J Prima Med Sains (2023) 5(2):218-222
https://doi.org/10.34012/jpms.v5i2.4523

ORIGINAL ARTICLE

Effectiveness of durian peel ethanol extract for lowering blood sugar levels in alloxan diabetic wistar rats

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Abstract

High blood sugar levels can be influenced by several factors, including high-carbohydrate food consumption and a lack of physical activity. To minimize the side effects of hyperglycemic treatment, efforts have been made to explore anti-hyperglycemic compounds from other sources, such as durian peel (*Durio zibetthinus Murr.*). This study aimed to determine the effectiveness of ethanol extract from durian peel in lowering alloxan-induced blood sugar levels in Wistar rats (*Rattus novergicus*). The study is an experimental research employing an alloxan-induced diabetic rat model. The rats were divided into five different groups: Group I (negative control), Group II (positive control), Group III (dose 25 × 10–30/gBW), Group IV (dose 50 × 10–30/gBW), and Group V (dose 100 × 10–30/gBW). The durian peel used in this study was extracted using the maceration method with ethanol as the solvent. The results of this study indicate that ethanol extract from durian peel significantly reduced blood sugar levels after 10 to 15 days of durian peel extract administration ($p < 0.05$).

Keywords: durian peel, ethanol, alloxan, wistar rat

Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by chronic hyperglycemia resulting from damage or deficiency in insulin secretion, impaired response to insulin, or both.[1] Risk factors contributing to the occurrence of diabetes mellitus include non-modifiable factors (age, sex, and family history of diabetes mellitus) and modifiable factors (excess weight, lack of physical activity, hypertension, disturbances in blood lipid profile, triglycerides > 250 mg/dL, and an unhealthy diet high in sugar and low in fiber).[2] In 2022, the International Diabetes Federation reported that 537 million adults (20-79 years) worldwide were living with diabetes. This number is estimated to increase to 643 million (one in nine adults) by 2030 and 784 million (one in eight adults) by 2045. Diabetes mellitus caused 6.7 million deaths in 2021, with an estimated 44% of adults living with diabetes (240 million people) remaining undiagnosed. Globally, 541 million adults, or 1 in 10, experience impaired glucose tolerance, putting them at a high risk of developing type 2 diabetes.[3] The Ministry of Health of the Republic of Indonesia reported 19.47 million cases of diabetes mellitus in 2021.[4]

Indonesia is rich in biodiversity, including traditional medicinal plants.[5,6] According to the World Health Organization (WHO), in 2008, approximately 80% of the world's population used traditional medicine for their primary health needs owing to its accessibility and relatively low cost.[7] Durian is a plant that thrives in tropical climates, particularly in Southeast Asia, particularly Indonesia. Durian plants have various components and benefits. Durian fruit peel contains essential oils, flavonoids, saponins, cellulose elements, lignin, and starch. Its leaves contain saponins, flavonoids, and polyphenols, whereas the roots contain tannins. Durian also contains significant amounts of vitamins B1, B2, and C, as well as potassium, calcium,

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and phosphorus. Durian leaves and roots are used as antipyretics, durian leaves can be used to treat fever, and durian fruit can serve as a dietary supplement, particularly for patients with hypercholesterolemia and diabetes mellitus, and as a natural source of antioxidants.[8]

Anti-hyperglycemic compounds originate from herbal plants such as durian peel. A phenomenon in society suggests that after consuming durian fruit, it is advisable to drink the water used to rinse durian peel. This practice is believed to alleviate dizziness that may occur after excessive durian consumption. Dizziness can elevate blood glucose levels, resulting in thickened blood. Consequently, the heart works harder to pump blood into the brain, and the brain signals to restore stable blood sugar levels. This effect is attributed to the phytonutrients found in durian peel, including Mn, organosulfur, and secondary metabolites.[9] A study by Yuan et al.[10] indicated that durian peel exhibits various pharmacological activities, such as antioxidant, anti-inflammatory, and regulation of glucose and lipid metabolism. The aim of this study was to investigate the effectiveness of ethanol extract from durian peel for lowering blood sugar levels in alloxan diabetic wistar rats.

