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Effect of red betel (*Piper crocatum* Ruiz and Pav) leaves extract on blood glucose levels and ankle brachial pressure index (ABPI) among patients with type 2 diabetes mellitus

Bios Cendekia Wigatiningtyas*, Ta'adi, Walin

Politeknik Kesehatan Kementerian Kesehatan Semarang

Corresponding author: *E-mail: bioscendekia@gmail.com

Abstract

Background: Hyperglycemia often occurs in DM patients even though they have received pharmacological therapy, thus encouraging people to consume herbal medicines. The dosage of herbal therapy consumed by the community is not appropriate, only the dosage of community assumptions, resulting in negative impacts. Chronic hyperglycemia causes worsening of the Ankle Brachial Pressure Index (ABPI) score. Giving red betel extract with the right dose can be a solution, because red betel extract contains flavonoids that can inhibit α -amylase and α -glucosidase so that the body can control blood sugar levels and improve ABPI scores.

Purpose: To determine effectiveness of red betel extract on fasting blood sugar levels and ABPI.

Method: A quasy experiment approach, specially focusing on pretest and posttest group. The study took place from October-November 2024, in Padangsari and Srandol Health Centers, Semarang. The independent variable was red betel leaf extract the dependent variables is fasting blood sugar levels and ABPI. Using purposive sampling and Lemeshow formula, 70 respondents were selected which were divided into 2 groups, who met specific inclusion and exclusion criteria. Analysis proceeded with a univariate test to determine the frequency distribution of respondent's characteristics, followed by bivariate analysis using man whitney test.

Results: Red betel leaf extract significantly reduced blood sugar levels in patients with type 2 diabetes mellitus with an intervention value of 112.83 ± 15.227 compared to control of 191.46 ± 72277 with a large Cohen's d effect of 0.87 and increased the value of the Ankle Brachial Pressure Index or ABPI in the intervention group by 0.855 ± 0.045 compared to control by 0.674 ± 0.094 with a large d effect of 1.22 These findings suggest that red beet extract has potential as an adjuvant therapy in glycemic control and improvement of peripheral circulation.

Conclusion: Betel leaf extract has been shown to be effective in reducing fasting blood sugar levels and improving Ankle Brachial Pressure Index (ABPI) scores in patients with type II diabetes mellitus

Keywords: Betel Leaf Extract; Blood Sugar; Glycemic Control; Type 2 Diabetes Mellitus.

INTRODUCTION

Diabetes Mellitus is disease degenerative that gets attention important Because become four priority disease No contagious that experienced increase. Disease degenerative this is disease chronic that occurs because failure in produces insulin in the pancreas or body no can using insulin effective. Diabetes mellitus is disease chronic metabolic which has manifestation clinical

improvement blood sugar levels and have complications damage serious on the heart, blood vessels blood, eyes, kidneys, and nerves (Ingrosso, Primavera, Samvelyan, Tagi, & Chiarelli, 2023).

Degenerative diseases such as diabetes mellitus are chronic conditions that arise due to the body's inability to produce sufficient insulin or to utilize insulin effectively. This metabolic disorder is

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characterized by persistent hyperglycemia and, if not managed properly, can lead to a range of serious complications involving multiple organ systems. These include cardiovascular disease, damage to blood vessels, retinopathy leading to vision problems, nephropathy affecting kidney function, and neuropathy causing nerve damage. The progressive nature of diabetes makes early detection, continuous management, and lifestyle modification crucial in preventing long-term complications and improving the quality of life for affected individuals (Li, Zou, Lin, Chi, Hao, Chen, & Liu, 2024).

The International Diabetes Federation in 2022 stated that 537 million people aged 20-79 years live with diabetes worldwide. The number of the estimated will increase to 643 million in 2030 and 784 million in 2045. It is estimated there are 44% of adults living with diabetes but no diagnosed, meaning there is 1 of 10 who experienced disturbance tolerance glucose and risk tall affected by type 2 diabetes (Wahyuni, Hasanah, & Lusiana, 2023). The prevalence of DM in Indonesia is experiencing improvement from 10.9% in 2018 to 11.7 % in 2023. Based on Health Profile of Central Java Province in 2021 prevalence DM sufferers reached 13.91% who occupied proportion the biggest second in disease no infectious after disease hypertension so that by 2021 diabetes mellitus become priority control PTM disease in Central Java. According to Health Office Data Central Java Province in 2023 estimated amount diabetes mellitus sufferer as many as 121.753 people with distribution of 41.468 each year. Increase Diabetes Mellitus sufferer caused by heredity, obesity, lack of activity physical, pattern eat no health, stress, and medication. Increase amount Type II DM sufferers are also stimulated by behavior public awareness in ongoing treatment for type II DM not enough (Hartono, & Ediyono, 2024).

