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Hypoglycemic Potential of Sungkai (*Albertisia papuana* Becc) Soaking Water in Alloxan-Induced Diabetic Rat

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ABSTRACT

Diabetes mellitus (DM) is a chronic disease characterized by blood glucose levels that exceed normal. One alternative treatment is to use herbs that have the potential as hypoglycemic compounds. Sungkai is one of the plants used by the Dayak tribe for generations to treat diabetes. This study aims to determine whether each organ of the Sungkai plant has the potential as a diabetes drug. The parameters measured in this study were antioxidant activity and total phenolics. This study used a completely randomized design with 25 white rats (*Rattus norvegicus*) as diabetic animal models, which were divided into five treatment groups which included normal rat (K-), DM positive rat K(+), and DM rat + soaking water from Sungkai leaf, DM rat + soaking water from Sungkai stem, and DM rat + soaking water from Sungkai root. The data obtained were analyzed statistically by ANOVA with sequence, normality test, homogeneity, and further test using Duncan's test. The results showed that the antioxidant activity and total phenol of each part of the Sungkai plant were significantly different ($p<0.05$). The highest antioxidant activity is found in the leaves. Blood glucose levels of DM rats decreased after 30 days of Sungkai treatment. Sungkai plant has different antioxidant activity in each organ, and the Sungkai plant has hypoglycemic potential in overcoming diabetes mellitus.

1. Introduction

The disease pattern in Indonesia is currently shifting from infectious to degenerative diseases. This pattern is accompanied by the problem of the double burden of diseases [1]. The case of degenerative diseases increases as life patterns and the environment change. One of the threats of degenerative diseases to public health is diabetes. Diabetes mellitus (DM) is a chronic disease that occurs because the pancreas does not produce enough insulin or the body is ineffective in using insulin [22].

There are several ways to treat DM disease, for example, by taking patent drugs that are usually provided in community health centers in each region. Patent drugs are generally from the sulfonylurea group of drugs,

the earliest type of oral hypoglycemic drug found [19]. Sulfonylurea group drugs stimulate insulin secretion in the pancreatic glands. Therefore, they are only effective if the pancreatic β-cells in the islets of Langerhans can still function normally. This nature of excitation is different from excitation by glucose because it turns out that when glucose (or hyperglycemia condition) fails to stimulate insulin secretion, these medicinal compounds are still able to increase insulin secretion [2].

The use of patent drugs for diabetes mellitus treatment still has a diverse impact, such as nausea, headaches, and muscle pain, which can be caused by the patient's age and the presence or absence of comorbidities [11]. One alternative to reduce the side effects of using patent drugs is to use plants that contain antioxidants and can potentially be diabetes mellitus drugs. Sungkai is one of the local Kalimantan plants which contains bisbenzylisoquinoline alkaloids. These alkaloids are found in stems and roots, which have antiplasmodial activity. Leaf and stem extracts contain saponins which have antibacterial activity against *Staphylococcus aureus* bacteria. Sungkai leaves contain saponin compounds that have antibacterial activity [15].

Apart from acting as an antibacterial, saponins also function as antidiabetics because they act as inhibitors of the α-glucosidase enzyme [3]. The enzyme α-glucosidase is an enzyme that plays a role in converting carbohydrates into glucose. Thus, if the enzyme α-glucosidase is inhibited, glucose levels in the blood will decrease [8]. Sungkai plants also contain flavonoids which are one type of antioxidant that is useful as an inhibitor of oxidative stress in people with diabetes mellitus by giving electrons to inhibit oxidation reactions through the binding of free radicals, which are reactive molecules, as a result of which cell damage can be prevented [10].

Oxidative stress and oxidative damage to tissues usually end with the onset of chronic diseases, including atherosclerosis, diabetes, and rheumatism arthritis [6]. In people with diabetes mellitus, glycosidation and liposidation in plasma and tissues increases due to oxidative stress. Therefore, alternative medicines made from natural ingredients such as plants are needed, which have the potential to contain antioxidants and are hypoglycemic to reduce free radical production [7].

