Jurnal Riset Kesehatan, 12 (2), 2023, 98 - 103
DOI: 10.31983/jrk.v12i2.9826

Jurnal Riset Kesehatan

http://ejournal.poltekkes-smg.ac.id/ojs/index.php/jrk

SOURSOP LEAF NANOPARTICLES ON BLOOD GLUCOSE LEVELS AND ANKLE BRACHIAL PRESSURE INDEX (ABPI) VALUES IN TYPE-2 DIABETES MELLITUS PATIENTS

Ta'adi[a*], Mardiyono[b], Umi Margi Rahayu[c], Niken Anggraini Sri Saputri[d]

[a,b,c,d] *Poltekkes Kemenkes Semarang ; Pedalangan Banyumanik ; Kota Semarang 50268 ; Indonesia*

Abstract

Chronic hyperglycemia will cause legs and blood circulation disorders. Treatment with insulin is still quite expensive and with some side effects of oral hypoglycemic drugs. This experience made the management of DM switch to herbal treatment, namely soursop leaves (Annona muricata). The study used a pre and post test control group design with random allocation. Quasy experimental study with a two group pre tpost-testest – post tepost-testst design at 36type-2 DM patients in the Pekalongan City area. Blood glucose levels in the treatment group were measured before and after administration of soursop leaf nanoparticles500 ml/20 gBB 3 times a day for 6 days and 500 mg metformin. Giving soursop leaf nanoparticles at a dose of 500 ml/20 grBW 3 times a day for 6 days is effective on fasting blood glucose levels clinically with a change in value of 65 mg/dL, and has a statistically significant effect on reducing fasting glucose levels (p=0.035).

Keywords: *soursop leaf nanoparticles, blood glucose, ABPI, Type II Diabetes Mellitus*

1. Introduction

Diabetes Mellitus (DM) is a chronic disease characterized by blood glucose levels exceeding normal and disturbances of carbohydrate, fat, and protein metabolism caused by a relative or absolute deficiency of the hormone insulin. If this is left uncontrolled, acute metabolic complications and long-term vascular complications can occur, both microangiopathy and macroangiopathy (Patricia Gonce Morton DF, Carolyn M. Hudak 2014)

In Pekalongan City, patients with type 2 diabetes mellitus are ranked second after hypertension with a percentage of 39.7%, namely with a total of 2887 cases out of 7264 cases of non-communicable diseases (Anon 2016). The increasing number of Diabetes Mellitus (DM) patients, mostly type 2 DM with several factors, namely risk factors that cannot be changed and risk factors that can be changed. Non-modifiable risk factors include a family history of DM; (first degree relative), age over 45 years, ethnicity, history of giving birth with a birth weight of more than 4 kg and less than 2.5 kg. The modifiable risk factors include obesity, physical activity, hypertension, dyslipidemia and unhealthy diet (Islam 2017). The higher the incidence of DM, the higher the risk of complications, one of which is neuropathy which will be the cause of diabetic ulcers (Suriadi 2015).

Based on interviews with several patients with type 2 DM, it was found that some patients did not perform routine examinations and had never taken alternative drugs that could lower fasting blood sugar levels and had never had an ABPI examination. Patients with high blood glucose and occur for a long time will cause blood circulation disorders in the legs. Blood circulation is the flow of blood pumped by the heart into the blood vessels and flowed by the arteries to all organs of the body, one of which is the legs (Dr. dr. Fatimah Eliana S 2016). The Ankle Brachial Pressure Index (ABPI) is the result of dividing the lower extremity systolic blood pressure value divided by the upper extremity (brachial) systolic blood pressure value which describes the quality of blood flow to the lower extremities (Suriadi 2015). Normal blood circulation in the legs according to Vowden (2001) (in Suriadi, 2014) is

*) Corresponding Author (Taadi)
E-mail: taadisamsuri@gmail.com

1.0 which is obtained from the ABPI (Ankle Brachial Pressure Index) formula. Abnormal conditions can be obtained if the ABPI value <0.9 indicates there is a high risk of injury to the foot, ABPI >0.5 and <0.9 patients need follow-up care, and ABPI <0.5 indicates the leg has had a necrotic foot, gangrene, ulcers, ulcers that need treatment by a vascular surgeon (Suriadi 2015).

