Effectiveness Of Red Betel Leaf (*Piper crocatum*) Decoction Water On Blood Glucose Levels Of Male Mice (*Mus musculus*) Diabetes Mellitus Model

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ABSTRACT

The incidence of Diabetes Mellitus in Indonesia has surged dramatically, rising from about 8.4 million people 1 2000 to an estimated 21.3 million by 2030. Antidiabetic drugs and insulin treatments frequently lead to side effects, highlighting the need for alternative therapies through traditional medicine. One promising option is the red betel plant (Piper crocatum), which contains chemical compounds such as flavonoids, alkaloids, and tannins that may help regulate blood glucose levels.

Keywords: Diabetes Mellitus, Red Betel, Blood Glucose Level, Mice.

INTRODUCTION

Diabetes mellitus (DM) is a chronic condition characterised by elevated blood glucose levels due to the body's inability to produce or use insulin efficiently. DM is also often referred to as the Mother of Disease and is at the root of many other health problems, such as hypertension, stroke, kidney failure and blindness. (Yanti et all, 2022).

Diabetes is of particular concern in Pacific island countries, where fruits and vegetables are expensive, fast food is common, and genetic factors may increase the risk of diabetes. (IDF). Natural treatment with traditional medicinal plants is one alternative to overcome diabetes mellitus, one of which is using the red betel plant (*Piper crocatum*). Red betel leaf (*Piper crocatum*) is known to contain chemical compounds such as flavonoids, alkaloids, and tannins, which have the potential to control blood glucose levels. (Budiman, 2021).

LITERATURE REVIEW

According to the World Health Organization (WHO) in 2019, there were still 382 million people suffering from DM in the world. (WHO, 2023). According to the latest statistics from the IDF, about 537 million people, or about 10% of all people aged 20-79 years in the world, are living with DM in 2021. It is estimated that this number will increase to 643 million in 2030 and 783 million in 2045. In addition, there are an estimated 240 million people who have diabetes but are undiagnosed. Diabetes is of particular concern in Pacific island countries, where fruits and vegetables are expensive, fast food is common, and genetic factors may increase the risk of developing diabetes. (IDF).

Indonesia is experiencing a significant increase in people with DM, which was around 8.4 million people in 2000 and is predicted to reach 21.3 million people by 2030. WHO states that Indonesia ranks 4th largest in the number of people with Diabetes Mellitus in the world. When viewed by province, North Sumatra reaches 2% or approximately 36,410 patients. (Kemenkes, 2018).

In Indonesia there are more than 30,000 types of plants, and about 1,000 of them are medicinal plants that can be used by the community in everyday life 5. Traditional medicinal plants have the advantage of being cheap and easy to obtain by picking directly or can be dried. So, natural treatment with traditional medicinal plants is one alternative to overcome diabetes mellitus, one of which is using the red betel plant (*Piper crocatum*). Red betel leaf (*Piper crocatum*) is known to contain chemical compounds such as flavonoids, alkaloids, and tannins, which have the potential to control blood glucose levels. (Budiman, 2021).

To date, user experience and empirical data have been the only basis for the use of red betel (*Piper crocatum*) in medicine. Therefore, research is needed to determine whether boiling red betel leaves (*Piper crocatum*) in water can cause a reduction in blood glucose levels. (Listiana, 2019). It is anticipated that the findings of this study will be used as evidence by science to support the potential of the red betel plant (*Piper crocatum*) as a drug that lowers blood glucose levels.

This study aims to observe the effect of red betel leaf (*Piper crocatum*) decoction water on blood glucose levels of male mice (*Mus musculus*) that were induced for 7 days and given red betel leaf decoction water with a total dose of 0.4 ml/20g BW and 0.5 ml/20g BW for 7 days. The findings of this study can lead to the application of red betel leaf (*Piper crocatum*) decoction water as a component in the production of herbal medicines.

METHODS

The tools used in this study were mice cages, mice food and drink containers, glucometers, containers and stoves for making boiled water, flannel cloth, filters, and oral sonde.

The materials used in this study were 32 male mice, husks, red betel leaf cooking water, standard mice feed, PAM water, gloves, alloxan, alcohol cotton, glucose strips, and syringes. This research is a laboratory experiment with a pretest-posttest control group design. The research was conducted at the UMI Medical Phytochemistry Laboratory to manufacture red betel leaf cooking water and at the Pharmacology and Pharmacy Laboratory of UMI Medicine to carry out the acclimatization process and administer treatment to experimental animals from May to June 2024.

For Population and Samples, male rats (Mus musculus) measuring 20-30 grams and 2- 3 months old formed the population used. Federer's experimental sample size formula (Federer, 1963) was used in this study to determine the sample size. This formula requires 6 rats in each group, plus 2 additional rats for backup. This study was referred to and under the supervision of the ethical committee of Universitas Prima Indonesia, number 044/KEPK/UNPRI/VIII/2024.

