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Article

Influence Giving Ethanol Extract of Nipah Fronds (Nypa Fruticans Wurmb) on the Lipid Parameters of Male Diabetic Rats of the Wistar Strain

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Abstract: Diabetes mellitus is gathering disease metabolic with hyperglycemia caused by abnormalities in insulin secretion , insulin action , or both of them . Loss central type 2 diabetes is caused by insulin resistance in muscles and liver as well failure pancreatic beta cells . Purpose This research is to find out How extract ethanol leaf stalk palm affect the lipid values of diabetic rats. Type This research is a experimental . This research is divided into 6 groups with different treatment namely normal, control negative CMC-Na (0.5%), control positive glibenclamide (0.45mL), 125mg/kgBW extract , 250mg/kgBW extract and 500mg/kgBW extract . The results of the lipid parameter data were analyzed with SPSS 22 with level 95% confidence level Results study show extract ethanol dose 250 mg/kgBW and 500 mg/kgBW or more Lots lower level total cholesterol , triglycerides , and LDL as well increase HDL levels ..

Keywords: Influence, Nypa fruticans Wurmb, lipid parameters

1. Introduction

Diabetes mellitus is gathering disease metabolic with hyperglycemia caused by abnormalities insulin secretion , insulin action , or both of them . Insulin resistance in muscles and heart as well as failure pancreatic beta cells has known as pathophysiology damage central to type 2 diabetes (Purwandari et al., 2022).

Global Burden of Disease The global prevalence of Diabetes Mellitus reached 382 million people in 2013, especially in the 45-59 year age group , and is estimated to... increase to 592 million by 2035. In particular , approximately 80% of individuals diagnosed with diabetes live in countries earn low and medium . Indonesia is positioned as country the seventh most affected impact globally , with an estimated 8.5 million people suffer from diabetes mellitus. According to Study Health 2018 basis , reported that prevalence of Diabetes Mellitus, as diagnosed by a health professional medical for individuals aged 45-54 years, has develop to 3.9%, different with 2013 statistics of 3.3%. In addition to age, the segmented data based on type gender and location geographical show that demographics Woman has experience improvement prevalence to 1.8%, compared to with the 2013 figure was 1.7%. (Purwandari et al., 2022). Although there has been progress achieved in the treatment of diabetes, the use of term long can result in various effect side effects and complications . Therefore That is so it is important to investigate source natural that has potential characteristic antidiabetic to facilitate development intervention more therapeutic safe and more productive (Fitri et al., 2023)

Plant has used since centuries ago as drug traditional for treating various type disease . Ability plants to produce metabolit secondary with nature and activities diverse biology make plant as one of the source the most important natural ingredients that can be developed as medicine (Sukma et al., 2018)

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Indonesia is country tropical with Lots forest as well as reaching 3.3 million hectares where most mangrove forest . Nipah (Nypa fruticans Wurmb) has utilized public from era in the past (Khairi et al., 2020). Leaf palm beneficial as drug traditional and as immunostimulant Because contain antioxidants and ingredients active that helps prevent disease bacteria (Ika June Putri et al., 2013).

Study previously that plant leaf nipah (Nypa fruticans Wurmb) contains phenolics , flavonoids, saponins, tannins , and triterpenoids, indicating that That originate from plant leaf nipah . (Nypa fruticans Wurmb) has prospecting in providing material standard biopharmaceuticals (Gazali & Nufus , 2019). A number of studies have done to prove various content material important contents contained in fruit and also sap nipah . Results extract endosperm fruit ripe nipah show content phenolics , flavonoids, and high antioxidant capacity (Prasad et al ., 2013).

Based on background behind above , formula problem from This research is whether the extract ethanol leaf stalk leaf nipah and differences the dosage own effect significant to lipid profiles of mice compared with group control . Purpose This research is to find out influence extract ethanol leaf stalk leaf palm to lipid profile of mice as well as to evaluate difference effect based on the dose given .

2. Preliminaries or Related Work or Literature Review

2.1. Subsection 1

Research conducted by Gazali & Nufus (2019) entitled " SCREENING PHYTOCHEMISTRY OF FRESH NYPA LEAVES fruticans "Wurmb ORIGIN OF THE WEST ACEH COAST " aims to identify content phytochemicals on leaf fresh Nypa fruticans Wurmb who came from from West Aceh coast . This research is very relevant Because give description about potential leaf palm as source material standard biopharmaceuticals . Results study Gazali & Nufus (2019) showed that that leaf Nipah (N. fruticans) contains various compound beneficial phytochemicals , including phenolics , flavonoids, saponins, tannins , and triterpenoids.

Compounds the known own various activity biological that can utilized in development herbal medicines . Phenolic known Because characteristic its powerful antioxidants , flavonoids have various activity biological like anti-inflammatory and anticancer , saponins are known Because characteristic hemolytic and its ability to form foam , tannin own characteristic astringent that can helps in healing wounds , and triterpenoids have various activity biological like anti-inflammatory and anticancer . Findings Gazali & Nufus (2019) indicated that leaf nipah (N. fruticans) has promising prospects in providing material standard biopharmaceuticals . With content compound diverse and beneficial phytochemicals , leaves palm potential to be developed more carry on as source material active in industry pharmacy and health . Research more carry on required to confirm effectiveness and safety use leaf nipah in clinical applications .