The aim of this research is to determine the effect of soursop leaf nanoparticles on ankle brachial pressure index (ABPI) values and fasting blood glucose levels in patients with type 2 diabetes mellitus. Treatment with insulin is still quite expensive and comes with some side effects from oral hypoglycemic drugs. This experience made DM management switch to herbal medicine, namely soursop leaves (Annona muricata). This is related to the secondary metabolic content in soursop such as flavonoids and tannins. Flavonoid and tannin compounds have a hypoglycemic effect by several mechanisms, namely by inhibiting glucose absorption, stimulating insulin release, increasing glucose uptake by peripheral tissues and regulating enzymes that play a role in carbohydrate metabolism. So it is hoped that soursop leaves can play a role in reducing blood sugar levels (Rekha N 2017).

2. Method

This research uses a non-randomized quasi-experimental pre and posttest control group design. A number of samples that meet the requirements, with random allocation, half of the samples will be treated by giving soursop leaf nanoparticles at a dose of 500 mg 3x1 a day for 6 days, and the other half as a control will be given meteor 500 mg 3x1 a day for 6 days. The sample size was calculated using the Lameshow formula with the results for each group being 18 people. Determination of samples using the following inclusion criteria: Type 2 DM patients, minimum age 30 years, under routine modern treatment, and using oral medication. Analysis of the data using a computer program with univariate analysis test, the research data were tabulated for further analysis using the Statistical Package for The Social Science (SPSS) 24.0 for window program. Independent test t-test to see differences in fasting blood glucose levels and ABPI values between groups before and after being given treatment, and paired t-test to see differences in fasting blood glucose levels and ABPI values before and after being given treatment in each study group. This research has received ethical permission No.421/EA/KEPK/2021 issued by the Ethics Committee of the Polytechnic Health Ministry of the Ministry of Health, Semarang.

3. Result and Discussion

The research was carried out from September to October 2021 in the Pekalongan City area.

a. Description of Respondents Characteristics, Levels of GDP, GDS, and ABPI values

1) Characteristics of Respondents

The following is a description of the characteristics of the respondents including the research confounding variables.

Table 1. Frequency Distribution of Respondents' Characteristics in the Control Group and the Intervention Group

Characteristic	Control Group (n=18)		Intervention Group (n=18)		Total		p
Age							
Age (mean±SD)	50.9 ± 6.014		53.50 ± 5.894		52.22 ± 6.010		0.471
Min-Max	40 - 59		34 - 60		34 - 60		
Gender							
Woman	7	38.9	4	22.2	11	0.6	0.444
Man	11	61.1	14	77.8	25	69.4	
Genetic History							
Yes	8	00	17	94.4	35	7.2	0.041
No	0	0	1	5.6	1	2.8	
Work							
Laborer	5	27.8	6	33.3	11	30.6	0.904
Retired	2	11.1	1	5.6	3	8.3	
civil servant	2	11.1	1	5.6	3	8.3	
entrepreneur	6	33.3	9	50	15	41.7	
Not Working	3	3	1	5.6	4	11.1	

Based on table 1, it was found that the average age in the control group was 50.9 years with a minimum age of 40 years and a maximum age of 59 years, for the average age in the intervention group was 53.5 years with a minimum age of 34 years and a maximum age of 60 years. Both the control group and the intervention group were in the adult age range. For gender, 69.4% of the research group (25 respondents) were women. Almost all respondents have a genetic history from a family suffering from diabetes mellitus (97.2%), and for the type of work, most of the respondents are self-employed (41.7%).

