experience hyperglycemia. Uncontrolled hyperglycemia in non-insulin-sensitive tissues results in increased phosphorylation of glucose-6-phosphate. This will activate the polyol pathway, where glucose is metabolized by aldose reductase to sorbitol using NADPH as a cofactor, resulting in reduced inositol

levels. The activity of the polyol pathway will increase oxidative stress with the mechanism of carbohydrate metabolism producing energy equivalent to encouraging ATP synthesis in the mitochondria which will produce free radicals and superoxide. The increased production of free radicals causes tissue damage, including DNA damage, initiating the peroxidase process of carbohydrates, proteins, and lipids in cell membranes which is characterized by increased protein damage, increased malondialdehyde, and decreased SOD. Malondialdehyde is used to determine the presence of oxidative stress in plasma or serum (Guney, 2012).

Hyperglycemia in muscle and adipose tissue results in a glycation reaction of cell membrane proteins which is characterized by the formation of AGEs. This condition affects the insulin receptor which causes a decrease in the ability of insulin receptor activity to respond to blood glucose, resulting in an increase in insulin resistance.

Insulin resistance causes a decrease in the amount of GLUT-4 on the cell surface which results in a decrease in glucose uptake by tissue cells, resulting in an increase in blood glucose levels and activation of muscle cells and adipose cells. Increased activity of glycogenolysis and lipolysis will increase mitochondrial activity so that it will result in an increase in ROS and cause hyperglycemia in people with T2DM.

DM management is needed to improve the quality of life of people with DM which consists of four pillars, namely education, nutritional therapy, physical activity, and pharmacology (PERKENI, 2019). One of the DM management that can be done is pharmacology using bajakah extract which is thought to have antioxidant compounds (Ayuchecaria dkk., 2020; Fitriani dkk., 2020). Bajakah tampala is one of the herbal plants that can be found in the Kalimantan region. Bajakah stems or roots are widely used by the people of the interior of Kalimantan or the Dayak tribe as traditional medicine to restore stamina during activities in the forest and treat various diseases.

The pirated extract has an antioxidant activity of 8.25 ppm, which indicates that the extract has a very strong antioxidant activity (Iskandar & Warsidah, 2020). High antioxidant content in food is very necessary for DM patients because DM sufferers experience a decrease in endogenous antioxidants in their bodies, thereby increasing oxidative stress (Sharma dkk., 2013). Increased intake of exogenous antioxidants from food can improve antioxidant status and be able to capture free radicals, and turn them into a more stable form (Dal & Sigrist, 2016). Administration of antioxidants is an attempt to inhibit the production of intracellular free radicals or increase the ability of enzymes to defend against free radicals to prevent oxidative stress and vascular complications related to diabetes. (Bajaj & Khan, 2012).

The antioxidant compounds contained in the pirated extract are in the form of tannins, saponins, flavonoids, and phenolics. The average pirated extract contains a total phenolic content of 12.33 mg GAE/g (Ayuchecaria dkk., 2020). The average tannin content in the pirated extract is 635.63 ppm (Fitriani dkk., 2020). The content of these secondary metabolites can treat various degenerative diseases, such as DM, cancer, tumors, and others. Bajakah tampala has bioactivity as an anticancer, antidiabetic, asthma drug, stroke drug, and rheumatism (Zhang dkk., 2015). However, research related to the right dose of bajakah extract in preventing or reducing the effects of complications for DM sufferers is still very limited so that researchers are interested in obtaining the right dose and studying further the effects of giving bajakah extract as a prevention or treatment in DMT2 patients.

The aim of this study was to examine the effect of bajakah extract on serum malondialdehyde in male Wistar strain rats induced by streptozotocin. The

expected benefit is that the results of this study can be used as a reference for further research on the role of pirated extracts against diabetes mellitus in humans.

## METHOD

This study is an experimental study on male wistar rats with a Randomized Post-Test Only with Control Group design. This research began in December 2021 – January 2022 for five weeks, consisting of one week of adaptation (acclimatization), two weeks of streptozotocin induction, and two weeks of pirate extract intervention.

The sample of this study was male wistar rats. The sample size was obtained based on the formula for the sample size for experimental research from Federer, namely: (t-1)(n-1) 15, and the results were 25 rats. The sample was divided into 5 groups randomly. Wistar rats were randomly divided into 5 groups, namely group K1 (n=5) rats were given standard feed without streptozotocin (stz) and bajakah extract, group K2 (n=5) rats were given stz induction and without bajakah extract, group P1 (n =5) rats were given stz induction and bajakah extract 50mg/kgBB, group P2 (n=5) rats were given stz induction and bajakah extract 100mg/kgBB, and group P3 (n=5) rats were given stz induction and bajakah extract 150mg/kgBB .

Inclusion criteria were male wistar rats, aged 2 – 3 months, weight 150 – 200g, rats were in good health and had no anatomical abnormalities, and had never been used as experimental animals in the study. The exclusion criteria were the rats had decreased physical condition, did not want to eat, and died.

