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EFFECT OF ETHANOL EXTRACT OF SEA PANDAN FRUIT (PANDANUS TECTORIUS) ON BLOOD GLUCOSE LEVELS IN MALE WHITE RATS (RATTUS NORVEGICUS) INDUCED BY DEXAMETHASONE

Ghifara Kireina Annisa[1], Nita Pranitasari[2]*, R. Varidianto Yudo Tjahjono[3], Roostantia Indrawati[4]
[1]Faculty of Medicine, Universitas Hang Tuah, Jl. Arif Rahman Hakim No. 150, Keputih, Sukolilo, Surabaya, Jawa Timur 60111, Indonesia
[2]Department of Histology, Universitas Hang Tuah, Jl. Arif Rahman Hakim No. 150, Keputih, Sukolilo, Surabaya, Jawa Timur 60111, Indonesia
[3]Department of Microbiology, Faculty of Medicine, Universitas Hang Tuah, Jl. Arif Rahman Hakim No. 150, Keputih, Sukolilo, Surabaya, Jawa Timur 60111, Indonesia
[4]Head of Pharmacy-Medical section, Faculty of Medicine, Universitas Hang Tuah, Jl. Arif Rahman Hakim No. 150, Keputih, Sukolilo, Surabaya, Jawa Timur 60111, Indonesia
*dr.nitnot@gmail.com

ABSTRACT
Diabetes mellitus is a metabolic disorder with increased blood glucose due to decreased insulin production or sensitivity. Chronic hyperglycemia can lead to endothelial dysfunction and vascular complications. Dexamethasone as a synthetic glucocorticoid can cause hyperglycemia through increased gluconeogenesis and insulin resistance. The antioxidant content in sea pandanus (Pandanus tectorius) has the potential to lower blood glucose levels. This study aims to determine the effect of ethanol extract of sea pandan fruit on blood glucose levels of male white rats (Rattus norvegicus) induced by dexamethasone. This study aims to determine the effect of ethanol extract of sea pandan fruit (Pandanus tectorius) on blood glucose levels in male white rats (Rattus norvegicus) induced by dexamethasone. Experimental research with a post test only control group on 30 mice grouped into 3 groups. Namely, K(-) which was only given standard feed, K(+) which was induced by dexamethasone at a dose of 5 mg/KgBB, and KP which was induced by dexamethasone at a dose of 5 mg/KgBB and given Pandanus tectorius fruit extract at a dose of 100 mg/KgBB, then at the end of the study a blood sample was taken to measure blood glucose levels and then terminated. The sample was selected using simple random sampling technique. The data was analyzed using the One Way Anova test. In the results of the study, the average blood glucose level K(-) = 170.37 was obtained; K(+) = 274.62; KP = 243. In the One Way Anova parametric test, a significant result was obtained which was 0.005 ($p<0.05$). Then in the Post Hoc Games-Howell test, K(-) and K(+) had a significance of 0.001 ($p<0.05$), while the K(-) and KP groups as well as K(+) and KP showed no significant results. This suggests that ethanol extract of Pandanus tectorius fruit did not successfully inhibit the increase in blood glucose levels in dexamethasone-induced white rats. The administration of ethanol extract of Pandanus tectorius fruit as a therapy was able to reduce the blood glucose level of male Rattus norvegicus induced by dexamethasone compared to a K(+) positive control of 31.62 mg/dL (11.5%).

Keywords: blood glucose; dexamethasone; diabetes; hyperglycemia; pandanus tectorius

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INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by an increase in blood glucose due to reduced insulin production, decreased sensitivity of the body to the action of insulin, or a combination of both. Type 1 diabetes mellitus occurs due to damage to pancreatic cells that play a role in producing insulin so that the production of the hormone decreases, while type 2 diabetes mellitus occurs as a result of a decrease in the sensitivity of insulin action which is generally related to metabolic syndrome (Petersmann et al., 2019). The endothelium is a layer of cells that lines the lumen of blood vessels and can be disrupted due to hyperglycemia. This can lead to decreased endothelial function which contributes to long-term complications including blood vessel damage to cardiovascular disease (Schmidt, 2018).

The main treatments used to treat diabetes mellitus are the administration of insulin from outside the body (exogenous) and antidiabetic drugs. In addition to pharmacotherapy therapy, the implementation of a healthy lifestyle that includes a balanced diet and exercise routine is an important part of managing diabetes (Akil et al., 2021).

