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The Effect of Sungkai (*Peronema canescens* Jack) Leaf Extract on Malondialdehyde Levels in Diabetic Rats Model

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ABSTRACT

The chronic illness known as diabetes mellitus is typified by elevated blood glucose levels brought on by an insulin shortage, or hyperglycemia. Oxidative stress is caused by hyperglycemia, which also deactivates the antioxidant system and causes reactive oxygen species (ROS) to build up. Lipid peroxidation is brought on by this stress, and malondialdehyde (MDA) is one of the by-products. This study used a diabetic rat model to examine how sungkai leaf extract affected MDA levels. This study used 30 rats in six groups: negative control (NC), positive control (PC) with alloxan induction, diabetes control (DC) with glibenclamide, and administration of sungkai (*Peronema canescens* Jack) leaf extract T1 (Dose 150 mg/kgBW), T2 (Dose 300 mg/kgBW), and T3 (Dose 600 mg/kgBW) for 30 days. The study was experimental and used a post-test-only control group design. The TBARS method was used to measure MDA levels. The One-way ANOVA test and the Bonferroni Post Hoc test were used to evaluate the data. According to the findings, MDA levels were considerably lowered by the sungkai leaf extract. It can be concluded that sungkai leaf extract lowers MDA levels in a model of diabetic rats.

Keywords: Diabetes Mellitus, Hyperglycemia, Malondialdehyde, *Peronema canescens* Jack.

INTRODUCTION

A major global health concern, diabetes mellitus (DM) has seen a sharp rise in cases over time. Globally, diabetes mellitus has become more common, particularly in low- and middle-income nations. The International Diabetes Federation (IDF) claims that, there will be 536.6 million diabetics in 2021; by 2045, that number is expected to rise by 46% to 783.2 million. With 19.5 million people living with diabetes mellitus, Indonesia was the fifth most prevalent country in the world in 2021 [1].

Protein kinase C pathway activation, the glycolysis process, polyols, hexosamines, and the generation of Advanced Glycation End Products (AGEs) are some of the route by which hyperglycemia in diabetes mellitus causes oxidative stress. In addition to endoplasmic reticulum stress and hyperglycemia-induced mitochondrial dysfunction, these pathways also lead to the accumulation of reactive oxygen species (ROS). Protein expression can undergo irreversible oxidative alterations as a result of reactive oxygen species' ability to modify intracellular signaling pathways and directly damage lipids, proteins, and DNA [2].

Reduced antioxidant enzyme activity and elevated ROS levels are the main causes of oxidative stress in diabetes patients. This may result in further glycation and lipid peroxidation. Through the glycolysis of proteins, elevated glucose levels in diabetes mellitus can inactivate antioxidant mechanisms, leading to oxidative stress. Consequently, elevated levels of malondialdehyde (MDA) indicate lipid peroxidation [3].

An endogenous chain reaction is necessary for lipid peroxidation, whereby phospholipids are oxidatively degraded by free radical species (ROS) to produce a variety of oxidation products. Lipids with carbon-carbon bonds, like polyunsaturated fatty acids (PUFA) in cell membranes, are vulnerable to assault by free radical species. The main byproducts of lipid peroxidation include malondialdehyde (MDA), lipid hydroperoxides (LH), thiobarbituric acid reactive substances (TBARS), and 4-hydroxy-2-nonenal. As the main aldehyde metabolite of lipid peroxidation, MDA has been thoroughly investigated as a lipid peroxidation biomarker. These byproducts contribute to the development and severity of a number of diseases, including diabetes, by oxidatively damaging cells, DNA, and proteins. They can also alter signaling pathways that are part of the oxidative cascade [4].

Peroxidative damage is implicated in the development of diabetic problems, as evidenced by elevated MDA levels in diabetics. Reduced enzymatic and nonenzymatic antioxidant defense systems are also indicated by elevated lipid peroxidation [5]. Lipid peroxidation, also referred to as oxidative lipid breakdown, is one harmful effect of oxidative stress. It causes damage to cell membranes, which speeds up apoptosis, the process by which cells die. Oxidative damage, which is brought on by increased ROS generation, not only aids in the development of diabetes but also has a major impact on the long-term progression of microvascular and macrovascular problems associated with the disease [4].