Based on the above provisions, a total of 4 groups were obtained with each group

- Only Given Standard Feed, Group
- Induced Alloxan 4.76 Mg/20grbb Only, Group (3) Induced Alloxan 4.76 Mg/20grbb Then Given Red Betel Leaf Decoction Water 0.4 Ml/20grbb And Group (4) Induced Alloxan 4.76 Mg/20grbb Then Given Red Betel Leaf Decoction Water 0.5 Ml/20grbb.

RESULTS

Based on **Table 1**, it was found that the average blood glucose levels of male mice (Mus musculus) diabetes mellitus models in K1, K2, K3, and K4 were 140.17 ± 23.74 mg/dL;

467.67 ± 38.47 mg/dL; 280.33±110.87 mg/dL; and 158.50±46.06

mg/dL. From the results of this study, it can be seen that the treatment groups of male mice with diabetes mellitus models (K3 and K4) have lower blood glucose levels compared to the control group (K2), but these levels are still higher than the control group of male mice without treatment.

Reporting Research Results

Table 1. Blood glucose levels of male mice after treatment for 7 days

	Blood glucose levels	
Group	**Mean**	**SD**
K1	190,17	84,05
K2	467,67	38,47
K3	280,33	110,87
K4	158,50	46,06

After obtaining the data, normality and homogeneity tests will be carried out first. The data is tested and shows the results of regular and homogeneous data. Then, the Oneway ANOVA test will be continued, and the results obtained are shown in Table 2.

Table 2 shows that p-value = 0.003 ($p<0.05$), which means that all groups have a significant difference in mean blood glucose levels. Thus, these results show that red betel leaf decoction water (Piper crocatum) influences blood glucose levels in male mice (Mus musculus) diabetes mellitus model.

Table 2. Difference in Mean Blood Glucose Levels of Male Mice

Group	***Mean***	***p value***
K1	190,17	
K2	351	
		0,003*
K3	297	
K4	158,50	

Description: Oneway ANOVA *Significant

DISCUSSION

Based on the research, it can be stated that red betel leaf decoction water (Piper crocatum) has a significant effect on blood glucose levels of male mice (Mus musculus) diabetes mellitus model with the most effective dose of red betel leaf decoction water in this study is 0.5 ml/20grBB compared to a dose of 0.4 ml/20grBB. This is due to the more significant the dose of red betel leaf decoction water, the higher the decrease in blood glucose levels.

The findings of this study are consistent with previous research by Wati et al. (2020), which found that red betel leaf decoction (Piper crocatum) lowers blood glucose levels in patients with diabetes mellitus. Arman (2021), using a quasy experiment with a Two- Group Pre-Test Post-Test design, also supports the findings of this study, which found that the administration of red betel leaf decoction can reduce blood glucose levels with a p-value = 0.000 ($p<0.05$) when examining the effects on the control and intervention groups, whose mean value was 42.0 mg/dL.

The effect of red betel leaf (Piper crocatum) boiled water as antihyperglycaemic in this study can be caused by the activity of several active compounds contained therein. The active compounds include flavonoids, alkaloids, saponins, polyphenolic compounds, tannins, and essential oils with high phenol content. The flavonoid content has an antihyperglycemic mechanism of action, including inhibiting the activity of glucosidase enzymes and hypoglycemic activity or reducing blood glucose levels.

Flavonoids can also inhibit phosphodiesterase, thus increasing the amount of cAMP in pancreatic β-cells. Increased cAMP will stimulate the release of protein kinase A (PKA), which can stimulate insulin secretion. Flavonoids from betel leaf also have antioxidant effects. These antioxidants can bind to hydroxyl radicals that damage pancreatic islets of Langerhans β-cells, maximizing insulin formation.

Red betel leaf (Piper crocatum) cooking water contains tannins, which, similar to how insulin increases phosphorylation of the glucose transport system, have anti-diabetic effects. Alkaloids are the most common type of secondary metabolite produced by plants. They are nitrogen-containing heterocyclic chemical compounds. Another characteristic of alkaloid compounds is their hypoglycaemic activity, which lowers blood glucose levels.

CONCLUSION

Based on the research results, it is concluded that there is a significant difference in mean blood glucose levels between all groups (p-value = 0.003 <0.05). Red betel leaf decoction water (Piper crocatum) with a dose of 0.4 and 0.5 ml/20grBB can reduce blood glucose levels in male mice (Mus musculus) diabetes mellitus model, and the most effective dose of red betel leaf decoction (Piper crocatum) in this study was a dose of 0.5 ml/20grBB.

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