Dexamethasone is a synthetic glucocorticoid that has a role as an anti-inflammatory and immunosuppressive. Long-term administration of dexamethasone may result in hyperglycemia. This condition occurs due to the stimulation of gluconeogenesis in the liver which plays a role in increasing liver glycogen and decreasing glucose absorption by skeletal muscle and fat tissue, thereby contributing to an increase in blood glucose and a decrease in the body's sensitivity to insulin (Niu et al., 2018).

The administration of exogenous glucocorticoids will stimulate lipolysis in adipose tissue as well as protein breakdown in muscles, both of which are used as ingredients for liver gluconeogenesis. Glucocorticoids are also associated with insulin resistance, namely by inhibiting the work of GLUT 4 in adipose tissue and muscles. The production of GLUT 4 is not disrupted but there is a disruption in the translocation of GLUT 4 to the plasma membrane. Glucocorticoids also work on GLUT 2 which acts as a transporter into the ß pancreatic cells, so glucose cannot enter the cell which functions to stimulate insulin release. Glucocorticoids can also cause death of pancreatic ß cells by stimulating the proapoptosis proteins BAX, BAD, p38 and inhibiting the prosurvival protein Bcl-2 which acts as an anti-apoptosis (Martinez et al., 2024).

Herbal medicine is an alternative in treating type 2 diabetes mellitus, one of which can be used to use sea pandan (Pandanus tectorius) (Sundus et al., 2021). The content of caffeoylquinic acid (CQA) found in Pandanus tectorius can lower blood sugar levels by inhibiting glucogenesis in the liver (Rustamsyah et al., 2022). Pandanus tectorius extract has the potential to be an antioxidant, antidiabetic, and anti-inflammatory so that the extract can be used to treat hyperglycemia (Balamurugan et al., 2024).

Based on this description, the author wants to know the effect of ethanol extract of sea pandan fruit (Pandanus tectorius) as an antidiabetic on blood glucose levels as evidenced by laboratory experimental research using male white rats (Rattus norvegicus) induced by dexamethasone.

METHOD

Research Design

This experimental research used a post test only control group design, at the Integrated Biomolecular and Hyperbaric Laboratory, Faculty of Medicine, Hang Tuah University from April to September 2025.

Subject

This research method uses a post-test only control group design involving white rats (Rattus norvegicus) as test animals. The study was divided into three groups, each consisting of 10 mice, including: (1) The negative control group (K−) was not given any treatment and blood glucose sampling was carried out on day 15; (2) The positive control group (K+) was subcutaneously induced dexamethasone at a dose of 5 mg/kgBB/day on days 8 to 14, then blood glucose sampling was carried out on day 15, and (3) The treatment group was given subcutaneous dexamethasone induction at the same dose, namely 5 mg/kgBB/day, and was given ethanol extract therapy of Pandanus tectorius fruit at a dose of 100 mg/kgBB/day on days 8 to 14. After all treatments were completed, blood glucose sampling in the treatment group was carried out on day 15.

The selection of white rats (Rattus norvegicus) used a simple random sampling technique with inclusion criteria including: (1) Male rat sex; (2) White rat type (Rattus norvegicus) of the wistar

strain; (3) In good health and active; (4) Age 7-9 weeks, and (5) Body mass of Rattus norvegicus from 100 g to 200 g.

Instruments Research

The bound variable was the blood glucose level of male white rats (Rattus norvegicus) of the wistar strain. The independent variable was ethanol extract of sea pandan fruit (Pandanus tectorius). Blood samples were taken from the heart vein through the left side of the rat's chest to measure fasting blood glucose levels (mg/dL). Glucose levels were determined enzymatically using the GOD-PAP method. This method produces a quinonimine-colored complex compound through a reaction between glucose and the GOD-PAP reagent. The intensity of this complex color is then measured using a spectrophotometer in the visible light spectrum . The research ethics permit was obtained from the Health Research Ethics Commission, Faculty of Medicine, Hang Tuah University Surabaya No. I/062/UHT. KEPK.03/VIII/2025.