DM type II This is disease metabolic consequence glucose blood increase Because decline insulin secretion by pancreatic beta cells or existence insulin resistance. Patients with level glucose blood high and happening in term long time will cause disturbance circulation in the legs (Parekh, Athavale, & Kelshikar, 2024). The ankle brachial

pressure index value is used as noninvasive method for detect existence and assess level severity disease artery peripheral, because DM is risking independent factors for development disease artery peripheral. DM patients with Abnormal ABPI values will cause existence plaque atherosclerotic prone own more distal and diffuse distribution as well as presentation more disease aggressive (Suryasa, Rodriguez, & Koldoris, 2021).

The Ankle Brachial Pressure Index (ABPI) is a valuable noninvasive method used to detect and assess the severity of peripheral artery disease (PAD), particularly in individuals with diabetes mellitus (DM). As DM is recognized as an independent risk factor for the development of PAD, regular monitoring of ABPI becomes essential in diabetic care. A low ABPI value indicates reduced blood flow to the lower extremities, which can signal the presence of arterial blockages or narrowing, commonly seen in diabetic patients due to chronic hyperglycemia-induced vascular damage. By incorporating ABPI assessments into routine diabetic evaluations, healthcare providers can identify early signs of peripheral circulation impairment, allowing for timely intervention to prevent further complications such as foot ulcers, infections, or even amputations (Argyropoulou, Nomikos, Terzis, Tataki, Geladas, & Paschalis, 2025).

Level glucose blood in patients with diabetes mellitus proven experience decline after given therapy leaf betel red, namely from 209.30 mg/dl (pretest) to 186.30 mg/dl (posttest). Betel leaves red own flavonoid, tanni, alkaloid and polyphenol content as activity antidiabetic or lower blood sugar levels. Flavonoid content in betel red show existence activity inhibition against glucosidase, meaning that the flavonoid content can control blood sugar within normal limits. Increase high blood sugar levels in type II DM patients are caused by because activity glucosidase enzymes that convert incoming starch to in body become glucose. Content betel red can form insulin so that reduce oxidative stress, activity antihyperglycemic, and decrease glucose (Sari, 2022).

Bios Cendekia Wigatiningtyas*, Ta'adi, Walin

Politeknik Kesehatan Kementerian Kesehatan Semarang
Corresponding author: *E-mail: bioscendekia@gmail.com

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RESEARCH METHOD

A quasy experiment approach, specially focusing on pretest and posttest group. The study took place from October-November 2024, in Padangsari and Srandol Health Centers, Semarang. The independent variable was red betel leaf extract the dependent variables is fasting blood sugar levels and ABPI. Using purposive sampling and Lemeshow formula, 70 respondents were selected which were divided into 2 groups, who met specific inclusion and exclusion criteria.

The inclusion criteria required age > 56 years, fasting blood sugar level (gdp) in the range of 126-450 mg/dl, do not have renal and cardiovascular disease, currently not using other complementary therapies, patients with mild to moderate physical activity scale, willing as a respondent in this study marked, with the signing of an informed consent. Exclusion criteria included Patients who receive intramuscular (IM) insulin therapy, have gangrenous wounds or ulcers, patients with severe stress, type II DM patients with a duration of <5 years, presence of limb weakness (paresis) and paralysis (plegia).

Data obtained from Global Physical Activity Questionnaire (GPAQ), Depression Anxiety Stress Scale (DASS), Ankle Brachial Pressure Index (ABPI) and food recall questionnaire. The Global Physical Activity Questionnaire (GPAQ) includes 16 questions covering three main domains of physical activity: physical activity at work, physical activity during commuting (transportation), and physical activity during leisure time (recreation), as well as the duration of time spent sitting or staying still (sedentary behavior). This total score is used to categorize physical activity levels: low (<600 MET minutes/week), moderate (600-2999), and high (≥ 3000).

The Depression Anxiety Stress Scale (DASS-21) consists of 21 statements divided into three subscales, namely depression, anxiety, and stress, each consisting of 7 items. Each item is scored using a scale of 0 to 3, then the total score for each subscale is summed and multiplied by 2. For the stress subscale, the total score is categorized as follows: 0-13 is categorized as mild stress, 14-26 as

moderate stress, and scores above 26 indicate severe stress. The Food Recall Questionnaire is a method of assessing dietary intake by asking the type and amount of food and drink consumed in the last 24 hours. Respondents are asked to remember the time of the meal, the portion, and the way the food was processed. The data obtained was analyzed to determine daily nutrient intake, such as energy, protein, fat, vitamins, and minerals.