Method

This study used an experimental method with a pre and post-test control group design. Utilizing this design, both the experimental and control groups had similar characteristics, as they were randomly selected from a homogeneous population. In this design, both groups underwent an initial test (pre-test) using the same assessment.

This study was conducted at the Integrated Research Laboratory of the Faculty of Medicine, Dentistry, and Health Sciences, Universitas Prima Indonesia, Medan, from April 2023 to October 2023. The study was approved by the Health Research Ethics Committee (KEPK) of Universitas Prima Indonesia (approval number 020/KEPK/UNPRI/X1/2023). Male Wistar rats were used as the experimental animals. Through the application of the Federer formula, a sample size of five rats or more was determined for testing in each experimental group, resulting in a total of 25 rats. The independent variable in this research was the durian peel extract, with percentages in groups receiving durian peel extract (25 × 10-30/gBW), groups receiving durian peel extract (50 × 10–30/gBW), and groups receiving durian peel extract (100 × 10-30/gBW). The dependent variable was blood sugar levels in rats. The control variable was the type of experimental animal, namely normal Wistar strain rats aged 2 months with a weight of approximately 150-300 g.

The tools and materials used in the study included Erlenmeyer flasks, beakers, volumetric flasks, rotary evaporator, desiccator, atomic absorption spectrophotometer, Mohr pipette, test tubes, oven, blender, funnel, filter paper, analytical balance, water bath, porcelain dish, mortar, durian peel, Wistar rats, distilled water, and acarbose. The procedures involved in the research included preparation of durian peel simplicia, durian peel extraction, determination of water content, preparation of alloxan solution, phytochemical testing, preparation of experimental animals, blood sugar level examination, and data analysis using one-way ANOVA.

Results

Table 1. Characteristics of leaf skin extract

Characteristics	Value
Fresh simplisia weight (g)	1,000
Dry simplisia powder weight (g)	358
Solvent volume (ml)	3,000
Extract weight (g)	7.1
Yield (%)	1.98

From 1,000 g of fresh durian peel, 358 g of durian peel powder was obtained (Table 1). Subsequently, this durian peel powder was macerated using 3,000 mL of ethanol solvent. After the rotary evaporator process, of durian peel extract was obtained in the amount of 7.1 grams. Based on these data, the yield was determined to be 1.98%. Phytochemical screening results indicated that the durian peel extract contained alkaloids and saponins (see Table 2).

The initial weight serves as one of the measured parameters in this study. Initially, the data for the initial weight were analyzed for its distribution using the Shapiro-Wilk test (see Table 3). In Table 3, it can be observed that the P-values for the weight data in Groups II, III, and IV are less than 0.05, indicating that the distribution of initial weight data is not normal. Therefore, the initial weight data is analyzed using the Kruskal-Wallis' test.

Table 2. Phytochemical screening results of durian peel extract

Phytochemical	Method	Result
Alkaloid	Bouchardart	-
	Mayer	+
	Dragendorf	-
	Wagner	+
Terpenoid/Stroid	Lieberman-Burchard	-
	Salkovski	+
Saponin	Aquadest + Alkohol 96%	+
Flavonoid	$FeCl_3$ 5%	-
	Sinoda Test (Mg + $HCl_{(p)}$	-
	Alkaline (NaOH 10%)	-
	$H_2SO_{4\ (p)}$	-
Tannin	$FeCl_3$ 1%	-

Table 3. Results of analysis of initial weight data distribution

Treatment group	p	Data distribution
Group I	0.119	Normal
Group II	0.046	Not Normal
Group III	0.046	Not Normal
Group IV	0.046	Not Normal
Group V	0.146	Normal

Table 4. Comparison of initial weight of rats across all treatment groups

Treatment group	Initial weight (g)			p
	Median	Min	Max	
Group I	164	163	165	< 0.05
Group II	146	146	148	
Group III	160	160	162	
Group IV	158	156	158	
Group V	155	153	156	