Data Analysis

In this study, the ethanol extract variable of sea pandan fruit (Pandanus tectorius) has a nominal data scale. The blood glucose levels of white rats (Rattus norvegicus) have a scale of ratio data. The normality test used the Saphiro-wilk method. To test the homogeneity of the variants, use the Levene method. Data were analyzed with the One-way anova test if it met the normality requirements, but if it did not meet the requirements using the Kruskal Wallis test.

RESULT

Descriptive Analysis

Based on Table 1, the negative control group (K−) had an average blood glucose level of 170.37 mg/dL, with a minimum value of 120 mg/dL and a maximum of 221 mg/dL, which reflects a relatively lower blood glucose condition compared to the other groups. The positive (K+) control group, which was induced by dexamethasone, showed the highest average blood glucose levels, which was 274.62 mg/dL, with a minimum value of 218 mg/dL and a maximum of 345 mg/dL, indicating that dexamethasone induction significantly improved blood glucose levels. Meanwhile, the treatment group (KP) that received ethanol extract therapy from Pandanus tectorius showed an average blood glucose level of 243 mg/dL, lower than the K(+) group but still higher than the K(−) group.

Table 1.
Blood Glucose Level Test Results in the Research Group

Groups	Mean (mg/dL)	Maximum (mg/dL)	Minimum (mg/dL)
Negative control group (K-)	170,37	221	120
Positive control group (K+)	274,62	345	218
Treatment Group (KP)	243,00	323	107

Bivariate Analysis

Based on Table 2, the results of the normality test in the negative control group (p = 0.958), the positive control group (p = 0.083); and the treatment group (p = 0.278) showed a p-value of >0.05 so that the data was normally distributed in all three groups.

Table 2.
Normality Test Results

Groups	p-value	Remarks
Negative control group	0,958	Normal distribution
Positive control group	0,083	Normal distribution
Treatment Groups	0,278	Normal distribution

After obtaining the normal distribution results on the normality test, the homogeneity test is performed. The *Levene* test is used to determine whether the data is homogeneous or not. Based on Table 3, it was found that the data was inhomogeneous. These results indicate that the data

assumption requirements of the three groups vary so that the One Way Anova test can be carried out.

Table 3.
Results of the Levene Homogeneity Test for Blood Glucose Levels

Variable	p-value
Blood Glucose Levels	0,005

The *One Way Anova test* was conducted to find out if there was a difference in the blood glucose levels of rats in the three groups. Based on Table 4, a significant difference was found from the administration of sea pandan fruit extract in the treatment group (p = 0.005). So to find out which group has the influence of the three groups, a Post-Hoc analysis test is carried out.

Table 4.
Parametric Test Results with *One Way Anova*

Variable	p-value
Blood Glucose Levels	0,005

The *Post-Hoc* test, which is an advanced version of Anova's *One Way parametric test*, is used to evaluate whether there is a significant or insignificant difference between the two groups. The *Post-Hoc Games-Howell* test is a viable option because the data is not homogeneous. Based on Table 5, it can be seen that there was a significant difference in blood glucose levels in the negative control group vs the positive control group (p = 0.001). There was no significant difference in blood glucose levels in the negative control group vs. the treatment group (p = 0.086). There was no significant difference in blood glucose levels in the positive control group vs. the treatment group (p = 0.625).

Table 5.
Post-Hoc Games-Howell Test Results of Blood Glucose Levels

Groups	p-value
Negative control group vs Positive control group	0,001
Negative control group vs treatment group	0,086
Positive control group vs treatment group	0,625

DISCUSSION

Effects of Dexamethasone Induction on Blood Glucose Levels

Based on the research and the process of checking blood glucose levels in Rattus norvegicus, the average rat in the K(-) group had the lowest blood glucose levels among the other 2 study groups. Meanwhile, the highest blood glucose level was found in the K(+) group, followed by the treatment group (KP). The K(+) group induced dexamethasone 5 mg/kgBB/day for 7 days was shown to improve blood glucose levels in study mice.

In a rat model, dexamethasone administration caused prolonged hyperglycemia, that is, a sustained increase in blood glucose levels, indicating a hyperglycemic effect after exposure to glucocorticoids such as dexamethasone (Uto et al., 2021). The choice of dexamethasone induction is also based on research by Mahmoud (2022) who showed that the use of dexamethasone can cause signs of insulin resistance similar to type 2 diabetes mellitus, namely hyperglycemia.