Oral antidiabetic medications and insulin injections are currently the primary methods used to control hyperglycemia and reduce the risk of diabetes-related complications. Although there are several oral medications available, such as sulfonylureas, biguanides, and gliclazide, they are associated with potential side effects. As a result, researchers have been exploring natural products for new drugs with fewer side effects [3]. In recent years, numerous natural compounds derived from plants have demonstrated antidiabetic properties. Bioactive compounds found in medicinal plants offer a promising alternative for diabetes treatment due to their affordability and potential for minimizing side effects. This affordability is a critical consideration in drug development [6].

There are multiple alternative candidates for diabetes mellitus drugs that aim to minimize side effects by using medicinal plants, such as the Sungkai plant (*Peronema canescens* Jack). The sungkai plant contains various bioactive compounds, which can act as antidiabetic, antimalarial, antiplasmodial, antibacterial, analgesic, and immunomodulatory agents. Bioactive substances including flavonoids, alkaloids, steroids, tannins, phenols, and saponins are found in sungkai leaves [7].

Alkaloids, flavonoids, and saponins are antioxidants found in sungkai leaf extract. By lowering oxidative stress, blocking caspase cascades, and avoiding DNA damage, flavonoids shield beta cells. By raising enzymatic and non-enzymatic antioxidants, flavonoid treatment improves the antioxidant capacity of beta cells in diabetic rats, decreasing the buildup of ROS and lipid peroxidation in beta cells [8]. The presence of many -OH groups in saponins' structure increases their antioxidant activity and allows them to function as metal chelators [9]. Alkaloids inhibit ROS formation by increasing the activity and expression of enzymes that produce antioxidants, such as glutathione (GSH), catalase (CAT), and superoxide dismutase (SOD) [10].

Research on the use of sungkai leaf extract to address hyperglycemia is still limited. Sungkai leaf extract may be able to reduce mice's blood glucose levels, according to a 2021 study by Latief et al. According to the study, mice's blood glucose levels may be lowered most effectively at a dose of 350 mg/kg body weight of sungkai leaf extract. [7]. As a result, researchers are interested in investigating the effect of sungkai leaf extract (*Peronema canescens* Jack) on the levels of malondialdehyde (MDA) and superoxide dismutase (SOD) in the serum of diabetes mellitus rats model. This research aims to provide scientific insights into the antioxidant effects of sungkai leaves on diabetes mellitus.

MATERIALS & METHODS

Place and Time

From October 2023 to July 2024, this study was carried out at Universitas Andalas' Faculty of Medicine's Biomedical Laboratory and Biochemistry Laboratory.

Material

Alloxan, aquadest, dried sungkai leaves, 96% ethanol, sodium carboxymethylcellulose (NaCMC), sungkai leaf extract, glibenclamide, whole blood sample, lancet, glucometer and glucose strip (Elvasense), serum sample, MDA standard solution, TCA reagent 5%, TBA reagent.

Animals

Male Wistar strain Wistar rats weighing 200–280 grams were utilized in this investigation. They were acquired from the Biomedical Laboratory of the Faculty of Medicine at Universitas Andalas. This study was approved by the Universitas Andalas Faculty of Medicine Ethics Commission with authorization number 189/UN.16.2/KEP-FK/2024.

Extract Preparation

Using a 96% ethanol combination and the maceration process, sungkai leaf was extracted. In a dark container, away from direct sunlight, in a shaded area, and with periodic stirring, the maceration process lasts for seventy-two hours. To get a full extract, the re-maceration procedure is continued for two more days. A rotary evaporator will be used to filter the collected macerate after it has been evaporated by vacuum distillation, producing a thick, pure sungkai leaf extract.