2. Materials and Methods

2.1 Materials

Sungkai plants (*Albertisia papuana* Becc) were obtained from the Ngaju Dayak tribe area in Tumbang Jiga Village, Katingan Hulu District, Katingan Regency, Central Kalimantan Province, Indonesia. The samples used in this study were Sungkai plant parts, including roots, stems, and leaves. The study used a completely randomized design (CRD) with five treatment groups.

2.2 Methods

This research has been approved by the Health Ethics Commission of the Faculty of Medicine, Diponegoro University Semarang with No. 08/EC/H/FK-UNDIP/I/2022.

2.3 Antioxidant Activity Test

Antioxidant activity testing was carried out using the DPPH method. The steps for measuring antioxidant activity included extracting Sungkai plant organs (roots, stems, leaves) and standard solutions with concentrations of 2, 4, 6, 8, and 10 mg/ml. The mixed solution was then put into a test tube, and 2 ml of 0.002% DPPH was added. The solution is then vortexed so that the solution becomes homogeneous. The solution was then incubated for 30 minutes, and the absorbance was measured with a UV-Vis

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spectrophotometer at a wavelength of 517 nm, then the inhibition percentage value was calculated [20].

2.4 Preparation of Experimental Animal Model

The experimental animal model of diabetes mellitus (DM) in this study used white rats (*Rattus norvergicus*) which were injected with a diabetic agent, namely 96% alloxan monohydrate dissolved in NaCl solvent [16]. Alloxan was injected intraperitoneally. After injecting 96% alloxan monohydrate, the test animals were given a sugar solution of 20 g/rat for 24 hours. Alloxan is one of the agents that carry free radicals into the body so that the number of free radicals increases and attacks the target organs [9].

2.5 Treatment

The treatment consisted of five groups, namely DM negative control, DM positive control, P1 (DM rat + soaking water from Sungkai leaf), P2 (DM rat + soaking water from Sungkai stem), and P3 (DM rat + soaking water from Sungkai root). Sungkai soaking water was given orally using a special rat sonde of 2 ml/day. The treatment was observed for 30 days.

2.6 Feed and Drinking Consumption

Each treatment group was fed as much as 20 g/day and drank as much as 100 ml/day. Feed and drinking consumption is calculated by measuring the initial amount of feed and drinking minus the remaining feed consumption and drinking per day.

2.7 Data Analysis

The data were analyzed with SPSS (24.0 version) with a one-way ANOVA test, followed by the Duncan's Multiple Range Test (DMRT). The test was declared significant at $p<0.05$.

3. Results

3.1 Total antioxidant and phenolic activity of Sungkai plants

The antioxidant activity results showed a significant difference ($p<0.05$) between the organs of the Sungkai plant. The results of the total phenolic test also showed a significant difference ($p<0.05$) between leaves with roots and stems (Table 1).

Table 1. Total antioxidant and Phenolic activity of Sungkai Plants

Sample	Mean ± Standard Deviation	
	Antioxidant Activity (%)	Total Phenolic (mg As.gallat)
Root	85.04±0.22[a]	6.89±0,12[a]
Stem	91.26±0.11[b]	6.94±0,08[a]
Leaf	92.99±0.22[c]	9.41±0,04[b]

Description: [a-c]Superscript is different in the same column showing a noticeable difference ($P<0.05$)

The different antioxidant activities in each organ of the Sungkai plant show that each organ has different effectiveness as an antioxidant. According to [12], if the antioxidant activity of a plant reaches 81.35%, it means that antioxidant activity is very high, while the results of this study show that the value of antioxidant activity in each Sungkai plant organ exceeds the research results of [12]. The high content of antioxidant activity in the roots, stems, and leaves of Sungkai is related to the habitat and biotic or abiotic factors of the growing environment, one of which is the intensity of light that can influence the content of compounds in

plants.