Effects of Pandanus tectorius Extract on Blood Glucose Levels in White Rats

In this study, there was 1 treatment group. Where in the treatment group (KP), dexamethasone induction was carried out subcutaneously with a dose of 5 mg/kgBB/day and given Pandanus tectorius ethanol extract at a dose of 100 mg/kgBB/day on days 8-14. The treatment group given Pandanus tectorius extract showed lower blood glucose levels than the positive control group induced dexamethasone, although the SPSS statistical test showed insignificant results.

In this study, the decrease in blood glucose levels in the treatment group (KP) statistically showed insignificant results when compared to the negative control group (K-), just as the average blood glucose level in the treatment group (KP) statistically showed insignificant results when compared

to the positive control group (K+). This means that the administration of ethanol extract of Pandanus tectorius fruit at a dose of 100 mg/kgBB/day was able to reduce blood glucose levels by 11.5% in the treatment group (KP) when compared to the K(+) positive control group even though it showed statistically insignificant results.

This study is different from the research conducted by Sundus et al. (2021), where Pandanus tectorius extract has been proven to reduce blood glucose levels in research mice. The study showed a decrease in blood glucose levels in rats after being given ethanol extracts of Pandanus tectorius stems, roots, and leaves at a dose of 200 mg/kgBB for 3 days and using alloxan 100 mg/kgBB for 3 days as an inducer to increase blood glucose levels. Ethanol extract shows the highest antioxidant potential obtained from the stem of Pandanus tectorius, while in water extract the highest antioxidant potential is found in the root of Pandanus tectorius (Sundus et al., 2021). In the study, we used whole extracts from the stems, roots, and leaves of Pandanus tectorius, while in the study we used whole extracts from the fruits of Pandanus tectorius. It can be said that the amount of dosage of Pandanus tectorius extract has an effect on the results of the study, with the dose of ethanol extract of Pandanus tectorius fruit given being too little, which is 100 mg/kgBB/day.

Several factors can be involved both externally and internally that affect the results of the research. The extraction process can affect the effectiveness of a compound. The commonly used phenolic compound extraction process is maceration using ethanol or methanol solvents. The use of a shaker incubator and temperature regulation can speed up the process but too high a temperature can damage phenolic compounds and evaporate solvents. The efficiency of extraction is affected by the length of time, the ratio of solvent to sample, and the size of the particle. A longer time will reach equilibrium levels, a ratio of solvents larger than the sample will increase the yield but when it is excessive it becomes less efficient, and smaller particles will produce higher phenolics due to a larger surface area (Shi et al., 2022). Research shows that when Pandanus tectorius is grown under drought stress, it will produce stronger biological activities such as antioxidants, anti-inflammatory, and antidiabetic. This happens because drought stress conditions will stimulate the production of plant active compounds (Balamurugan et al., 2024).

The effectiveness of Pandanus tectorius fruit extract can also be increased by making it in the form of SNEDDS (Self-Nanoemulsifying Drug Delivery System) rather than in the form of coarse extract. SNEDDS produces a stable lipid solution so that it is stable in gastric and intestinal fluids for 4 hours without deposition. This results in increased antioxidant activity as the extract becomes more soluble, more stable, and more effective as an antioxidant making it suitable for oral use (Kholieqoh et al., 2022).

In a study by Tanggu et al. (2022) using Pandanus tectorius leaf extract, it showed antidiabetic activity. The dosage given varied at 125,250, and 375 mg/kgBB/day for 14 days. The results showed that the optimal dose to reduce blood glucose levels was 375 mg/kgBB/day (Tanggu et al., 2022). It can be said that the dose and duration of administration have an effect on the results of the study.

Research Limitations

The limitation of this study is the lack of variation in the dosage and duration of administration of ethanol extract of Pandanus tectorius fruit. As well as the use of extracts that are still in the form of whole extract, not in the form of a single component that has been isolated.

CONCLUSION

This suggests that ethanol extract of Pandanus tectorius fruit did not successfully inhibit the increase in blood glucose levels in dexamethasone-induced white rats. The administration of ethanol extract of Pandanus tectorius fruit as a therapy was able to reduce the blood glucose level of

male Rattus norvegicus induced by dexamethasone compared to a K(+) positive control of 31.62 mg/dL (11.5%).

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