International Journal of Research and Review
Volume 11; Issue: 12; December 2024
Website: www.ijrrjournal.com
Research Paper *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Sungkai Leaf Extract (*Peronema canescens* Jack) Decrease Blood Glucose Levels in Rat Models of Diabetes Mellitus

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DOI: https://doi.org/10.52403/ijrr.20241201

ABSTRACT

Diabetes mellitus (DM) is a long-term metabolic condition marked by hyperglycemia, which, if it persists, will generate an excess of free radicals, contributing to problems from diabetes. Sungkai (*Peronema canescens* Jack) is a plant that provides antioxidants and antidiabetic properties. Finding out how sungkai leaf extract affects blood glucose levels in diabetic rat models is the aim of this study.

In this study, the Post Test-Only Control Group is used as part of an experimental design. The 35 rats were split up into six groups: the DM control group (KDM) of rats given glibenclamide, the positive control group (K+) of rats given alloxan, the negative control group (K-), and the group that received sungkai leaf extract (*Peronema canescens* Jack) P1 (dose 150 mg/kgBB), P2 (dose 300 mg/kgBB), and P3 (dose 600 mg/kgBB) for 30 days. Using a spectrophotometer and the GOD-PAP technique, blood glucose levels were assessed.

According to the findings, sungkai leaf extract (*Peronema canescens* Jack) reduced blood glucose levels ($p<0.05$). In summary, sungkai leaf extract may be used as an antidiabetic treatment.

Keywords: Hyperglycemia, Sungkai Leaf Extract, Antidiabetic

INTRODUCTION

Diabetes mellitus affected 537 million individuals worldwide in 2021, ranging in age from 20 to 79, according to the American Diabetes Foundation. One person every five seconds, or 6.7 million people, has a statistically significant chance of dying from diabetes mellitus. The prevalence has increased by 9% in females and 9.7% in males, respectively, and is impacted by age and gender characteristics. By 2030, this number is expected to rise to 643 million, and by 2045, it will reach 783 million [1]. 19.46 million Indonesians suffer from diabetes, placing the country fifth after the US, China, India, and Pakistan. By comparison, the number was 81.8% higher than in 2019. Only Indonesia is listed among the top 10 nations in Southeast Asia with the highest number of cases [1].

An autoimmune disease called type 1 diabetes damages the pancreatic cells, resulting in insufficient insulin production [2]. According to Merovci et al [3], damage to the beta cells in the pancreas prevents the hormone insulin from being released appropriately, which results in type 1 diabetes mellitus. Because insulin inhibits the tissues' ability to absorb glucose, a

severe catabolic state called hyperglycemia occurs, causing blood glucose levels to rise.

Both hereditary and environmental factors contribute to the occurrence of type 1 diabetes mellitus, which is typified by the death of pancreatic β cells. Mutations and activation of the HLADQ8, HLADRB1*04:01, and HLADRB1*04:05 haplotypes in HLA (Human Leukocyte Antigen) class II are genetic variables that increase the likelihood of developing pancreatic beta cell autoimmunity. This type of haplotype is often associated as an autoantibody trigger on insulin and is susceptible to the incidence of type 1 diabetes mellitus [4]. Environmental factors that cause type 1 diabetes mellitus include vitamin D deficiency, occlusive stress, inadequate nutrition during infancy, and viral infection (viruses from the Togaviridae, Paramyxoviridae, Retroviridae, and Picornaviridae families that produce viral RNA and DNA viruses) [5]. Because it typically manifests before the age of 25, type 1 diabetes mellitus is also known as adolescent-onset diabetes.

Oxidative stress can be brought on by hyperglycemia. Oxidative stress, sometimes referred to as reactive oxygen species (ROS) and reactive nitrogen species (RNS), is a condition brought on by an increase in free radicals or a decrease in endogenous antioxidant defense activity [6]. The development and proliferation of free radicals, or ROS, as a result of glucose autooxidation, polyol metabolic pathway activation, protein glycation, hexamine metabolism activation, C kinase protein activation, and Advanced Glycation End products (AGEs), which lead to complications in diabetes mellitus [7].