The content of antioxidants in plants can inhibit or delay the oxidation of a molecule by ending the chain reaction of initiation and propagation. Antioxidants also act to neutralize free radicals that have the potential to cause negative impacts on the body. The application of antioxidants to DM model animals aims to prevent the disruption caused by free radicals so that they can be inhibited and prevent damage caused by degenerative diseases [4].

One part of the plant that often produces secondary metabolites is the leaf part. The content of secondary metabolites in the leaf is influenced by the size and age of the leaves [18]. One of the bioactive compounds that can usually be found in the roots and stems of plants is flavonoids. Flavonoid compounds are one of the constituent compounds of phenolic compounds [21]. Flavonoids and tannins are compounds in the phenolic compound group in plants, which function as antioxidants that catch free radicals to inhibit damage due to diseases caused [5]. Flavonoids and tannins also have the potential to be hypoglycemic by regenerating damaged pancreatic β-cells and catching free radicals as antioxidants [14].

3.2 Blood Glucose Levels of Diabetes Mellitus Rats

The results of blood glucose levels measured in this study showed that the control group (-) (normal rat), DM rat (control rat +), P2 (DM rat + soaking water from Sungkai stem), and P3 (DM rat + soaking water from Sungkai root) significantly differed with rats of group P1 (DM rat + soaking water from Sungkai leaf) in ($p<0.05$) (Table 2).

Table 2. Blood Glucose Post Injection Alloxan Monohydrate

Treatment	Blood Glucose day-0 (mg/dL)
K(-) Normal	110.80±10.93[a]
K(+) DM	123.00±1.30[a]
DM + Sungkai leaf	160.00±13.75[b]
DM + Sungkai stem	133.60±5.60[a]
DM + Sungkai root	127.60±2.06[a]

Description: [a-b]Superscript is different in the same column showing a noticeable difference ($P<0.05$)

3.3 Blood Glucose Measurement

After being treated using soaking water of Sungkai for 30 days, statistical data analysis showed that on the 0th day, it was found that the negative control group, P2, and P3, were significantly different ($p<0.05$). After 15 days post-treatment was given results if the positive control group was significantly different ($p<0.05$) from the negative control group, P1, P2, and P3, and decreased blood glucose of DM rats with the treatment reached 16% of blood glucose 15 days earlier. The data obtained after treatment obtained blood glucose results from the DM positive control rat group were significantly different ($p<0.05$) from the normal control rat group, P1, P2, and P3, as well as a decrease in blood glucose from the 0th day to 30th day, decreased by 31% (Table 3).

Table 3. Blood glucose of DM rats after treatment for 30 days

	Mean ± Standard Deviation

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Treatment	Blood Glucose day-0 (mg/dL)	Blood Glucose day-15 (mg/dL)	Blood Glucose day-30 (mg/dL)	Percentage decrease in blood glucose day-15	Percentage decrease in blood glucose Day-30
K(-) Normal	110.80±10.93[a]	105.20±8.74[b]	98.20±1.24[b]	4%	7%
K(+) DM	123.00±1.30[a]	84.20±4.87[a]	76.20±4.19[a]	32%	38%
DM + Sungkai leaf	160.00±13.75[b]	145.00±4.44[c]	110.00±4.48[b]	9%	31%
DM + Sungkai Stem	133.60±5.60[a]	118.20±8.82[b]	103.60±6.16[b]	12%	22%
DM + Sungkai root	127.60±2.06[a]	107.00±4.87[b]	97.20±2.29[b]	16%	24%

Description: [a-c]Superscript is different in the same column showing a noticeable difference (P<0.05).

Low blood glucose levels in experimental rats were assumed to be the result of the hypoglycemic action of the Sungkai plant organs. Flavonoids contained in the roots, stems, and leaves of Sungkai have the potential to be hypoglycemic. The results showed that the blood glucose levels of DM + treatment rats from day 0 to day 30 decreased, characterized by an increase in the percentage decrease in blood glucose during treatment (Table 3). The percentage of decrease in blood glucose of DM rats in this study can be seen 15 days post-treatment. Based on these results, it is suspected that a more effective treatment to lower blood glucose for 30 days of treatment is soaking water from Sungkai leaf.