2.2 Subsection 2

Research conducted by Khotimah Khusnul A (2016) entitled " The Influence of Giving Faction n-Hexane , Ethyl Acetate and Water From Extract Leaf Soursop (Annona muricata L)" aims to find out influence giving faction from extract leaf soursop to decline level sugar blood . Results study show that group extract leaf soursop faction n-hexane , fraction ethyl acetate , and water fractions have an effect significant to decline level sugar comparable blood with control positive . Fraction n-hexane , which is known Because characteristic its lipophilicity , indicating effect significant in reducing level sugar blood , shows existence compound active that can interact with metabolism glucose . Fraction ethyl acetate , which is capable of extract semi-polar compounds , also have an effect significant to decline level sugar blood . While that , the water fraction , which is known Because his ability extract polar compounds , showing effect significant in reducing level sugar blood .

These findings indicate that leaf soursop (Annona muricata L) has content compound diverse and useful activities , so that potential to be developed more carry on as source material standard biopharmaceuticals in the treatment of diabetes. Research more carry on required to confirm effectiveness and safety use leaf soursop in clinical applications ..

2.3 Subsection 3

Research conducted by Hikmah & Khaerati (2016) entitled " The Influence of Giving Extract Bay Leaf (Syzygium polyanthum Wight) against Glibenclamide in Lowering Level Glucose Blood Mice (Mus musculus) which is Induced Aloxan " aims to find out influence giving extract leaf regards to glibenclamide in reducing level glucose blood . Results study show that giving extract leaf regards influential in a way significant to glibenclamide in reducing level glucose blood , with effective dose is combination dose glibenclamide 0.65 mg/kg BW and extract leaf greeting 250 mg/kg BW. This finding indicates that leaf greetings (Syzygium polyanthum Wight) has content compound active that can Work synergistic with glibenclamide to reduce level glucose blood .

Leaf regards known Because content compound active such as flavonoids, tannins , and polyphenols which have various activity biological , including antidiabetic . These compounds can help increase insulin sensitivity and reduce absorption glucose in the intestine . Glibenclamide , as drug antidiabetic , works with stimulate pancreas to produce more lots of insulin. Findings that combination dose glibenclamide 0.65 mg/kg BW and extract leaf greeting 250 mg/kg BW is the most effective show existence synergy between second This material , which can give effect decline level glucose more blood significant compared to with use each material in a way separated .

These findings indicate that leaf greetings (Syzygium polyanthum Wight) has promising prospects in providing material standard biopharmaceuticals for the treatment of diabetes. With content compound diverse and useful active , leaves regards potential to be developed more carry on as source material active in industry pharmacy and health . Research more carry on required to confirm effectiveness and safety use leaf greetings in clinical applications , as well as to explore mechanism Work synergistic between extract leaf greetings and glibenclamide .

3. Proposed Method

This research is a study experimental which aims to study influence giving extract ethanol from leaf stalk nipah (Nypa fruticans Wurmb) on diabetes. This research was conducted in the Laboratory Biology Ahmad Dahlan University Yogyakarta and Laboratory Pharmacology Duta University Study between July and November 2024. Variables free in this study is dose extract ethanol from leaf stalk nipah , while variable bound covers change total cholesterol , LDL, HDL, and triglyceride levels in diabetic mice. To minimize influence from other variables , variables controlled in this study include condition measurement , laboratory environment , and characteristics physique from test animals such as heavy body , age, type gender , and strain of mice.

The tools used in this study include : scales analytical (Ohaus PR224), vessel maceration , rotary evaporator, water bath, and Glucose Monitoring System type AGM-4000 from Germany . Besides that , the materials used in this study consist of from powder leaf stalk nipah , ethanol 96%, male white rat line Wistar , paper filter Whatman , aquadest , Carboxy Methyl Cellulose (Na-CMC), glibenclamide , and glucose . Samples leaf stalk palm taken from beach Jatimalang , Regency Purworejo , Central Java , and carried out sorting wet to separate a decent part use from what is not .

After taking sample , leaf stalk palm washed use running water to remove dirt and objects foreign . Drying process done with oven on temperature of 50 degrees Celsius for not enough more two days to reduce water content in the material , so can hinder growth microbes and other chemical reactions . After drying , leaf stalks nipah which has dry Then blended until become powder , and powder the filtered use mesh 40 to get uniform size .

Screening phytochemicals carried out to identify compound active in extract leaf stalk nipah . Testing performed for flavonoids, alkaloids, phenolics , steroids, triterpenoids, and saponins. For example , flavonoid testing is performed by tube method and thin layer chromatography (TLC), where there is sediment chocolate show the presence of flavonoids. The test animals used in this study were 24 Wistar rats . with heavy body between 180-250 grams. The mice were weighed and given sign , then shared become six each group consists of from four rat tail .

