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Research Article

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Eugenia polyantha leaf extract as an antidiabetic alternative medicine on *Rattus norvegicus*

Joko Waluyo, Kamalia Fikri*, Fadhila Siti Cahyani

Biology Education Department, Jember University, Jember, Indonesia
Email: jokowaluyo.fkip@unej.ac.id[a], kamalia.fkip@unej.ac.id[b]*, fadhilacahyani2404@gmail.com[c]
* Corresponding author

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ABSTRACT

The public does not yet know the potential of *Eugenia polyantha* as an alternative medicine for diabetes mellitus. In fact, the content of chemical compounds such as flavonoids in *Eugenia polyantha* can minimize damage to the pancreas. This study aimed to determine the antidiabetic activity of the ethanolic extract of *Eugenia polyantha* leaf against streptozotocin-induced Wistar rats. The sample for this study were male white rats of the Wistar strain, consisting of 30 rats. It was divided into 6 test groups, group P1 was negative control (aqua dest), group P2 was positive control (glibenclamide), and group P3, P4, and P5 was treated with 70% ethanol extract of *Eugenia polyantha* leaf with doses of 312.5, 625 and 1250 mg/kg respectively. The blood glucose level on the 11th day was tested by ANOVA which is then tested by Duncan. The results showed *Eugenia polyantha* leaf extract has an effect on reducing blood glucose in Wistar rats (*Rattus norvegicus*) with doses 312.5, 625, and 1250 mg/kg body weight. The most effective dose of 70% ethanol extract of *Eugenia polyantha* leaf for reducing blood glucose is 1250 mg/kg body weight. Furthermore, the findings of this study can be tested in more depth so that it can be recommended to the public as an alternative medicine for diabetes mellitus in humans.

Keywords: Antidiabetic; *Eugenia polyantha*; *Rattus norvegicus*

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IKIP Budi Utomo, Malang, Indonesia

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INTRODUCTION

Diet and physical activity have a major influence on the incidence of DM. A risky diet is a diet that often consumes high-carbohydrate food sources (rice, bread, and noodles), sweet drinks and foods, fatty meats, sources of fat, fast food, and preserved foods (Lee et al., 2021). Likewise, low physical activity is

a factor that influences the incidence of DM. The physical activity carried out by a person will be able to affect blood sugar levels because the use of glucose by muscles will increase when a person has high physical activity (Jais et al., 2021).

Setting inappropriate eating patterns such as schedule, amount, and type can result in an increase in blood sugar levels. The more excessive food intake, the greater the possibility of causing an increase in sugar levels. Intake of foods such as carbohydrates or sugar and excessive energy can cause an increase in blood sugar levels so it becomes an early risk factor for diabetes mellitus (Susanti & Bistara, 2018). It is estimated that in 2025 there will be an increase in the number of people with diabetes mellitus from 5 million to 12 million people with diabetes mellitus in the world (Hakim et al., 2009). The number of diabetics in Indonesia is expected to double from 8.4 million in 2000 to 21.3 million in 2009-2030 (Munadjad, 2010). One of the factors that is thought to be the cause of diabetes mellitus is an unhealthy diet (Mahendra et al., 2018).

Diabetes mellitus is characterized by hyperglycemia resulting from insulin secretion, insulin action, or both, in which the pancreas does not produce enough insulin or the body cannot use insulin effectively. Insulin is a hormone that regulates the balance of blood sugar levels. Symptoms of hyperglycemia are characterized by polyuria, polydipsia, weight loss, and sometimes with polyphagia and blurred vision. Decreased growth and susceptibility to certain infections may also accompany chronic hyperglycemia (Yulianti et al., 2020).

One of the preventions of diabetes mellitus is by using alternative medicine from plants (Kasole et al., 2019). The use of traditional medicine among people is still in great demand, not inferior to the use of chemical drugs (Liu et al., 2019). However, traditional and chemical medicines both have side effects, and people rarely think about the side effects of using these drugs. There are almost no side effects from using herbal medicines, even if there is a reaction it is a process of adaptation or adjustment because the body has received high levels of food (Marwati & Amidi, 2018). Traditional medicines are still in great demand by the public because the use of these traditional medicines goes directly to the source of the disease and is reconstructive in nature, namely repairing organs and rebuilding damaged organs, tissues, or cells (Marwati & Amidi, 2018). *Eugenia polyantha* is a plant that can treat diabetes mellitus (Firdausya & Amalia, 2020; Simson & Basuki, 2019). It is one of the herbal medicines that is widely consumed by the public and is used by the community to lower cholesterol, diabetes, hypertension, gastritis, and diarrhea. *Eugenia polyantha* leaves are known to contain flavonoids, selenium, vitamin A, and vitamin E which function as antioxidants (Firdausya & Amalia, 2020). Flavonoids are polyphenol compounds that have benefits as antiviral, antimicrobial, antiallergic, antiplatelet, anti-inflammatory, antitumor, and antioxidants as the body's defense system because flavonoids are known to have been synthesized by plants in response to infection microbes to be effective (Harismah & Chusniatun, 2016).