The Ankle Brachial Pressure Index (ABPI) is measured by obtaining the systolic pressure in the arm (brachial) using doppler and then measuring the pressure in the dorsalis pedis or posterior tibial artery at the ankle. The ABPI is calculated by dividing the leg systolic pressure by the highest arm pressure. Interpretation of ABPI: A value of 1.0-1.4 is normal, 0.9-0.99 indicates mild Peripheral Arterial Disease (PAD), 0.6-0.89 moderate PAD (claudication-like symptoms), and <0.5 severe PAD (critical ischemia). If >1.4, stiff arteries may be present (e.g. in diabetes).

The control group was given management of fasting blood sugar levels according to the standard operational procedures of the health center, namely only in the form of pharmacological treatment. Measurement of fasting blood glucose levels in this group was carried out twice, namely on day 1 (as baseline) and day 8 (as final evaluation). The intervention group received a combination of pharmacological treatment and red betel leaf extract. Fasting blood glucose measurements in the intervention group were conducted more intensively, namely 8 times consisting of 1 pre-intervention measurement (before the administration of red betel leaf extract) and 7 post-intervention measurements (every day for 7 consecutive days after the administration of red betel leaf extract).

The analysis proceeded with a univariate test to determine the frequency distribution of respondent's characteristics, followed by bivariate analysis using man whitney test. This research has obtained permission from the Research Ethics Committee Polytechnic of Health Semarang with number No.1253/EA/F.XXIII/38/2024.

Bios Cendekia Wigatiningtyas*, Ta'adi, Walin

Politeknik Kesehatan Kementerian Kesehatan Semarang
Corresponding author: *E-mail: bioscendekia@gmail.com

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RESEARCH RESULTS

Table 1. Characteristic of Respondents (N=70)

Variabel	Results	
	Intervention (n=35)	Control (n=35)
Age (Mean±SD)(Range)(Year)	(59.71±2.094) (56-65)	(62.40±16.364) (56-85)
Age (n/%)		
56-65 years old	35/100.0	16/45.7
66-75 years old	0/0	18/51.4
7-85 years old	0/0	1/2.9
Gender (n/%)		
Male	11/31.4	15/42.9
Female	24/68.8	20/57.1
Education Level (n/%)		
Elementary School	4/11.4	2/5.7
Junior High School	7/20.0	8/22.9
Senior High School	13/37.1	13/37.1
Bachelor	11/31.4	12/34.3
Long Suffering (n/%)		
<5 years	0/0	0/0
>5 years	35/100.0	35/100.0
Dietary (n/%)		
Yes	35/100.0	35/100.0
No	0/0	0/0
Activity (n/%)		
High	12/33.4	2/5.7
Moderate	23/66.6	33/94.3
Low	0/0	0/0
Depression Anxiety Stress Scale (n/%)		
Low	33/94.3	33/94.3
Moderate	2/5.7	2/5.7
Extreme	0/0	0/0

Table 1 shows the intervention group's participants range in age from 56-65 years old, with an average age of 59.71 and a standard deviation of 2.094. In contrast, the control group, which has members ages ranging from 56-85, has an average of 62.40 and a standard deviation of 16.364. The majority of respondents in both groups were female, 68.8% in the intervention group and 57.1% in the control group. The highest level of education was at the senior high school (SMA) level with the same percentage in both groups, 37.1%. All respondents had been suffering from the disease for more than 5 years (100%), and all were also on a recommended diet (100%). Most physical activities were in the moderate category, namely 66.6% in the intervention group and 94.3% in the control group while high activity was only found in a small proportion of respondents. Most respondents were in the low stress category at 94.3%, while the rest were in the moderate category 5.7% and no respondents were found in the extreme stress category.

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Table 2. Wilcoxon Test

Variable	Pretest (Mean±SD)	Posttest (Mean±SD)	p-value
Blood Sugar Level			
Control	166.6±55.421	191.46±72.277	0.000
Intervention	181.43±58.604	112.83±227	
ABPI			
Control	0.67±0.094	0.68±0.80	0.000
Intervention	0.68±0.076	112.83±0.045	

Tabel 2. Shows intervention group, there was a significant decrease in blood sugar levels from an average of 181.43±58.604 to 112.83±227, while in the control group it increased from 166.6±55.421 to 191.46±72.277, with a p value = 0.000 indicating statistical significance. Meanwhile, the ABPI value in the control group experienced a small increase from 0.67±0.094 to 0.68±0.80, and in the intervention group showed a more stable increase from 0.68±0.076 to 112.83±0.045, with a p value of 0.000 indicating that the changes were statistically significant.