The mice used in this study were induced with alloxan to create diabetes condition . Induction done with dose of 125 mg/kgBW, and after 96 hours, the level glucose blood measured to ensure that the mouse fulfil diabetes criteria with level glucose more of 200

mg/dL. In vivo testing was performed with give dose extract ethanol to diabetic and normal mice, where measurements level glucose blood done on the 3rd day until 21st after treatment .

Data analysis was performed using descriptive methods and devices SPSS software edition 23rd . Normality and homogeneity test done to ensure Data validity . The one-way ANOVA method is used to test homogeneous and normal data , with the expected significant value . not enough from 0.05. Results study expected can give better understanding Good about effect extract ethanol leaf stalk palm against diabetes, as well as his contribution to the development therapy alternative for this disease .

Research process started with taking sample leaf stalk nipah done on the beach Jatimalang , Regency Purworejo , Central Java . After taking , stem palm dissorted wet to separate a decent part use from those that don't , and then washed using running water . After that , the stem palm dried in the oven at temperature of 50 degrees Celsius for two days to reduce water content . The next process is milling leaf stalk nipah which has dry become powder , which is then filtered to get uniform size .

Screening phytochemicals carried out to identify compound active in the extract , including flavonoid, alkaloid, phenolic , steroid, triterpenoid, and saponin testing . Flavonoid testing was carried out with the tube and TLC methods , while alkaloid testing using Mayer and Dragendorff reactions . Test animals used are 24 Wistar rats induced with diabetes with alloxan , and levels glucose blood measured to ensure that the mice fulfill diabetes criteria .

After induction , mice were given solution 5% sugar after 8-9 hours of induction , and on the following day , the mice were given eat and drink ad libitum. The level of glucose blood measured on the 3rd day until 7th to make sure that the mouse have diabetes. Measurement done Again on days 7 , 14, and 21 after day 0 to evaluate effect from the treatment given .

4. Results and Discussion

Phytochemical screening is a preliminary stage that can provide an overview of the content of certain compounds in natural materials that will be researched. This method can be used to identify the content of secondary metabolite compounds in these natural materials. Phytochemical screening is carried out using the tube method (color complex) and thin layer chromatography (TLC) to identify the chemical compounds contained therein. Based on the results of the study, it contains secondary metabolites such as alkaloids, flavonoids, phenolics or tannics, and steroids or triterpenoids. The phytochemical results of the Nipah Leaf Stem extract (*Nypa fruticans Wurmb*) using the tube test method (reagent) can be seen in table 4.10.

Table 1. Results of Phytochemical Tests of Ethanol Extract of Nipah Leaf Stems (*Nypa fruticans. Wurmb*)

Compound	Reagent	Positive Signs	Results	Kt
Alkaloid	Mayer	Presence of white/yellow sediment (Aziza *et al.,* 2022)	The presence of a thin white sediment	+
	Dragendoff	The presence of red brown sediment (Aziza *et al.,* 2022)	The presence of a thin reddish brown sediment	+
	Bouchardat	The presence of red brown sediment (Aziza *et al.,* 2022)	Presence of reddish brown sediment	+
	Flavonoid	Mg powder + concentrated HCl (Aziza *et al.,* 2022)	Color changes to red, purple red or orange	

Phe-nolic/Tannin		FeCl3 5% (Aziza *et al.,* 2022)	Formed blue or blue black color	+
Steroid		Chloroform + anhydrous acetic acid + concentrated sulfuric acid (Aziza *et al.,* 2022)	There are brownish or violet rings	+
Triterpenoid		Chloroform + anhydrous acetic acid + concentrated sulfuric acid (Aziza *et al.* , 2022)	A bluish green color is formed	+
Saponins	Aquadest	Stable foam is formed (3 cm foam for 30 minutes) (Aziza *et al.,* 2022)	No foam formed	-

Using the test tube method, the results showed that the phytochemical compounds contained in Nipah fronds (*Nypa fruticans Wurmb*) include alkaloids, flavonoids, phenolics/tannins, and steroids/triterpenoids. The phytochemical compound content of Nipah fronds is the same as the study conducted by (L. Wijayanti *et al.,* 2022) which stated that the phytochemical compound content of Nipah leaves *(Nypa fruticans Wurmb)* includes alkaloids, flavonoids, phenolics/tannins and steroids/triterpenoids.