Siregar (2015) explained that *Eugenia polyantha* leaves can treat diabetes mellitus, diarrhea, hypertension, gastritis, and cholesterol, but this explanation is through a comprehensive literature review study. While in this study using laboratory research methods with animal samples (*Rattus norvegicus*) streptozotocin was induced through extraction techniques to determine the decrease in blood sugar levels. Research by Lelono & Tachibana (2013) explained that *Eugenia polyantha* leaf extract was effective in inhibiting the activity of the alpha-glucosidase enzyme where *Eugenia polyantha* leaves were extracted using a methanol-water solvent. Sutrisna (2016) explained that *Eugenia polyantha* leaf extract can lower blood sugar whereas *Eugenia polyantha* leaves are extracted using 96% ethanol solvent. In

this study the solvent used in the extraction was 70% ethanol, this was done to maximize the phenol concentration. If the ethanol concentration exceeds 70%, the phenol concentration will decrease (Suhendra et al., 2019). Thus, the purpose of this study was to determine the antidiabetic activity of the ethanolic extract of *Eugenia polyantha* leaves against streptozotocin-induced Wistar rats.

RESEARCH METHODS

This study is an experimental study with the aim to determine the effect of 70% ethanol extract of *Eugenia polyantha* leaves on decreasing sugar in Wistar rats (*Rattus norvegicus*) and knowing the concentration of the dose of 70% ethanol extract of *Eugenia polyantha* leaves which was most effective against the blood sugar content of white rats (*Rattus norvegicus*). The sample for this study were male white rats of the Wistar strain which were reared and developed at the Biology Education Department laboratory, Jember University, aged 4-8 weeks, consisting of 30 rats. The 30 white rats were divided into 6 test groups, each test group consisting of 5 white rats with 4 repetitions. Group P1 was negative control (aqua dest), group P2 was positive control (glibenclamide), and group P3, P4, and P5 was treated with 70% *Eugenia polyantha* leaf extract with doses of 312.5, 625, and 1250 mg/kg respectively. After the acclimatization process for 7 days, the Wistar rats (*Rattus norvegicus*) were induced by streptozotocin on the 8th day (Furman, 2015; Saputra et al., 2018). Then on the 11th day blood glucose levels were measured. 70% ethanol extract of *Eugenia polyantha* leaves treatment was carried out for 7 days, and on the 18th-day blood glucose levels were measured. The data obtained then performed normality and homogeneity test using Saphiro-Wilk. Because the data is homogeneous, it is continued with the ANOVA test and DUNCAN.

FINDING AND DISCUSSION

The results of the data were obtained from measuring the blood glucose levels of white rats (*Rattus norvegicus*) in group K (-) which was only given distilled water, K (+) induced by 150 mg/kg Body Weight (BW) streptozotocin and given glibenclamide, groups P1, P2, and P3 which were induced by streptozotocin 150 mg/kg BW and treated with *Eugenia polyantha* leaf ethanol extract at a dose of 312.5 mg/kg BW, 625 mg each /kg BW and 1250 mg /kg BW. The research results can be seen in Table 1.

Table 1. The Average Blood Glucose Level Day-to 0, 11, and 18 White Rats (*Rattus norvegicus*) for groups K (-), K (+), P1, P2, and P3

Treatment	Data Day-0 (mg/dl)	Data Day-11 (mg/dl)	Data Day-18 (mg/dl)	Data Day 11-18 Decrease (mg/dl)
K-	101.4 ± 9.76	472.2 ± 103.95	524.8 ± 67.09	-52.6
K+	105.4 ± 8.96	466.8 ± 56.74	302.8± 51.13	164
P1	107.4 ± 12.09	513.8 ± 68.79	361.6 ± 44.89	152.2
P2	108.4 ± 15.86	427 ± 99.18	267.6 ± 39.48	159.4
P3	101,6 ± 7.98	398 ± 110.71	192 ± 58.60	206

Based on Tabel 1, the average blood glucose level on day 11 of white rats (*Rattus norvegicus*) for groups K (-), K (+), P1, P2, and P3 after *streptozotocin* induction increased from 398.00 to 513.80. While the average blood glucose level after treatment with 70% ethanol extract of *Eugenia polyantha* leaves, on day 18 was decreased, except for negative control. Based on data on the difference between after being

induced by *streptozotocin* and after being treated with ethanol extract of *Eugenia polyantha* leaves, the highest decrease was in P3.