At present, insulin injections and oral antidiabetic medications are the primary methods for managing hyperglycemia and mitigating the risk of diabetes-related complications. Despite the availability of numerous oral hypoglycemic agents, including sulfonylureas, biguanides, and gliclazide, apprehensions regarding their adverse effects persist. Consequently, researchers focused on discovering novel pharmaceuticals derived from natural sources that exhibit low adverse effects. The World Health Organization (WHO) advocates for the assessment of traditional herbal remedies utilized in diabetes management due to their efficacy and reduced toxicity relative to synthetic oral hypoglycemic medications [8].

To prevent pharmacological side effects, it is best to consume natural antioxidants produced by plants, such as vegetables, fruits, spices, tea, or enzymes and proteins. [9] According to prior study, the use of chemical antidiabetic medicines can cause significant negative effects. As a result, efforts to find traditional medicines as alternatives to chemical pharmaceuticals are ongoing. The World Health Organization supports traditional medicine and herbs for disease control and public health. Traditional medicine is regarded safer due of its very few adverse effect.

Sungkai leaf (*Peronema canescens* Jack) is a plant that can be used as an alternative medication for diabetes. The sungkai leaf contains numerous bioactive chemicals, which have antimalarial, antiplasmodial, antibacterial, analgesic, and immunomodulatory properties. Sungkai leaves have bioactive substances include flavonoids, alkaloids, steroids, tannins, phenols, and saponins [10]. Several studies have shown that flavonoids in sungkai leaves have antiviral, antibacterial, anticancer, antioxidant, and anti-inflammatory properties, hence they are classified as phenolic substances [9] Many factors influence the bioavailability of flavonoids in diet, such as their molecular weight, which dramatically impacts their absorption, glycosylation, and metabolic conversion [11]. Furthermore, flavonoids work as antioxidants to moderate oxidative stress in the body by neutralizing the effects of reactive oxygen and nitrogen, therefore preventing many diseases [10].

Based on this, researchers want to see how sungkai extract leaf (*Peronema canescens* Jack) affects blood glucose levels. The

usage of sungkai extract leaf (*Peronema canescens* Jack) in this study is intended to develop sungkai extract leaf as a diabetes preventative.

MATERIALS & METHODS

Materials

Aquades (Aquabidest); 96% ethanol (Merck); sterilised water for injection (Otsu-WI); Alloxan (Sigma-Aldrich); Blood, blood glucose reagent, blood glucose standards, 70% alcohol, and hands-choen Sungkai leaf extract; and rats were used for this research.

Method

Animals

Male Wistar rats are the experimental animals used in this study, which is an experimental laboratory study employing the Post Test-Only Control Group design. 30 rats made up the research sample, which was subsequently split up into 6 experimental groups: DM control (KDM) treatment with glibenclamide dose 5 mg/kgBW, treatment group (P1) dose of 150 mg/kgBW, treatment group (P2) dose of 300 mg/kgBW, treatment group (P3) dose of 600 mg/kgBW, and negative control group (K-) and positive control group (K+) alloxan induction. The Universitas Andalas Faculty of Medicine Ethics Commission has authorized this study under authorization number 189/UN.16.2/KEP-FK/2024.

Alloxan Induction

For the male *Rattus novergicus* used in the experiment, the induction procedure will start with a 30-hour dietary restriction prior to injection. The rats only received water to drink; they were not provided any food. The rat will be manually restrained following the fasting period and given an intraperitoneal injection of 100 mg/kgBW alloxan in the lower right belly. The rats were then put back in their cages with unlimited access to commercial food and water.

Making Sungkai Leaf Extract

The maceration process is used to make sungkai leaf extra using a 96% ethanol mixture. Three thousand grams of sungkai (*Peronema canescens* Jack) leaves are immersed in 1000 millilitres of 96% ethanol for seventy-two hours till they settle. The maceration process will be conducted for three days in a dark container and shaded area away from direct sunlight, with periodic stirring. In an evaporation flask, the macerate, or soaking product, is placed. The output of the extraction is placed in a glass bottle and kept in a freezer or refrigerator.

Phytochemical Test of Sungkai Leaf Extract (*Peronema canescens* Jack)

The objective of the qualitative analysis used for the phytochemical test of sungkai leaf extract was to preserve the stability of the components that were already present in the extract. The chemical components of sungkai leaf extract will be assessed using Dragendorff's reagent, feCl3, vanillin sulphuric acid, and the alkaloid, phenol, terpenoid, and flavonoid tests, respectively.