The alkaloid compound test of the ethanol extract of Nipah fronds (*Nypa fruticans Wurmb*) was carried out using Mayer and Dragendorff reagents. The results of the alkaloid test showed a reaction of the formation of a thin layer of white and brownish red deposits, indicating that nipah fronds may have antioxidant content. The alkaloid test also showed a reaction of the formation of a thin layer of deposits, indicating that nipah leaves may have antioxidant content. Depending on the age of the leaves, the plant produces various metabolites and bioactive compounds (L. Wijayanti *et al.,* 2022)

Test of flavonoid compounds of ethanol extract of Nipah leaves (*Nypa fruticans Wurmb*), the test sample was added with mg powder and concentrated HCl solution. The aim is to reduce the glycoside bond with flavonoids by adding hydrochloric acid and magnesium powder. The presence of a color change to reddish brown indicates that flavonoids have a positive effect. Flavonoids are widely found in plants as pigments. Their medicinal functions include preventing enzyme and non-enzyme oxidation reactions. In addition, flavonoids function as hydroxyl radical sinks (L. Wijayanti *et al.,* 2022)

Positive tannin compound test contains white sediment, the sediment is due to tannin and protein forming hydrogen bonds in gelatin. Tannin compounds can react with proteins to form co-polymers that are insoluble in water. Tannins in plants will make the flow of water passing through them have a bitter and astringent taste. Tannins also have antibacterial and antioxidant properties (L. Wijayanti *et al.,* 2022)

Test of steroid and triterpenoid compounds in ethanol extract of Nipah leaves *(Nypa fruticans* Wurmb *)* using *Liberman-Burchard reagent* (a mixture of sulfuric acid and acetic anhydride). Triterpenoid compounds will experience dehydration during the formation of strong acid H2SO4 and also acetic anhydride acid which causes the formation of rings on the two solvent

boundaries. Positive steroid results indicate the formation of a purplish violet ring and positive triterpenoids form a greenish red color.

Test of saponin compounds from ethanol extract of Nipah leaves *(Nypa fruticans Wurmb)* using heated distilled water. The results of this test showed negative results because no foam was formed for 30 minutes and as high as 3 cm above the surface of the liquid (Aziza *et al.,* 2022) .

A. Acute Antidiabetic Testing

Influence testing extract administration ethanol of nipah fronds using 30 rats. The rats used were male wistar strain rats with weight. The rats were divided into 5 groups, namely negative control Na-Cmc 0.5% positive control glibenclamide 0.45 kg / bw, dose group 1 is 250mg kg / bw, dose 2 125mg kg / bw and dose 3 is 500mg kg / bw. The rats were adapted for 7 days in the Laboratory and fasted for 15 hours then fasting blood glucose levels were measured and found out day 0. before treatment while still being given water. The purpose of fasting the rats before treatment is to normalize metabolism in the body of the test animals and to reduce food interaction factors and accelerate gastric emptying time.

The chemical compound that causes diabetes in mice is alloxan. Glucose levels from day 3 to day 7, glucose levels are measured. Checking the blood sugar levels of mice is done by cutting the tip of the mouse using *a cutter* . The tools used to check the blood sugar levels of mice are *check strips* (*Accu-chek ® instant S*) and glucometers (*Accu-chek ® instant S*). If there is an increase in glucose levels to 200 mg / dL, the mouse is considered diabetic.

Table 2. 1of Fasting Blood Sugar Reduction Test

Group	Blood Sugar Decrease (%)
Normal	-0.38 ± 2.85 [b]
Negative Control (CMC Na 1%)	-11.85 ± 4.60 [a]
Positive Control (Glibenclamide 0.45 mg/khBW)	62.39 ± 1.69 [c]
Extract 125mg/kgBW	53.49 ± 4.87 [c]
Extract 250 mg/kgBW	61.04 ± 2.38 [c]
Extract 500 mg/kgBW	61.71 ± 1.75 [c]

Note: Different letters indicate differences in Duncan's Test subsets (p >0.05)

The data tested with Duncan's Test obtained 3 subsets, with the relationship between subsets being significant (p = <0.05) so that subset 1 (negative group) was significant to subset 2 (normal group), also significant to subset 3 (positive group, 125 mg/kgBW extract group, 250 mg/kgBW extract group, and 500 mg/kgBW extract group). Likewise, subset 2 was also significant to subset 3. It is known that the administration of extract (subset 3) affects the percentage of blood sugar level reduction compared to the normal group (subset 2) and the negative group (subset 1). This is in accordance with study previously (Nasution *et al.,* 2024) . show effect giving extract ethanol bone leaf palm show decline level sugar blood on mice .

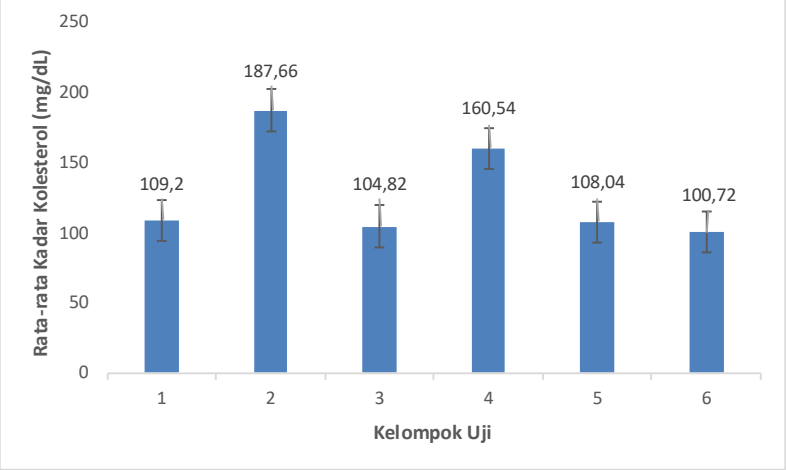

Figure 1. Average cholesterol levels

Based on the graphic image, it can be seen that on normal group , levels cholesterol has a value of 109.920 mg/dL, while on group control negative given Na-CMC 0.5% , levels cholesterol increase in a way significant to 187.660 mg/dL. Group control positive given glibenclamide (0.45 mg/kgBW) showed level higher cholesterol low , namely 104.820 mg/dL. This indicates that glibenclamide own effect decline cholesterol , which is in line with study (Monika & Lestariyana, 2014) who reported that giving combination quercetin and glibenclamide can lower level higher LDL cholesterol Good .