Animal rearing and blood sampling were carried out at the Biochemistry Laboratory, Faculty of Medicine, Airlangga University. Bajakah extract, phytochemical content testing of bajakah extract, and malondialdehyde serum were carried out at the Nutrition Laboratory, Faculty of Public Health, Airlangga University. After being treated for two weeks, all groups of rats were anesthetized using ketamine and xylazine and intracardiac blood was taken. Blood was put into a sample tube and immediately centrifuged to obtain serum to be examined for malondialdehyde serum by spectrophotometric method.

The measurement results were analyzed using the SPSS program with the MANOVA (Multivariate Analysis of Variance) test method if the data were normally distributed and homogeneous. Then proceed with the post hoc Tukey HSD test to find out the differences between each control and treatment group. All actions in this study have received approval recommendations from the Health Research Ethical Clearance Commission FEPK), Faculty of Dentistry (FKG), Airlangga University. The recomendation number is 597/HRECC.FODM/XI/2021.

## RESULT AND DISCUSSION

During the experiment, the control and treatment groups were feed standard BR-512. In groups K2, P1, P2, and P3, mice were given additional treatment, is streptozotocin induction, then in groups P1, P2, and P3 were given the intervention of pirated extract as shown in Table 1.

**Table 1. The Amount of Feed Given to Control and Treatment Groups**

| Feed Type | K1 | K2 | P1 | P2 | P3 |
|---|---|---|---|---|---|
| BR-512 (g)/ feed standard | 20 | 20 | 20 | 20 | 20 |
| STZ induction (mg/kgBB) | 0 | 30 | 30 | 30 | 30 |
| Bajakah extracts (mg/kgBB) | 0 | 0 | 50 | 100 | 150 |

The results of the phytochemical test of the bajakah extract using the spectrophotometric method were that the total phenols, flavonoids, saponins, and tannins were 4.64%, 2.48%, 1.06%, and 0.028% (Table 2).

**Table 2. Phytochemical Content Test Results of Bajakah Extract**

| Parameter | Result (%) |
|---|---|
| Total phenol | 4,64 |
| Flavonoid | 2,48 |
| Saponin | 1,06 |
| Tannin | 0,028 |

Measurement of malondialdehyde serum was carried out at the end of the study using experimental animal blood samples. The mean of malondialdehyde serum after being given the intervention of bajakah extract for 14 days in each group can be seen in Table 3.

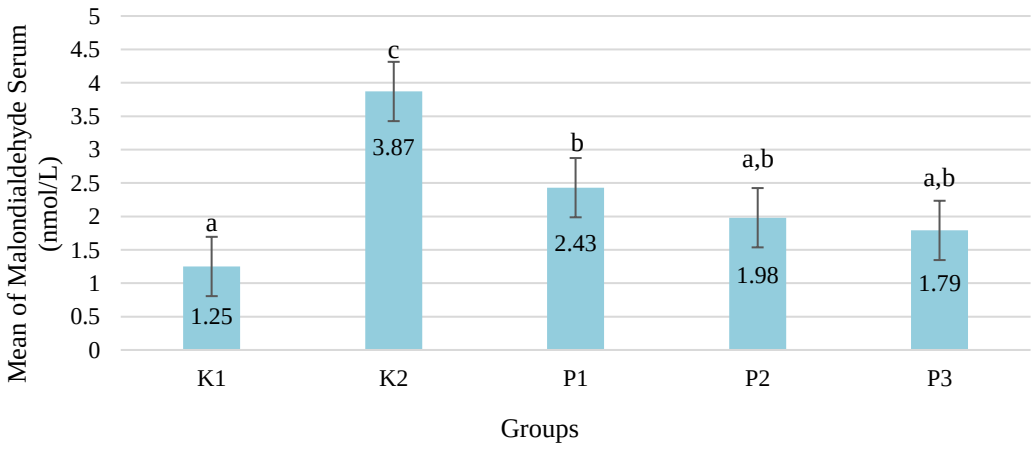
**Table 3. The Data of Malondialdehyde Serum After Intervention of Bajakah Extract**

| Malondialdehyde serum | Mean ± SD (nmol/L) | *p* value |
|---|---|---|
| K1 | 1,25 ± 0,09 | |
| K2 | 3,87 ± 0,70 | |
| P1 | 2,43 ± 0,33 | 0,000 |
| P2 | 1,98 ± 0,50 | |
| P3 | 1,79 ± 0,29 | |

Description:
K1: negative control group (standard feed); K2: DM positive control group (standard feed + STZ induction); P1: standard feed, STZ induction, and intervention of bajakah extract 50 mg/kgBB; P2: standard feed, STZ induction and intervention of bajakah extract 100 mg/kgBB; P3: standard feed, STZ induction, and intervention of bajakah extract 150 mg/kgBB

The highest mean malondialdehyde serum in the K2 group was 3.87 ± 0.70 nmol/L with a minimum value of 2.99 nmol/L and a maximum of 4.74 nmol/L. The lowest mean serum MDA level in the P3 group was 1.79 ± 0.29 nmol/L with a minimum value of 1.59 nmol/L and a maximum of 2.15 nmol/L. The administration of bajakah extract in experimental animals had the effect of reducing malondialdehyde serum in the treatment group. The malondialdehyde serum in the P3 group was close to the K1 control group.