2) Blood Glucose

a) Blood Glucose When

Table 2. Frequency Distribution of Blood Glucose Levels during the Control Group and the Intervention Group

DS	Control Group (n=18)		Intervention Group (n=18)		P
	Mean±SD	Mn-Max	Man±SD	Mn-Max	
Pre-Test	290±49.01	180-327	297±57.5	190-370	0.623
Post Test	186±52.19	110-320	174±51.5	123-305	0.087

Table 2 shows the average blood glucose level in the control group before treatment, which was 290 mg/dL with a minimum value of 180 mg/dL and a maximum value of 327 mg/dL, whereas after treatment it was 186 mg/dL. For the intervention group, the GDS value before treatment was 297 mg/dL with a minimum value of 190 mg/dL and a maximum value of 390 mg/dL and after treatment 174 mg/dL.

b) Fasting Blood Glucose

Table 3. Frequency Distribution of Fasting Blood Glucose Levels in the Control Group and the Intervention Group

GDP	Control Group (n=18)		Intervention Group (n=18)		P
	Mean±SD	Min-Max	Mean±SD	Min-Max	
Pre-Test	185±43.01	110-285	189±49.7	120-315	0.544
Post Test	156.1±47,3	107-265	124±42.2	100-275	0.456

Table 3 shows the average fasting blood glucose level in the control group before treatment, which was 185 mg/dL with a minimum value of 110 mg/dL and a maximum value of 156 mg/dL, whereas after treatment it was 156 mg/dL. For the intervention group, the GDS value before treatment was 189 mg/dL with a minimum value of 120 mg/dL and a maximum value of 315 mg/dL and after treatment it was 124 mg/dL.

c) *Ankle Brachial Pressure Index* (ABPI)

Table 4. Frequency Distribution of Ankle Brachial Pressure Index (ABPI) values Control Group and Intervention Group

ABPI	Control Group (n=18)		Intervention Group (n=18)		P
	Mean±SD	Min-Max	Mean±SD	Min-Max	
Pre-Test	1.00±0.01	0.8-1	1.00±0.01	0.8-1	0.002
Post Test	1.00±0.01	0.8-1	1.00±0.01	0.8-1	0.001

From table 4, it can be seen that in both the control group and the intervention group before and after treatment, there was no change in the ABI value.

b. Analysis of the Effect of Soursop Leaf Extract on Blood Glucose Levels and Ankle Brachial Pressure Index (ABPI) Values in Type 2 Diabetes Mellitus Patients

1) Fasting Blood Glucose Level (GDP)

Table 5. Analysis of the Effect of Soursop Leaf Nanoparticles on Fasting Blood Glucose Levels (GDP) in Type 2 Diabetes Mellitus Patients

GDS	Control Group (n=18)		Intervention Group (n=18)		P value
	Mean±SD	Min-Max	Mean±SD	Min-Max	
Pre-Test	290±49.01	180-327	297±57.5	190-370	0.525
Post Test	186±52.19	110-320	174±51.5	123-305	0.026
□	104±22.2		123±20.8		0.004
P value	0.001		0.001		

From table 5 above, it can be seen that in the control group there was a change in GDS levels before and after treatment as much as 104 mg/dL with a p value of 0.001 which means that there was a significant difference in GDS levels in the control group, while in the intervention group there was a change in GDS levels before and after intervention as much as 123 mg/dL with a p value of 0.001 which means that there is a significant difference in GDS levels in the control group. The test results between groups obtained p value of 0.004 which means that there is a significant difference in GDS levels between groups.