Dose 1 (125 mg/kgBW) shows level cholesterol of 160.540 mg/dL, which is still more tall compared to normal and control groups positive . However , dose 2 (250 mg/kgBW) showed level higher cholesterol low , namely 108.040 mg/dL, which is close to level cholesterol normal group . Effects the most significant decline seen on dose 3 (500 mg/kgBW), with level cholesterol reached 100.720 mg/dL. This result shows that extract ethanol leaf stalk leaf palm own potential as agent hypocholesterolemic , according to with (WF Sari & Suwondo, 2022) , which states that antioxidant compounds such as flavonoids, saponins, and tannins have been proven to have hypolipidemic effects that can lower cholesterol levels.

Cholesterol data was then analyzed using Spps 22 with a 95% confidence level. This normality test can be known using *Shapiro Wilk,* used on samples of less than 50. After obtaining normally distributed normality, the homogeneity test is continued to determine whether the data is homogeneous or not using the *Levene Statistic test* (Setyawan Dodiet Aditya, 2021) .

The normality test can be known to be normally distributed if the significance is > 0.05. In 6 treatment groups, the significance value is more than 0.05. The significance value of each group is respectively 0.904, 0.540, 0.696, 0.540, 0.397, 0.460, it can be concluded that all data are normally distributed. In the *Levene Statistic homogeneity test* , the result is 0.155, meaning > 0.05, it can be concluded that the data is homogeneous.

The spps test using *one way anova,* a type of parametric statistical test, aims to determine whether there is a difference in the average between two or more groups. After the *one-way anova test* , Tukey can be continued. The results of the one-way anova test show a significance value of 0.000, meaning <0.05, it is concluded that there is a difference in the six treatments that have been given.

The data was then continued with the Tukey test which aims to determine whether there is a significant difference between each treatment group. It is said that there is a significant difference between treatments if the sig value <0.05

Administration of dose 1 significantly increased cholesterol levels compared to normal, positive control and dose 3. Dose 2 did not show any significant difference with normal, Dose 3 also showed a significant decrease in cholesterol levels compared to dose 1 and negative control.

Table 3. 2Cholesterol Test Results

Test Group	Average Cholesterol	$\bar{x} \pm$ SEM
Normal	37.68	37.68 ± 3.754 [a]
Negative	84.76	84.76 ± 5.448 [c]
Positive Gliben	44.72	44.72 ± 3.114 [a]
Dosage 250 mg/kgbb	81.60	81.60 ± 2.903 [b]
Dosage 500 mg/kgbb	31.56	31.56 ± 4.772 [a]
Dosage 1000 mg/kgbb	30.00	30.00 ± 5.050 [a]

The results of the Duncan Test showed that the normal group with negative control and the positive control group with a dose of 125 mg/kgBW showed significant differences.

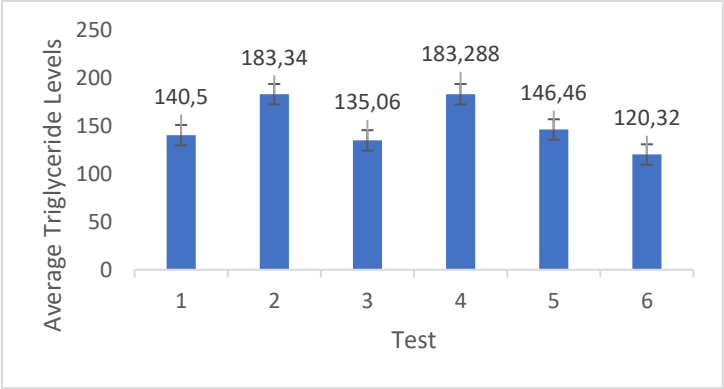

Figure 2. Average Triglyceride Levels

Based on Picture on show that giving extract ethanol leaf stalk palm influential to level triglycerides of male diabetic rats line Wistar . On normal group , levels triglycerides produced of 140.5 mg/dL, while on group control negative given Na-CMC 0.5 % content triglycerides increase to 205.34 mg/dL. This increase indicates that diabetes condition that is not get intervention can cause disturbance lipid metabolism . These results are in line with study previously mentioned that diabetes mellitus closely related to improvement level triglycerides consequence disturbance metabolism fat (Khadke et al., 2020).

Group control positive given glibenclamide (0.45 mg/kgBW) showed level higher triglycerides low , namely 135.06 mg/dL. This indicates that glibenclamide capable lower level triglycerides .