Table 5. Results of blood sugar level data distribution analysis

Parameter	Treatment group	p	Data distribution
Blood sugar level before induction	Group I	0.946	Normal
	Group II	0.482	Normal
	Group III	0.503	Normal
	Group IV	0.589	Normal
	Group V	0.839	Normal
Blood sugar level after induction	Group I	0.052	Normal
	Group II	0.094	Normal
	Group III	0.032	Not normal
	Group IV	0.745	Normal
	Group V	0.190	Normal
Blood sugar level (day 5)	Group I	0.287	Normal
	Group II	0.256	Normal
	Group III	0.448	Normal
	Group IV	0.689	Normal
	Group V	0.664	Normal
Blood sugar level (day 10)	Group I	0.955	Normal
	Group II	0.364	Normal
	Group III	0.974	Normal
	Group IV	0.442	Normal
	Group V	0.004	Not normal
Initial weight	Group I	0.306	Normal
	Group II	0.912	Normal
	Group III	0.277	Normal
	Group IV	0.063	Normal
	Group V	0.819	Normal

In Table 4, it can be observed that there was a significant difference in the initial weight of the rats used in this study ($p < 0.05$). The highest initial weight was found in Group I (164 g), followed by Group III (160 g), IV (158 g), V (155 g), and II (146 g).

The blood sugar levels of male Wistar rats were measured at five different times: before induction, after induction, on day 5, day 10, and day 15. Before comparing blood sugar levels in all treatment groups, the distribution of the entire blood sugar level data was analyzed using the Shapiro-Wilk test (Table 5). It can be observed that the distribution of blood sugar levels after induction and on day 10 shows a non-normal distribution. Meanwhile, blood sugar levels before induction, on day 5, and on day 15 exhibit a normal distribution. Based on the analysis of the data distribution, blood sugar levels after induction and on day 10 will be further analyzed using the Kruskal-Wallis test. Meanwhile, data on blood sugar levels before induction, on day 5, and on day 15 will be analyzed using the one-way ANOVA test (see Table 6).

Based on the comparison of blood sugar levels, it can be observed that the male Wistar rat blood sugar levels show significant differences among treatment groups on day 10 and day 15, as indicated by the P-value < 0.05. After 10 days of treatment, the trend of the highest blood sugar level is found in Group I at 489 mg/dL, followed by Group III (473 mg/dL), IV (289 mg/dL), V (211 mg/dL), and the lowest in Group II at 158 mg/dL. Furthermore, the blood sugar levels of rats after 15 days of treatment also tend to decrease, with the highest blood sugar level still found in Group I at 350.60 mg/dL, followed by Group III (362.20 mg/dL), IV (220.60 mg/dL), V (217.20 mg/dL), and the lowest in Group II at 144.00 mg/dL.

Discussion

Based on these results, it is clear that durian fruit peel extract significantly reduced blood sugar le vels after 10 days of administration. However, the blood sugar levels in the group receiving durian peel extract did not reach normal values (< 200 mg/dL), whereas those in the control group receiving acar-bose showed a significant decrease to normal levels. The findings of this study were consistent with those of previous studies. Muhtadi et al.[11] reported that durian peel extract had antidiabetic effects at doses of 125-500 mg/kgBW evaluated in an alloxan-induced diabetic rat model. The average blood sugar levels of diabetic rats receiving durian peel extract at doses of 500 mg/kgBW, 250 mg/kgBW, and 125 mg/kgBW after 28 days of treatment were 112.80 ± 8.29 mg/dL, 147 ± 8.69 mg/dL, and 189 ± 6.78 mg/dL, respectively. Furthermore, this study also reported a percentage decrease in blood sugar levels in rats receiving durian peel extract at doses of 500 mg/kg BW, 250 mg/kg

BW, and 125 mg/kg BW, which were 50.19 ± 3.66%, 35.09 ± 3.84%, and 16.55 ± 2.99%, respectively. This study is consistent with the results of a study conducted by Muhtadi et al.[12], where durian peel extract was also reported to reduce blood sugar levels within seven days. The average blood sugar levels of rats receiving durian peel extract at doses of 500 mg/kgBW, 250 mg/kgBW, and 125 mg/kgBW after 7 days were 112.8±8.29 mg/dL, 147±8.69 mg/dL, and 189±6.78 mg/dL.