2) Blood Glucose Level (GDS)

Table 6. Analysis of the Effect of Soursop Leaf Extract on Blood Glucose Levels (GDS) in Respondents with Diabetes Mellitus Type 2

GDP	Control Group (n=18)		Intervention Group (n=18)		P value
	Mean±SD	Min-Max	Mean±SD	Min-Max	
Pre-Test	185±43.01	110-285	189±49.7	120-315	0.186
Post Test	156.1±47,3	107-265	124±42.2	100-275	0.043
□	29±36.3		65±36.3		0.035
P value	0.001		0.001		

From table 6 above, it can be seen that in the control group there was a change in GDP levels before and after treatment as much as 29 mg/dL with a p value of 0.001 which means that there was a significant difference in GDP levels in the control group, while in the intervention group there was a change in GDP levels before and after intervention as much as 65 mg/dL with a p value of 0.001 means that there is a significant difference in GDP levels in the control group. The results of the test between groups obtained a p value of 0.035, which means that there is a significant difference in GDP levels between groups.

3) Ankle Brachial Pressure Index (ABPI) value

Table 7. Analysis of the Effect of Soursop Leaf Extract on the Ankle Brachial Pressure Index (ABPI) in Respondents with Type 2 Diabetes Mellitus

ABI	Control Group (n=18)		Intervention Group (n=18)		P value
	Mean±SD	Min-Max	Mean±SD	Min-Max	
Pre-Test	1.00±0.01	0.8-1	1.00±0.01	0.8-1	0.075
Post Test	1.00±0.01	0.8-1	1.00±0.01	0.8-1	0.074
□	0.002±0.001		0.002±0.001		0.317
P value	1,000		0.317		

From table 7 above, it can be seen that in both the control group and the intervention group there was no change in the ABPI value with a p value of 0.317, which means that there was no significant difference in the ABPI value between groups.

c. Analysis the effect of the intervention on GDP, GDS, and ABPI values by controlling for factors of age, sex, genetic history, and occupation

Table 8. Analysis the effect of the intervention on GDP, GDS, and ABPI values by controlling for factors of age, sex, genetic history, and occupation

Var Confounding	*P value* GDP	*P value* GDS	*P value* ABPI value
Age	0.948	0.828	0.476
Gender	0.793	0.603	0.437
Genetic History	0.849	0.999	0.831
Work	0.799	0.119	0.466
Work	0.799	0.119	0.466

Table 8 shows that age, gender, history of illness, and occupation have no effect on changes in both the GDP, GDS, and ABPI values. It can be concluded that changes in the value of GDP and GDS have changed due to the provision of intervention soursop leaf extract 500 mg 3 times a day for 6 days.

From the results of the study, it was found that there was a change in GDS levels in Type II Diabetes Mellitus patients as much as 123 mg/dL in the group of patients who were given additional soursop leaf extract capsule therapy at a dose of 500 ml/20 gBB 3 times a day for 6 days. This change when compared with changes in GDS levels in the group of patients who only consumed 500 mg metformin, which had a difference of 104 mmHg. This change indicates that soursop leaf extract has a significant effect on lowering GDS (0.004). For changes in GDP levels in the group of patients who were given soursop leaf nanoparticles also decreased more than the group of patients who were not given, statistically showing a significant difference with a difference of 36 mg/dL decrease. The small change in GDS is influenced by various factors, one of which is the type of carbohydrate intake consumed. There was no significant change in the ABPI values in the control and intervention groups, and statistically there was no effect (p=0.317).

Antioxidant activity has been proven in previous research. Soursop and Moringa extracts are effective in their single form in reducing blood sugar levels, accompanied by the ability to reduce the impact of oxidative stress (Dharma S 2014). There were 36 test animals divided into 6 groups, namely: normal group (aquadest), negative control (CMC Na 0.5%), positive control (glibenclamide dose 1.26 mg/kgBW), soursop extract 100 mg/kgBW, Moringa extract dose of 200 mg/kg BW and combination I (75:25), II (50:50) and III (25:75) in percent. All groups of test animals, except for the normal group, alloxan was induced at a dose of 160mg/kgBW on day 0, followed by treatment of test animals from day 1 to day 14. On the last day, the test animals were sacrificed for liver organ harvesting and measurement of oxidative stress levels which included lipid peroxidase and glutathione. The use of

moringa leaf extract and soursop leaf extract, both singly and in combination, was able to reduce oxidative stress, which was characterized by decreased levels of Lactoperoxide (LPO) and increased levels of Growth Stimulating Hormone (GSH) significantly ($p<0.05$). Optimal activity in 50:50 combination of Moringa soursop. This combination gives better results than the single form (Ta'adi, Mardi H, Sunarto 2019).