On group a dose of 125 mg/kgBW has level triglycerides of 183.288 mg/dL, which is still more tall compared to normal and control groups positive . A dose of 250 mg/kgBW shows level higher triglycerides low , namely 146.6 mg/dL.

Giving dose highest namely 500 mg/kgBW, indicating the most significant effect in reducing level triglycerides up to 120.32 mg/dL, even more low from group control positive . This shows that extract palm own potential can lower level triglycerides .

Besides that , the presence of saponins in the extract leaf nipah , which binds fat in the intestinal lumen , forming compound complex that is not dissolved which is not can absorbed by the mucosa intestines . Seaponin can also increase production and secretion of bile and also facilitates fat metabolism so that it can reduce blood triglyceride levels (Putri *et al.,* 2017)

Cholesterol data was then analyzed using Spps 22 with a 95% confidence level. This normality test can be known using *Shapiro Wilk,* used on samples of less than 50. After obtaining normally distributed normality, the homogeneity test is continued to determine whether the data is homogeneous or not using the *Levene Statistic test* (Setyawan Dodiet Aditya, 2021) .

The normality test can be known to be normally distributed if the significance is > 0.05. In 6 treatment groups, the significance value is more than 0.05. The significance value of each group is respectively 0.663, 0.800, 0.279, 0.699, 0.076, 0.797, it can be concluded that all data is normally distributed. In the *Levene Statistic* homogeneity test , the result is 0.625, meaning > 0.05, it can be assumed that the data is homogeneous.

The spps test using *one way anova,* a type of parametric statistical test, aims to determine whether there is a difference in the average between two or more groups. After the *one-way anova test* , the Post Hoc Test can be continued using Tukey. The results of the one-way anova test show a significance value of 0.000, meaning <0.05, it is concluded that there is a difference in the six treatments that have been given.

The data was then continued with the Tukey test which aims to determine whether there is a significant difference between each treatment group. It is said that there is a significant difference between treatments if the sig value <0.05

In the negative control group with dose 3 there was a significant difference compared to normal, positive control and dose 1. Dose 1 did not show a significant difference with normal, Dose 3 also showed a significant difference with the negative control.

Table 4. 3Triglyceride Test Results

Test Group	Average Triglycerides	$\bar{x} \pm$ SEM
Normal	140.50	140.50 ± 10.076 [a]
Negative Control	223.34	223.34 ± 7.801 [b]
Positive Control	135.06	135.06 ± 10.326 [a]
Dosage 125mg/kgbb	162.49	162.49 ± 4.833 [b]
Dosage 250 mg/kgbb	146.60	146.60 ± 9.838 [a]
Dosage 500 mg/kgbb	120.32	120.32 ± 14.474 [a]

The results of the Duncan Test showed that the normal group with negative control and the positive control group with a dose of 125 mg/kgBW showed significant differences.

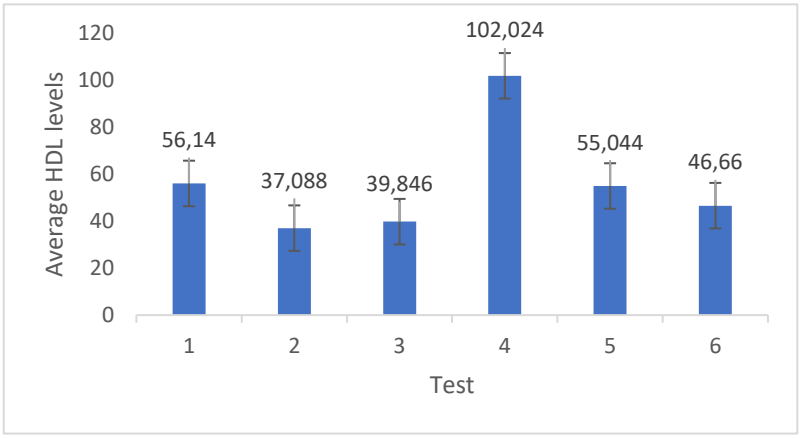

Figure 3. 1HDL levels

Based on the image above shows the results of the analysis of HDL levels in male diabetic rats of the Wistar strain. The data shows significant variations in HDL levels in various treatment groups. In the normal group, HDL levels produced a value of 56.14 mg/dL which indicates a healthy and normal HDL level value according to the standards for Wistar rats.

The negative control group given 0.5% Na-CMC showed HDL levels of 37.088 mg/dL. This decrease in HDL levels is commonly found in type 2 diabetes. A study by (Access & Pathophysiology, 2020) showed that HDL levels in type 2 diabetic rats decreased significantly compared to healthy controls, which illustrates a negative effect on lipid profiles. The positive control group given glibenclamide at a dose of 0.45 mg/kgBW showed an increase in HDL levels to 39.846 mg/dL.

Glibenclamide is drug antidiabetic used to reduce level sugar blood in type 2 diabetes (Mayasari, 2024) . Glibenclamide can control level sugar blood , increase HDL levels in group control positive No significant compared to with normal group . Research by (Access & Pathophysiology, 2020) , shows combination with glibenclamide and sertraline increase control serum glucose and increased HDL.