Tabel 3. Effect Red Betel Extract on Blood Sugar Levels and ABPI in Type II DM

Variable	(Mean±SD)	Cohen's Effect
Blood Sugar Level		
Control	191.46±72.277	0.87
Intervention	112.83±15.227	
ABPI		
Control	0.674±0.094	1.22
Intervention	0.855±0.045	

Tabel 3. Indicate red betel leaf extract significantly reduced blood sugar levels in patients with type 2 diabetes mellitus with an intervention value of 112.83 ± 15.227 compared to control of 191.46 ± 72277 with a large Cohen's d effect of 0.87 and increased the value of the Ankle Brachial Pressure Index or ABPI in the intervention group by 0.855 ± 0.045 compared to control by 0.674 ± 0.094 with a large d effect of 1.22 These findings suggest that red beet extract has potential as an adjuvant therapy in glycemic control and improvement of peripheral circulation.

DISCUSSION

Diabetes mellitus increasing in age elderly. Because existence insulin resistance, deficiency mass muscle, and the occurrence of vascular changes, activity poor physical and nutritional intake

food that is not controlled. Age carries on will influence sensitivity network to insulin which contributes moment body experience. Hyperglycemia, and the aging process also affect hormone in metabolism that can disturbing balance glucose which can increase blood sugar levels (Lariwu, Sarayar, Pondaag, Merentek, & Lontaan, 2024).

Age elderly women are also more often affected by DM because in women will happen insulin resistance due to concentration estrogen in postmenopausal women so increase body fat reserves and increase release free fatty acids. Hormones also have significant role in improvement blood sugar levels, one of them hormone estrogen where hormone this own effect protection to insulin resistance and women will experience decline level estrogen after menopause so that risky have

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diabetes (Rohmatulloh, Riskiyah, Pardjianto, & Kinasih, 2024).

Higher education more will accept himself as a sick person experience symptom or complaint whereas level education low will not enough accept with symptoms that arise from disease experienced. Higher education usually will more lots of knowledge related in the process of treatment Diabetes Mellitus Control Type II. Some factors influence somebody in DM management includes motivation, tendency learning and factors environment social (Risqi, Dewi, Barokah, & Susanti, 2024).

Individuals with higher levels of education tend to be more able to accept their health conditions, including when experiencing symptoms or complaints due to diseases such as type II diabetes mellitus. A better understanding of the disease process and its management makes them more open to treatment efforts and able to exercise better self-control. In contrast, individuals with lower levels of education often have difficulty accepting the symptoms that arise, due to limited understanding of the disease. In addition to education level, diabetes management is also strongly influenced by individual motivation, desire to learn, and social environment support. These three factors are interrelated in determining the extent to which a person can carry out effective self-management of their diabetes condition (Malik, Paria, Firdous, & Ghazzawy, Alqahtani, He, & Gouda, 2024).

Study this use food recall method every day in group intervention for see influence food to blood sugar levels and ABPI. Research before explaining that food play a role important in increase blood sugar. Researchers using food recall for 7 days for look at the food intake of the respondents with focus carbohydrate because carbohydrate broken down and absorbed as monosaccharides, especially sugars. Absorption, this will increase level glucose sweat and release insulin hormone for arrange blood sugar levels. The type of food you should eat be noticed that is protein multiplication as energy and carbohydrates and fats are restricted no excessive (Casey, Lanting, Oldmeadow, & Chuter, 2019).

The process of nutrient absorption, particularly glucose, affects blood sugar levels, which in turn stimulates the release of the hormone insulin to maintain blood sugar stability. Therefore, diet plays a

crucial role in diabetes management. Careful selection of food types is essential, where protein intake can be increased as an alternative energy source, while carbohydrate and fat intake should be limited to avoid excess. A well-balanced diet helps prevent spikes in blood sugar levels and supports insulin function in the body, making it essential for individuals with type II diabetes mellitus to follow dietary guidelines tailored to their metabolic needs (Rais, Ved, Ahmad, & Parveen, 2024).