Based on the results of previous research with the title blood glucose levels before and after administration of starfruit and soursop leaf extracts in diabetes mellitus sufferers, the results of the paired t-test with a confidence interval of the difference of 95% obtained a significant value = 0.000 means $p <0.05$, which means that H1 is accepted which shows that there is a significant difference between blood glucose levels in diabetes mellitus sufferers before and after administration of soursop leaf extract (Ta'adi, Mardi H, Sunarto 2019). In line with research entitled the effect of soursop leaf extract (Annona muricata L.) on reducing blood glucose levels 9, it was explained that flavounoids have a hypoglycemic effect by several mechanisms, namely by inhibiting glucose absorption, increasing glucose tolerance, stimulating insulin release or acting like insulin, increasing glucose uptake by peripheral tissues and regulating enzymes that play a role in carbohydrate metabolism (Rahmaningsih BY, Nur Hidayat SP, Iin Novita N 2016). Other research more specifically states that the compound quercetin (flavonol subclass) has the potential as a hypoglycemic agent through an inhibitory mechanism for the alpha amylase enzyme which plays a role in the breakdown of carbohydrates. In vitro research also shows that quercetin has the potential to act as an inhibitor of glucose transport by intestinal Glucose Transport 2 (GLUT2) and Glucose Transport 5 (GLUT5) which are responsible for glucose absorption in the small intestine. This is what causes quercetin to reduce blood glucose levels. Tannins are able to reduce blood glucose levels by increasing glucose uptake through the activation of Mitogen Activated Protein Kinase (MAPK) and Phosphoinositide 3-Kinase (PI3K) (Ta'adi, Mardi H, Sunarto 2019).

As for another study entitled the effect of giving soursop leaf extract (Annona muricata L.) on the blood sugar levels of Wistar rats (Rattus norvegicus) induced by alloxan, it was concluded that soursop leaf extract at a dose of 5000 mg/kg BW of rats had the effect of lowering blood sugar levels. measured at 30, 60, 90 and 120 minutes. This type of research is similar with the object of ticks with an experimental design laboratory pretest and posttest with control group design, the sample size is 30 mice, using alloxan to induce diabetes, and glucose levels are determined using the Glucose Oxidase-Phenol 4-Aminoantipyrine (GODPAP) method with results Soursop leaf extract had an effect on improving blood glucose levels in diabetic Wistar rats with an average reduction of 50.72 mg/dl, but the reduction was not significantly different from the glibenclamide group (Ta'adi, Mardi H, Sunarto 2019).

In this study, there was no change in the ABPI value, where this ABPI value indicates the state of circulation of blood flow to the lower extremities. In Type 2 DM patients with the onset of high blood glucose levels in a long time can cause vasoconstriction of blood vessels, causing blood vessel stiffness which will result in plaque buildup, this is what causes blood flow to be blocked, if this happens in the long term it can cause complications of neuropathy and a high risk of wound/diabetic foot ulcer (DFU). One of the causes of the formation of DFU is due to vascular abnormalities in the form of occlusion of peripheral blood vessels in the lower extremities due to hyperglycemia for a long time. ABPI is a non-invasive examination that is used as a diagnostic for arterial stenosis in the lower limbs, because it can describe the process of atherosclerosis, especially in people at risk of vascular disorders aged 40-75 years. The ABPI value has a specificity of 83.33-99.0% and a high accuracy (72.9-89.2%) indicating that a patient may have 50% stenosis if the ABPI value is 0.9. Improvements that can be made to this blood flow are 3 months without surgery.23 2%) indicates that a patient may have 50% stenosis if the ABPI value is 0.9. Improvements that can be made to this blood flow are 3 months without surgery.23 2%) indicates that a patient may have 50% stenosis

if the ABPI value is 0.9. Improvements that can be made to this blood flow are 3 months without surgery (Rahayu UM 2017).