On group dose of 125 mg/kgBW, occurred improvement significant in HDL levels , namely reached 102.024 mg/dL. This result shows that extract ethanol leaf stalk palm potential more effective in improving HDL levels compared with group control and normal. This effect could be caused by the content bioactive in extract those that can influence lipid metabolism in a different way from treatment conventional like glibenclamide .

Group with dose extract 250 mg/kgBW showed HDL levels of 55.044 mg/dL which is higher tall from group control , but more low than group dose of 125 mg/kgBW. Although more low compared to with dose of 125 mg/kgBW, HDL levels in This group shows effect quite an improvement significant compared to with group control . This shows that higher dose tall from This extract is still give effect in increasing HDL levels , although No as effective as possible dose previously . Research (Isdadiyanto et al., 2024) about extract ethanol seed mahogany show improvement HDL levels in induced mice with a high diet fat , although highest HDL levels recorded on dose 200 mg/kgBW. Group with dose extract 500 mg/kgBW showed low HDL levels more low compared to with dose of 125 mg/kgBW, which is 46.66 mg/dL. Although dose This extract is more high , the impact to HDL levels apparently more low . Research (Adhitama et al., 2023) , shows that on dose extract more kedondong tall of 450 mg/kgBW, occurs decline level significant total cholesterol due to side effects or metabolic imbalances produced by higher doses.

The normality test can be known to be normally distributed if the significance is > 0.05. In 6 treatment groups, the significance value is more than 0.05. The significance value of each group, respectively, is 0.187, 0.418, 0.386, 0.582, 0.163, 0.319. It can be concluded that all data is normally distributed. In the *Levene Statistic homogeneity test* , the result is 0.301, meaning > 0.05, it can be concluded that the data is homogeneous.

The spps test using *one way anova,* a type of parametric statistical test, aims to determine whether there is a difference in the average between two or more groups. After the *one-way anova test* , the Post Hoc Test can be continued using Tukey. The results of the one-way anova test show a significance value of 0.000, meaning <0.05, it is concluded that there is a difference in the six treatments that have been given.

The data was then continued with the Tukey test which aims to determine whether there is a significant difference between each treatment group. It is said that there is a significant difference between treatments if the sig value <0.05.

Administration of dose 1 showed significant HDL levels compared to normal, negative control, positive control dose 2 and dose 3. Dose 2 did not show any significant difference with normal, Dose 3 also showed a significant difference with dose 1 .

Table 5. 4HDL Test Results

Test Group	Average Hdl	$\bar{x} \pm$ SEM
Normal	56.14	56.14 ± 1.728 [b]
Negative Control	37.09	37.09 ± 3.583 [a]
Positive Control	39.85	39.85 ± 4.439 [a]
Dosage 125mg/kgbb	102.02	102.02 ± 3.530 [c]
Dosage 250 mg/kgbb	55.04	55.04 ± 4.921 [b]
Dosage 500 mg/kgbb	46.66	46.66 ± 3.494 [a]

Duncan's test results show that all groups show significant differences.

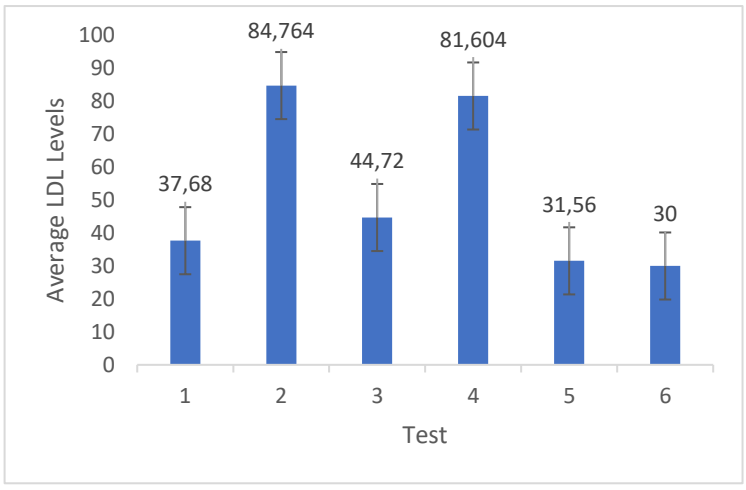

Figure 4. 2HDL levels

Based on the table above, the Normal group showed an average LDL level of 37.68 mg/dL, which is the reference value for LDL levels under normal conditions. This LDL level is an important indicator for assessing the risk of cardiovascular disease, where the higher the LDL level, the greater the potential for plaque buildup on the walls of blood