The results of the data obtained were then averaged and analyzed using the SPSS for Windows 23 program. Before carrying out the if the data has significant > 0.05 then the data is said to be the same or homogeneous. Based on Sig Value. shown in this table are shown on blood glucose levels on day 0, day 11, and day 18. The result from the homogeneity test on GD0 has a significant value (0.280 > 0.05) so the data is said to be homogeneous. The results of the homogeneity test on GD11 have a significant value (0.571 > 0.05) so the data is said to be homogeneous. Likewise, the results of the homogeneity test on GD18 have a signification. Because the data is homogeneous, it is continued with the test ANOVA and generated data as in Table 2. Table 2 shows the value of significant (0.000 < 0.05) so there is a significant difference on day 18. The test was continued by conducting DUNCAN's test. The results can be seen in the following Table 3.

Table 2. ANOVA Test Results from the Effect of *Eugenia polyantha* Leaf Extract on Reducing Blood Glucose Levels

	Sum of Square	Df	Mean Square	F	Sig.
Between Groups	313114.560	4	78278.640	27.706	0.000
Within Groups	56506.000	20	2825.300		
Total	369620.560	24			

Table 3. DUNCAN's Results the Effect of *Eugenia polyantha* Leaf Extract on Reducing Blood Sugar Levels

Group (Treatment)	(Mean ± SD)
K-	524.80±67.09^{d}
K+	302.80±51.13^{bc}
P1	361.60±44.89^{c}
P2	267.60±39.48^{b}
P3	192.00±58.60^{a}

Superscript $^{(abcd)}$ difference in the same column indicates a significant difference (sig < 0.05)

Based on Table 3, P3 showed very significantly different results from the K (-), K (+), P1, P2 treatments. Giving 70% ethanol extract of *Eugenia polyantha* leaves decrease blood glucose level even the value is smaller than the positive control treatment that was given glibenclamide (K+).

Groups P1, P2, P3 who were given 70% ethanol extract of *Eugenia polyantha* leaf at a dose of 312.5 mg/kg BW, 625 mg/kg BW, and 1250 mg/kg BW respectively also experienced a decrease in blood sugar levels. The highest reduction with a difference of 206 mg/dL was found at P3. This is because the ethanol extract of *Eugenia polyantha* leaves contains the main flavonoids in the form of quercitrin and fluorethin which function as antioxidants (Badan Pengawas Obat dan Makanan, 2004). Bahriul et al. (2014) explained that flavonoids have an antioxidant effect that acts as an antidote to free radicals such as Reactive Oxygen Species (ROS). Flavonoids work by inhibiting the reabsorption of glucose from the kidneys (Putakala et al., 2017). It works by regulating the work of enzymes involved in carbohydrate metabolism pathways, increasing insulin secretion (Brahmachari, 2011; Man et al., 2017). The positive control group that was treated with glibenclamide at a dose of 2 ml/gram BW experienced a decrease in blood glucose levels. Glibenclamide is an oral hyperglycemic drug in the sulfonylurea class which has a therapeutic effect on lowering blood glucose levels. This is because glibenclamide works primarily in increasing insulin secretion. The mechanism of action of glibenclamide is to stimulate insulin hormone secretion from the β-cell granules of the islets of langerhans in the pancreas (Maliangkay et al., 2019).

CONCLUSION

The results showed 70% ethanol extract *Eugenia polyantha* leaf extract reduces blood glucose in Wistar rats (*Rattus norvegicus*) with doses 312.5, 625, and 1250 mg/kg BW. The most effective dose of 70% ethanol extract *Eugenia polyantha* leaf on reducing blood glucose is 1250 mg/kg BW. Furthermore, the findings of this study can be tested in more depth so that it can be recommended to the public as an alternative medicine for diabetes mellitus in humans.

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