4. Conclusion and Suggestion

Soursop leaf nanoparticles, when administered three times daily over six days, showed significant and clinically relevant reductions in blood glucose levels and by a 123 mg/dL change. Fasting blood glucose levels also decreased significantly by 65 mg/dL with the same nanoparticle administration. However, soursop leaf extract at the identical dosage didn't impact the ABPI value in Type II Diabetes Mellitus patients.

Given the expense and side effects associated with oral hypoglycemic drugs for Type II Diabetes Mellitus, soursop presents itself as an alternative therapy. Its richness in secondary metabolites such as flavonoids and tannins positions it as a potential remedy for temporarily lowering blood glucose levels. Particularly, its accessibility as a traditional medicinal plant could be advantageous for community groups seeking readily available solution

The food intake of respondents plays a crucial role in regulating carbohydrate intake, potentially influencing variations in GDP, GDS, and ABPI values. Additionally, assessing changes in the ABPI value requires substantial time and deeper examination when administering soursop leaf extract, indicating the need for thorough evaluation to identify and understand its effects.s for managing blood sugar levels.

5. Acknowledgments

We would like to thank the head of Poltekkes Kemenkes Semarang, the head of the master of nursing study program, all the team, as well as the respondents who were willing to take part in this research.

6. References

Anon. 2016. *Health Profile of Kotra Pekalongan Health Office PDKK*.

Dharma S, Supanda. 2014. "Effect of Soursop Leaf Ethanol Extract (Annona Muricata L) on LDL Levels in Male White Mice." *Journal of Pharmacy Higea* 6(1):68–77.

Dr. dr. Fatimah Eliana S, KEMD. 2016. *DM Management According to the 2015 PERKENI Consensus*. edited by YARSI BPDF.

Islam, Md. Rabiul. 2017. "Association between Socio-Demographic Factors and Blood Sugar Levels in Type 2 Diabetes Mellitus Patients in Bangladesh." *Journal of Diabetes Mellitus* 07(03):151–59. doi: 10.4236/jdm.2017.73012.

Patricia Gonce Morton DF, Carolyn M. Hudak, Barbara M. Gallo. 2014. *Critical Nursing, Holistic Approach to Care*. Jakarta: ECG.

Rahayu UM. 2017. "Factors Associated with the Occurrence of Diabetic Ulcers in Patients with Type II Diabetes Mellitus. Proceedings of the National Seminar: Vocational Health Services in Supporting National Health Development; Semarang: Postgraduate Program in Applied Mast." 116.

Rahmaningsih BY, Nur Hidayat SP, Iin Novita N, PD S. 2016. "The Relationship between the Ankle Brachial Index Value and the Incidence of Diabetic Foot Ulcer in Type 2 Diabetes Mellitus Patients at Dr. Hospital. Moewardi Surakarta." *PSIK Journal* 11(3):123–31.

Rekha N. 2017. "The Effect of Soursop Leaves (Annona Muricata) on Lowering Blood Sugar Levels." *Journal of Majority, FKUI Univ Lampung* 6(3):144–48.

Suriadi. 2015. *Wound Assessment and Treatment*. Jakarta: Sagung Seto.

Ta'adi, Mardi H, Sunarto, Choiroel Anwar. 2019. "Effectiveness of Soursop Leaf Extracts on Decreasing Blood Sugar for Type - 2 Diabetes Mellitus Patients." *Indian Journal of Public Health Research & Development* 10(9):1306–10.