Treatment

Prior to the trial, the rats were acclimated for seven days. Six sets of experimental animals were employed in this investigation. Aquadest and a regular diet were the sole treatments administered to the negative control (NC) group. Alloxan induced the positive control group (PC). Rats in the diabetic control group (DC) were given glibenclamide at a dose of 5 mg/kg BW after being given alloxan. After being induced with alloxan, the rats in treatment group 1 (T1) were administered 150 mg/kgBW of sungkai leaf extract. Rats in treatment group 2 (T2) received 300 mg/kgBW of sungkai leaf extract after being induced with alloxan, whereas rats in treatment group 3 (T3) received 600 mg/kgBW of sungkai leaf extract after being induced with alloxan.

Prior to alloxan induction, blood glucose levels were assessed in the treatment groups (T1, T2, and T3), the diabetic control group (DC), the positive control group (PC), and a negative control group that did not receive any therapy. To continue with the therapeutic treatment, blood glucose levels were assessed once more following 72 hours of alloxan induction to see if there had been an increase. After 30 days of this treatment, whole blood samples were used to measure blood glucose levels, and serum samples were used to measure malondialdehyde levels.

MDA Levels Measurement

The TBARS technique was used to analyze the MDA levels. MDA levels were measured using the Spectronic 21D equipment, which has a wavelength of 530 nm. TBA, 5% TCA, and standard reagents were made. After adding 2.5 mL of 5% TCA reagent to each standard tube, the samples were mixed using

a vortex mixer and centrifuged for 15 minutes at 10,000 RPM. After collecting 1 mL of filtrate and adding 1 mL of TBA reagent, the mixture was incubated at 100°C for 30 minutes. A Spectronic 21D spectrophotometer was used to test the absorbance at 530 nm after cooling [11].

STATISTICAL ANALYSIS

The One Way ANOVA test and the Bonferroni Post Hoc test were used to evaluate the data. The findings are shown as an elementary ± average. When the p-value is less than 0.05, it indicates a significant difference.

RESULT

T1 (2.31 ± 0.27 nmol/mL), T2 (2.19 ± 0.20 nmol/mL), T3 (2.04 ± 0.09 nmol/mL), NC (1.44 ± 0.37 nmol/mL), PC (3.25 ± 0.48 nmol/mL), and DC (2.05 ± 0.29 nmol/mL) had the highest average MDA values. Positive control group and diabetic control (DC) group, negative control group and treatment 1 (T1) group, negative control group and treatment 2 (T2) group, positive control group and treatment 1 (T1) group, positive control group and treatment 2 (T2) group, and finally, positive control group and treatment 3 (T3) group were all significantly different from each other, according to the Bonferroni Post Hoc test.

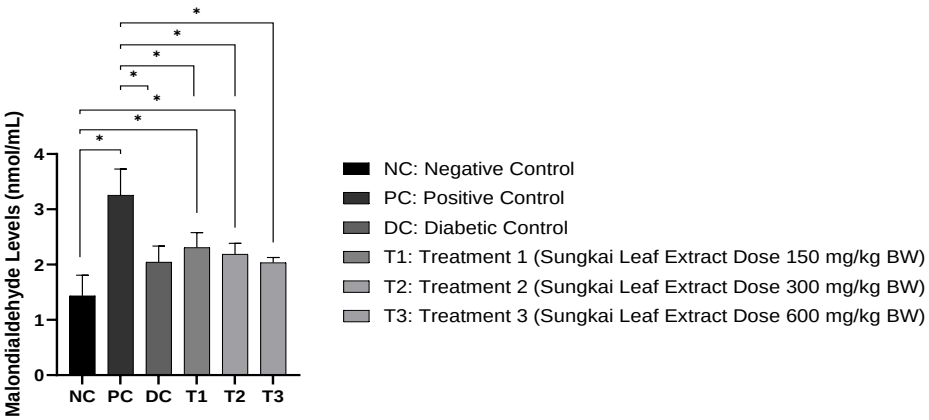

Figure 1. Mean of Malondialdehyde Levels (nmol/mL) After Administration of Sungkai Leaf Extract for 30 Days in Diabetic Rats Model (One Way ANOVA Test followed by Bonferroni Post Hoc Test.* p<0.05)

DISCUSSION

As illustrated in Figure 1, rats in the negative control group (NC) had the lowest average MDA levels, while rats in the alloxan-induced positive control group (PC) had the highest. The average MDA levels of the rats in the positive control group (PC) were therefore higher than those of the diabetic control group (DC) and the treatment groups 1 (T1), 2 (T2), and 3 (T3). MDA levels in the diabetic control group and all treatment groups (T1, T2, and T3) were considerably lower than those in the positive control group (PC).