Examination of Blood Glucose Levels

The GOD-PAP method was used to measure blood glucose levels. Get the Standard, Glucose Reagent, Aquabest, and Serum/plasma ready. A blank tube contains 10 µl of aquadest, a sample tube has 10 µl of serum, a standard tube contains 10 µl of standard, and a glucose reagent tube contains 1000 µl of blank, 1000 µl of sample, and 1000 µl of standard. After mixing until uniform, incubate for 10 minutes at 37°C or 20 minutes at room temperature. then read at a wavelength of 546 nm using Microlab 300.

STATISTICAL ANALYSIS

One-Way ANOVA was utilised only after the normality of numerical and categorical data has been established using the Shapiro-Wilks test.

RESULT

Phytochemical Test of Sungkai Leaf Extract (*Peronema canescens* Jack)

Examination of secondary metabolite components in sungkai leaf (*Peronema canescens* Jack) ethanol extract. To assess the existence of chemical components in the form of flavonoids, phenolics, saponins, triterpenoids, steroids, and alkaloids in the ethanol extract of sungkai leaf (Peronema canescens Jack), a qualitative analysis was conducted. The following outcomes were attained in the phytochemical test of sungkai leaf extract.

Table 1. Content of Secondary Metabolite Compounds in Sungkai Leaf Extract (*Peronema canescens* Jack)

Extract	Bioactive Compounds	Description	Observation result
Sungkai Leaf Extract (*Peronema canescens* Jack)	Flavonoid	+	Orange
	Phenolic	+	Blackish blue
	Saponin	+	There is foamy
	Triterpenoid	+	There is a red ring
	Steroid	+	There is a green ring
	Alkaloid	+	There is a white precipitate

Effect of Sungkai Leaf Extract (*Peronema canescens* Jack) on Blood Glucose Levels

To see how sungkai leaf extract affected blood glucose levels, blood glucose levels in the research group were measured. The One-Way Anova was used to statistically analyse the blood glucose measurement findings.

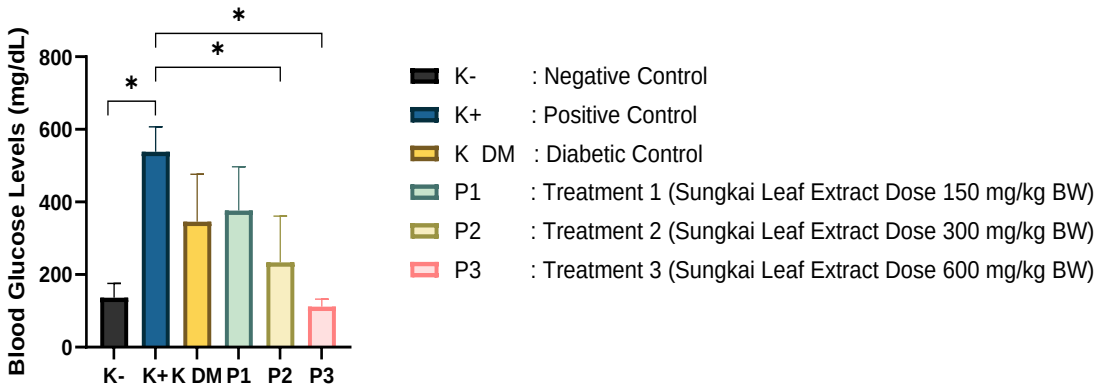

Figure 1. Blood Glucose Levels (mg/dL) were Decreased After Treatment by Sungkai Leaf Extracts (*Peronema canescens* Jack) in Diabetes Model Rats

The average blood glucose level in the positive control group animal produced by alloxan increased to 538,40 ± 68,54 (mg/dL), according to the data. Comparing the treatment group that received sungkai leaf extract to the positive control group (K+), the average blood glucose levels in groups P2 (300 mg/kg BW) and P3 (600 mg/kg BW) decreased. Sungkai leaf extract has an effect on blood glucose levels, according to statistical test results ($p<0.05$).