Based on the homogeneity test using the Levene test, it showed p = 0.085 (p > 0.05), which means the data is homogeneous so that it can be continued with the Manova test. Based on the test using the general linear Manova model which was analyzed with Wilk' Lambda, it showed a significance value of p = 0.000 (p <0.05), which means that there is a difference in the mean serum malondialdehyde levels of each group after being treated with the use of pirated extract. Testing the difference in serum malondialdehyde levels after being given the extract of bajakah stems between the control groups and the treatment using a follow-up test using the Tukey HSD test with a 95% confidence level. There was a significant difference in malondialdehyde serum in the K2 group with the K1, P1, P2, and P3 groups with p<0.05 (Picture 1).




Picture 1. Mean of Malondialdehyde Serum After Bajakah Extract Intervention
Description: The different alphabet above the diagram showed the difference based on the Tukey HSD test α=0.05

This study measures malondialdehyde serum at the end of the study or after the administration of the bajakah extract. Malondialdehyde serum is one of the most studied biomarkers to determine oxidative stress in cells. Malondialdehyde can be observed in plasma, serum, and various other tissues such as kidney tissue which has been reported in diabetic patients (Tiwari dkk., 2013).

The increase in malondialdehyde serum is influenced by the increased production of Reactive Oxygen Species (ROS) caused by hyperglycemia. This triggers oxidative stress due to the presence of excessive free radicals in the body compared to antioxidants. If there are excessive free radicals, it will have an impact on damage to cells, especially pancreatic cells through cellular mediated autoimmune action and increased lipid peroxidation products, namely malondialdehyde (Abou-Seif & Youssef, 2004).

The mechanism of increasing free radical production in hyperglycemic states is through increased activity of the polyol pathway, glucoautooxidation, and protein glycation. The formation of reactive oxygen compounds can increase the modification of lipids, DNA, and proteins in various tissues. Molecular modifications in these various tissues result in an imbalance between protective antioxidants (antioxidant defense) and an increase in free radicals. This is the beginning of oxidative damage or oxidative stress. One of the end products of lipid peroxidation in the body is malondialdehyde (Ayala dkk., 2014).

Malondialdehyde serum decreased due to the presence of antioxidant compounds in the bajakah extract. The mechanism of inhibition of increasing malondialdehyde serum by antioxidants is the flavonoid antioxidant content found in the bajakah extract which works to capture Reactive Oxygen Species (ROS) against hydroxyl radicals, superoxide anions, peroxyl and alkoxyl radicals as well as metal chelators. The use of bajakah extract is an alternative to prevent the effects of free radicals in diabetes mellitus. Bajakah tampala as a native plant of Indonesia is widely used for various diseases including as an anti-diabetic.

The antioxidants contained in the bajakah extract, namely phenolics and flavonoids, act as peroxyl radical scavengers (ROO-) which will be regenerated into more stable ROOH. Flavonoids, phenolics, and saponins will donate hydrogen ions to free radicals to form more stable compounds so that they can break oxidative chain reactions and help overcome oxidative stress. Flavonoids as antioxidants not only act as radical scavengers, but also act as chelating metal ions so that the damage caused by hydroxyl radicals produced by the reaction of hydroperoxides ($H_2O_2$) with metal ions can be reduced. Flavonoids are also able to inhibit the work of CYP enzymes in generating free radicals (Kumar & Pandey, 2013). Saponin compounds can act as antioxidants and have the ability to scavenge free radicals. The ability of saponin compounds to reduce oxidative stress in hyperglycemic rats. In addition, the content of saponins is also quite effective for alleviating diabetes by lowering the level of lipid peroxidation and increasing the antioxidant defense system in serum, liver and pancreas (Elekofehinti dkk., 2017).

## CONCLUSION

Based on the results of the research that has been done, it can be concluded that the bajakah extract contains antioxidant and antidiabetic compounds, namely phenols, flavonoids, saponins, and tannins. Based on the statistical results showed that there was a significant difference in the mean serum malondialdehyde in the control and treatment groups. Giving pirate extract can reduce malondialdehyde

serum. Antioxidants and antidiabetics in bajakah extracts are useful for the prevention of diabetes mellitus in humans.

The limitations of this study are that this study did not use variations in the length of time of giving bajakah stem extract, only using variations in doses so that it could not compare the effects on the duration of giving bajakah stem extract at different times. Future studies may be able to examine the histopathological features of pancreatic beta.

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