Table 6. Comparison of rat blood sugar levels across all treatment groups

Group	Initial Weight (mg/dl)				
	Before induction	After Induction	Day-5	Day-10	Day-15
I	95.20 11.73	299 (261-600)	446.80 136.35	489 (311-600)	350.60 73.28
II	92.00 6.32	294 (208-600)	326.20 191.41	158 (111-290)	144.00 38.71
III	98.40 23.86	384 (349-600)	423.40 101.11	473 (300-600)	362.20 98.87
IV	90.60 12.97	310 (227-412)	322.80 76.53	289 (212-389)	220.60 53.50
V	101.40 10.33	336 (206-379)	297.00 78.92	211 (200-380)	217.20 49.32

The differences between the results of the current study and those of previous studies may be attributed to various factors, including the quality of the extract and phytochemical content of the durian peel extract. In this study, the quality of the extract was determined based on the yield value. Muhtadi et al. used durian peel extract with a yield value of 16.93%. This yield value indicates that a higher yield indicates a poorer quality extract, whereas a lower yield indicates a better quality extract. In this study, the yield was 1.98%, indicating that the quality of durian peel extract was better than that reported by Muhtadi et al. (16.93%).[11,12] This variation may be due to the type of solvent used in the current study compared with the previous study by Muhtadi et al. In the current study, 96% ethanol was used as the solvent, whereas Muhtadi et al. used a maseration solvent in the form of a mixture of 96% ethanol and acetone. This aligns with the theory, as Pandey and Tripathi[13] reported that some factors influencing the quality of the extract include the plant part used as the starting material, solvent used for extraction, and extraction procedure.

The antidiabetic activity of durian peel extract is closely related to its phytochemical content present in durian peel. Charoenphun & Klangbud[14] reported that the total phenol content in two types of durian, Monthong and Chanee, was 3,471.98 ± 141.06 mg GAE/g and 3,576.74 ± 259.99 mg GAE/g, respectively. Furthermore, this phytochemical content is responsible for other pharmacological effects, including antioxidant and anti-inflammatory effects. Muhtadi et al.[11] reported that durian peel extract contains phenolic compounds in the form of flavonoids, such as catechin, quercetin, EGCG, and other phenolic compounds, such as polyphenols and tannins. In this study, phytochemical screening of durian peel extract revealed only alkaloids and saponins, which differs from previous studies reporting various phenolic compounds in durian peel extract, such as flavonoids and other polyphenols.

These phenolic compounds can reduce rat blood sugar levels by inhibiting glucose absorption through insulin release stimulation and indirectly through antioxidant activity, thereby preventing free radical-induced pancreatic damage.[11] In addition, alkaloids have been reported to have antidiabetic effects. Muhammad et al.[15] reported that alkaloids exert antidiabetic effects by inhibiting or inducing several candidate proteins, including AMP-activated protein kinase, glucose transporters, glycogen synthase kinase-3, sterol regulatory element-binding protein 1, glucokinase, glucose-6-phosphatase, and acetyl-CoA carboxylase. Adhikari[16] also reported that alkaloids can inhibit several enzymes involved in glucose absorption, including α-amylase, α-glucosidase, aldose reductase, dipeptidyl peptidase-IV, and protein tyrosine phosphatase-1.

Conclusion

The ethanol extract of durian peel, with a yield of 1.98%, contains phytochemicals, such as alkaloids and saponins. The results indicated that the ethanol extract of durian peel significantly reduced blood sugar levels after 10 to 15 days. After 10 days of treatment, the highest trend in blood sugar levels was found in Group I (489 mg/dL), followed by Group III (473 mg/dL), IV (289 mg/dL), and V (211 mg/dL), and the lowest in Group II (158 mg/dL). Meanwhile, after 15 days of treatment, the average highest blood sugar levels were still found in Group I at 350.60 mg/dL, followed by Group III (362.20 mg/dL), IV (220.60 mg/dL), V (217.20 mg/dL), and the lowest was in Group II at 144.00 mg/dL.

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