vessels which can cause atherosclerosis (Borén *et al.,* 2020) . In the test conducted, the Negative control (Na-CMC 0.5%) had an average LDL level of 84.764 mg/dL . The increase in LDL levels in this group shows that Na-CMC does not have an LDL-lowering effect, and even tends to increase LDL levels, which has the potential to increase the risk of atherosclerosis and cardiovascular disease. Positive Control (Glibenclamide 0.45 mg/kgBW) had an average LDL level of 44.72 mg/dL . Glibenclamide shows an LDL-lowering effect that is close to normal values, so it can be used as a comparison for the effectiveness of the extract. This is in accordance with research by (Shinde *et al.* , nd) , which showed a non-significant decrease in LDL was observed with Glibenclamide therapy . The 125 mg/kgBW extract had an average LDL level of 81.604 mg/dL . At this dose, the extract did not show a significant LDL lowering effect. Although LDL levels decreased slightly compared to the negative control, this decrease was not significant enough to indicate that the extract at this dose could effectively lower LDL levels. The 250 mg/kgBW extract had an average LDL level of 31.56 mg/dL . At this dose, the extract showed a significant decrease in LDL, even lower than the normal group and the positive control . The significant decrease in LDL at this dose indicates that the extract has the potential to reduce LDL levels in a more effective manner. This LDL lowering effect was also better compared to the positive control given Glibenclamide. (Singh & Cho, 2024) , indicating that non-statin LDL lowering therapy can provide a significant lowering effect. This supports the results that new LDL-lowering agents such as Nipah leaf stem extract have a greater impact in lowering LDL levels when compared to positive controls. Extract 500 mg/kgBW Average LDL levels were 30 mg/dL . At this dose, the extract showed the most effective LDL reduction, lower than the normal group and positive control. Extract ethanol acetate of nipah fronds at doses of 250 mg/kgBW and 500 mg/kgBW showed a significant LDL lowering effect. at a dose of 500 mg/kgBW , LDL levels were lower than the normal group and positive control. This indicates that the extract has the potential as an effective LDL lowering agent. research by Rahman et al (2017), reported that the extract of Nypa *fruticans* can reduce LDL levels by 20-30% in diabetic rats.

The normality test can be known to be normally distributed if the significance is > 0.05. In 6 treatment groups, the significance value is more than 0.05. The significance value of each group, respectively, is 0.152, 0.715, 0.185, 0.700, 0.145, 0.415. It can be concluded that all data are normally distributed. In the Levene Statistic homogeneity test, the result is 0.739, meaning > 0.05, it can be assumed that the data is homogeneous.

The spps test using one way anova, a type of parametric statistical test, aims to determine whether there is a difference in the average between two or more groups. After the one-way anova test, the Post Hoc Test can be continued using LSD. The results of the one-way anova test show a significance value of 0.000, meaning <0.05, it is concluded that there is a difference in the six treatments that have been given.

The data was then continued with the Tukey test which aims to determine whether there is a significant difference between each treatment group. It is said that there is a significant difference between treatments if the sig value <0.05.

The results of the Tukey HSD test analysis showed that there was a significant difference in LDL levels between the normal and control groups. The group of diabetic

rats given ethanol extract of Nipah leaf stalks at doses 1, 2, and 3 showed significant changes in LDL levels.

Table 6. 5LDL Test Results

Test Group	Average LDL	$\bar{x} \pm$ SEM
Normal	37.68	37.68 ± 3.754 [a]
Negative Control	84.76	84.76 ± 3.114 [c]
Positive Control	44.72	44.72 ± 3.114 [b]
Extract 125mg/kgbb	81.60	81.60 ± 2.903 [c]
Extract 250 mg/kgbb	31.56	31.56 ± 4.772 [a]
Extract 500 mg/kgbb	30.00	30.00 ± 5.050 [a]

The results of the Duncan Test showed that the normal group with negative control and the positive control group with a dose of 125 mg/kgBW showed significant differences.

5. Comparison

Table 7. Research Results of Nipah Leaf Stem Ethanol Extract on Lipid Profile

Parameter	Dosage (mg/kgBW)	Results (mg/dL)	Comparison with other groups	Supporting Journals
Cholesterol	500	100.72 mg/dL	More effective vs. glibenclamide (104.82 mg/dL)	(Monika & Lestariyana, 2014)
Triglycerides	500	120.32 mg/dL	Lower vs. positive control (135.06 mg/dL); negative control 205.34 mg/dL	(Putri et al., 2017)
HDL	125	102.02 mg/dL	Exceeding the normal group (56.14 mg/dL); decreased HDL at a dose of 500 mg/kgBW	(Isdadiyanto et al., 2024)
LDL	250	31.56 mg/dL	Lower vs. normal group (37.68 mg/dL); 500 mg/kgBW dose lowered LDL to 30.00 mg/dL	(Borén et al., 2020)
LDL	250	30.00 mg/dL	20-30% reduction effect according to previous studies; supports low cardiovascular risk	(Borén et al., 2020)

6 . Conclusions

Extract ethanol leaf stalk nipah (Nypa fruticans Wurmb) shows significant effect in reducing level total cholesterol , triglycerides , and LDL as well increase HDL levels in male diabetic rats line Wistar , with doses of 250 mg/kgBW and 500 mg/kgBW which are higher effective . For development more further , required study about isolation compound active nutritious flavonoids as reducer level sugar blood and testing using combination other herbal plants that have properties as antidiabetic to achieve more effects tall.

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