Acute stress can contribute to hyperglycemia in patients with type II DM. Research previously mention that concentration glucose statistically significant more tall when stressed because there is improvement activity system nerve otomom, especially alpha adrenergic stimulation. Activity be one of factor reason improvement blood sugar levels and ABPI due to with doing activities will change glucose and causes blood sugar levels decrease. Someone who doesn't be active so No will happen combustion and sugar content will save in body so that blood sugar levels will increase (Dias, Pinto, & Silva, 2021).

Physical activity is one of the key factors influencing the regulation of blood sugar levels and improvement of the Ankle Brachial Pressure Index (ABPI). Engaging in regular physical activity helps increase glucose uptake by the muscles, which in turn lowers blood sugar levels as the glucose is used for energy. On the other hand, individuals who are physically inactive will not experience sufficient glucose metabolism, causing excess sugar to accumulate in the body and resulting in elevated blood sugar levels. Additionally, physical activity improves blood circulation, which positively affects peripheral vascular health as reflected in increased ABPI scores. Therefore, incorporating consistent physical activity into daily routines is essential for individuals with type II diabetes mellitus to manage their blood sugar effectively and support overall vascular health (Mudassar, Lakho, Anwar, Rehman, Zakir, & Joher, 2025).

Betel leaf extract can stimulate insulin secretion and increase the process of glycogenesis and has astringent properties that can minimize intestinal epithelial membranes to reduce nutrient absorption, inhibit glucose intake, and prevent spikes in blood glucose levels that are too high. The decrease in

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blood sugar levels after the administration of red betel extract is due to the presence of flavonoid compound that is antioxidant, which can prevent the oxidation of pancreatic beta cells so that the existing cell damage in patients does not become more severe (Saeedi, Petershon, Salpea, Malanda, Karuranga, Unwin, & IDF, 2019).

The decrease in blood sugar levels after the administration of red betel extract is largely attributed to the presence of flavonoid compounds that act as powerful antioxidants. These flavonoids play a critical role in protecting pancreatic beta cells from oxidative stress, which is one of the major contributors to the progression of diabetes mellitus. By preventing further oxidation and cellular damage, flavonoids help maintain the function of insulin-producing cells, thereby supporting better glycemic control. In addition, flavonoids may also contribute to enhancing insulin sensitivity and inhibiting carbohydrate digestion, both of which further aid in lowering blood glucose levels. This highlights the therapeutic potential of red betel extract as an adjuvant treatment for managing type II diabetes mellitus through both pancreatic and extra-pancreatic mechanisms (Meyyazhagan, Kanagaraj, & Annamalai, 2025).

Flavonoids in red betel also play a role in preventing complications and progression of diabetes mellitus through the mechanism of clearing excess free radicals, breaking the chain of free radical reactions, binding metals, and inhibiting the polyol pathway by inhibiting the aldose reductase enzyme. In addition, flavonoids have an inhibitory effect on the alpha-glucosidase enzyme through hydroxylation and substitution bonds on the beta ring (Prayitno, & Murtini, 2018). This mechanism of action is like acarbose, which slows down the hydrolysis of carbohydrates and disaccharides, and inhibits the metabolism of sucrose into glucose and fructose. Therefore, betel leaf extract has the potential to be an effective herbal medicine in treating patients with diabetes mellitus, especially in reducing blood sugar levels and increasing ABPI values (Roshan, Chaudhary, Chouran, Huda, & Basu, 2024).

Bioactive compounds, especially flavonoids, not only exhibit antioxidant properties that protect pancreatic beta cells but also help regulate glucose metabolism by enhancing insulin sensitivity and

reducing intestinal glucose absorption. Moreover, the vascular benefits of betel leaf extract contribute to improved peripheral circulation, as evidenced by increased ABPI scores. This dual benefit glycemic control and vascular health positions betel leaf extract as a promising complementary therapy in the comprehensive management of type II diabetes mellitus (Dar, Gulya, Abass, Dev, Parveen, Ahmad, & Qureshi, 2024).

CONCLUSION

The use of betel leaf extract has been shown to be effective in reducing fasting blood sugar levels and improving Ankle Brachial Pressure Index (ABPI) scores in patients with type II diabetes mellitus. This blood glucose-lowering effect suggests that active compounds in red betel, such as flavonoids, tannins, and alkaloids, play a role in increasing insulin sensitivity and improving glucose metabolism.

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Bios Cendekia Wigatiningtyas*, Ta'adi, Walin

Politeknik Kesehatan Kementerian Kesehatan Semarang
Corresponding author: *E-mail: bioscendekia@gmail.com

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Politeknik Kesehatan Kementerian Kesehatan Semarang
Corresponding author: *E-mail: bioscendekia@gmail.com

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