Flavonoid activity lowers blood glucose levels by increasing the function of pancreatic cells and stimulating insulin secretion in the body. Flavonoids can also reduce glucose uptake and regulate the activity of enzymes in carbohydrate metabolism. In addition to flavonoids, the content of compounds that are thought to have the potential to be hypoglycemic is polyphenol compounds. Polyphenols can prevent the conversion of superoxide to hydrogen superoxide and prevent excessive oxidation, thereby protecting pancreatic cells during chronic hyperglycemia conditions [23].

3.4 Feed and Drink Consumption of DM Rats

The results of the analysis of feed consumption data showed a significant difference (p<0.05) between the normal rat group (K-) and DM rat (Table 4). Meanwhile, the feed consumption in the DM group of rats (control + and given Sungkai baths) showed no significant differences. The highest amount of feed consumption is found in the normal rat group. Drinking consumption also showed a significant difference between treatment groups (P<0.05) (Table 4). The highest amount of daily drinking consumption of rats was found in the group of DM rats who were given Sungkai leaf baths. The DM (control +) rats and DM rats fed with soaking water of stem and root from Sungkai had insignificant differences.

Table 4. Feed Consumption and Drinking Consumption of DM Rats During Treatment

Treatment	Parameter (Mean ± Standard Deviation)	
	Feed Consumption (g/day)	Drinking Consumption (mL/day)
K(-) Normal	18.35±1.80[b]	40.00±5.66[ab]
K(+) DM	14.04±1.68[a]	35.80±7.40[a]
DM + Sungkai leaf	14.41±1.82[a]	45.80±8.38[b]

DM + Sungkai stem	12.50±1.10[a]	33.40±3.36[a]
DM + Sungkai root	14.02±1.47[a]	35.20±2.49[a]

Description: a-bSuperscript is different in the same column showing a noticeable difference (P<0.05).

Rats with normal states tended to consume more feed than DM rats given Sungkai water. Normal rat feed consumption is not disturbed by any circumstances, so normal rats look healthier. They have a relatively high average amount of feed because they do not experience health problems [17]. In this study, the results of measuring rat feed consumption similar to [25] reported that normal white rat feed consumption could reach 100% of the feed given. The amount of feed consumed per day is about 10-20 g.

Feed consumption in DM conditions will generally increase due to cellular hunger and decreased energy storage due to impaired carbohydrate, fat, and protein metabolism. However, the feed consumption of DM rats in this study was relatively low compared to control (K-) rat feed. Low feed consumption in DM rats is thought to be related to the administration of root, stem, and Sungkai leaf baths. Based on the phytochemical analysis, Sungkai plants contain phenol components (Table 4).

The P1 mouse group was DM rats with a record of relatively high glucose during the study. One of the characteristics of the DM condition is polydipsia (drinking a lot). Polydipsia is compensation for the state of polyuria experienced by DM rats. The treatment of Sungkai leaf soaking water (P1) has not reduced the drinking consumption of DM rats compared to DM rats who received stem soaking water and Sungkai plant roots. Meanwhile, [13] showed that drinking consumption in white rats was 21.57-25.35 ml/day. The amount of drinking water consumed in DM rats in this study exceeded the required drinking water consumption.

DM rats have high blood glucose levels that cause hyperosmolarity of body fluids. Increased osmolarity is received by osmoreceptors in the hypothalamus as a thirsty sensation, so DM rats will increase drinking consumption to decrease or maintain the osmolarity of body fluids. In addition, the difference in the results of drinking water consumption in this study with the required amount of drinking water was due to differences in rat strains, treatment, health status, and maintenance management.

4. Conclusion

Sungkai plant (*Albertisia papuana* Becc) has the potential to be one of the plants that contain antioxidants and plants that contain hypoglycemic compounds that are beneficial in reducing blood glucose levels in people with diabetes mellitus.

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ISSN: 0005-2523
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