To determine the dose at which the impact became relevant or significant, a Post-Hoc test (Bonferroni Post-Hoc Test) was then conducted. Sungkai leaf extract's impact on blood glucose levels in mg/dL was determined using the Bonferroni Post-Hoct Test. The hyperglycemia group (K+) and the group that received a graded dose of sungkai leaf extract (*Peronema canescens* Jack) differed significantly.

DISCUSSION

To find out how feeding sungkai leaf extract affected rats with hyperglycemia, blood glucose levels in the rats were examined. On

the 31st day, blood glucose levels are measured. A Pasteur pipette or haematocrit tube is used to extract blood from the eye's retro-orbital sinuses. The average blood glucose level in rats with alloxan-induced hyperglycemia decreased, indicating that sungkai leaf extract may have antidiabetic effects based on the findings of the blood glucose level test. Treatment groups II and III experienced a reduction in blood glucose levels after receiving dosages of 300 mg/kgBW and 600 mg/kgBW of sungkai leaf extract (*Peronema canescens* Jack).

When sungkai leaf extract was administered orally to a group of rats, their blood glucose levels decreased on average. Chemical components found in sungkai leaves include flavonoids, phenolics, alkaloids, saponins, steroids, and triterpenoids, according to the findings of phytochemical studies carried out at Andala University's Organic Chemistry Laboratory of Natural Materials. Flavonoids are antioxidants that can absorb free radicals from the oxidation reaction of alloxan and decrease oxidative stress by boosting cellular antioxidant enzymes like SOD, catalase, and glycation peroxidase. These enzymes help prevent DNA damage to cells in the pancreas caused by alloxan and can repair damaged pancreatic β cells, thereby overcoming insulin deficiency [11].

Sungkai leaf extract's flavonoid concentration acts as an antioxidant by postponing, stopping, or removing oxidative damage to a target molecule. Flavonoids work in three ways: (1) they can capture free radical compounds by giving them one hydrogen atom; (2) they suppress enzymes that help form free radical compounds, including xanthine oxidase, protein kinase C, cyclooxygenase, NADPH oxidase, and lipoxygenase; and (3) they increase or stimulate the body's natural enzymatic antioxidants, such as glutathione peroxidase, catalase, and superoxide dismutase (SOD) [12].

This study demonstrated that giving each treatment group sungkai leaf extract with flavonoids reduced their blood glucose levels. By blocking GLUT2 in the intestinal mucosa, flavonoid compounds can decrease blood glucose levels by reducing the amount of glucose absorbed from the intestines. Flavonoids can also have hypoglycemic effects by decreasing the absorption of glucose and controlling the production of enzymes involved in the metabolism of carbohydrates. Because of their antioxidant and free radical-fighting properties, saponin compounds may be a natural source of antioxidants and play a significant role in therapeutic treatments that prevent or reduce the onset of diabetes [13]. Herbal plants include saponin chemicals that may help increase insulin action and stimulate the pancreas to produce more insulin. Because of the presence of β cells, which preserve homeostatic balance and facilitate the smooth release of insulin, glucose levels have decreased [9]. By promoting glycogenesis, tannin compounds have antihyperglycemic effects. Furthermore, tannins have an astringent effect that can cause the small intestine's epithelial membrane to shrink, which prevents the absorption of glucose and, ultimately, lowers blood glucose levels [14].

CONCLUSION

Research has shown that sungkai leaf extract (Peronema canescen Jack) affects blood glucose levels. The most efficient way to lower blood glucose levels is with a high dosage of 600 mg/kgBW.

Declaration by Authors

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

Acknowledgement: We acknowledge funding for this work from the Universitas Andalas (Faculty of Medicine).

Source of Funding: Grant Fundamental Scheme No.11/UN16.02/DD/PT.01.03/FK-UPPM/2024 from the Faculty of Medicine, Universitas Andalas, Padang, Indonesia, provided financial assistance for this work.

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

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How to cite this article: Siski Rahayu, Rauza Sukma Rita, Mohamad Reza. Sungkai leaf extract (*Peronema canescens* Jack) decrease blood glucose levels in rat models of diabetes mellitus. *International Journal of Research and Review*. 2024; 11(12): 1-6. DOI: *https://doi.org/10.52403/ijrr.20241201*

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