The positive group of rats who received alloxan developed diabetes as a result of the partial degradation of the pancreatic islet beta cells, which decreased the quantity and quality of insulin production. Pancreatic beta cells necrotize when alloxan is consumed by them because it inhibits glucose and generates reactive oxygen species (ROS). As a result, the cells become poisonous and selectively bioaccumulate. [12]. High hyperglycemia can enhance the production of free radicals. ROS and protection are out of balance because the body's defenses are weakened, making it impossible for it to combat the rising ROS generation [13].

Polyunsaturated fatty acids (PUFAs), which are found in cell membranes and other lipids containing carbon-carbon bonds, are vulnerable to assault by reactive oxygen species (ROS) and other free radical species. Malondialdehyde (MDA), one of the main consequences of lipid peroxidation, is known

to encourage oxidative damage to DNA, proteins, and cells. The pathophysiology of diabetes as well as the onset and severity of a number of other diseases can be influenced by these lipid peroxidation byproducts. The signaling pathways implicated in oxidative processes can also be modified by them [4].

Rats in treatment groups T1, T2, and T3 that received sungkai leaf extract had lower MDA levels than the positive control group (PC), which did not receive it. This is due to the antioxidant properties of the flavonoids, saponins, and alkaloids included in sungkai leaf extract, which reduce oxidative stress and hence affect MDA levels.

Flavonoids are antioxidants that can inhibit lipid peroxidation and reduce oxidative stress [14]. They are considered to be the main contributors to many therapeutic effects, including their antioxidant activity [15]. As scavengers of free radicals, flavonoids provide defense against lipid peroxidation and metal chelation [14]. Flavonoids can help β cells survive by lowering oxidative damage and inflammation. Furthermore, flavonoids shield β cells from death by inhibiting apoptosis via both extrinsic (death receptor-mediated) and intrinsic (mitochondria-mediated) routes. This decrease in reactive oxygen species (ROS) is associated with this anti-apoptotic action [16]. According to earlier studies, following four weeks of therapy, flavonoids can dramatically reduce MDA levels in diabetic rats [17].

Non-enzymatic protein glycation is a mechanism where glucose cytotoxicity occurs due to the formation of reactive oxygen species (ROS) through the autoxidation of glucose catalyzed by transition metals. Saponins function as effective metal chelators, preventing these metals from participating in glucose autoxidation. The numerous -OH groups present in the saponin structure contribute to its enhanced antioxidant activity [9]. A study by Weng et al. in 2014 showed that saponins could lower serum MDA levels in diabetic rats model after 28 days of treatment [18].

Alkaloids can act as antioxidant therapy in diabetes by responding to reactive radicals, accepting or donating electrons, decreasing the expression or activity of the enzymes that generate reactive radicals or boosting the expression and activity of the enzymes that generate antioxidants [17]. Research conducted by Alamzeb et al. in 2024 showed higher levels of MDA in the diabetes group due to lipid peroxidation caused by excessive production of free radicals, leading to tissue damage. Furthermore, the population of diabetics who were given alkaloids could significantly lower MDA levels [17].

CONCLUSION

Research has shown that sungkai (Peronema canescens Jack) extract lowers malondialdehyde levels. All treatment groups, including doses of 150 mg/kg BB, 300 mg/kg BB, and 600 mg/kg BB, showed a substantial decrease; the dose of 600 mg/kg BB showed the largest drop.

Declaration by Authors

Ethical Approval: Approved by The Ethics Commission of the Faculty of Medicine, Universitas Andalas with number 189/UN.16.2/KEP-FK/2024

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Conflict of Interest: The authors declare no conflict of interest.

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