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# Application of zanthoxylum acanthopodium fruit extract in reducing dyslipidemia in male wistar rats undergoing high-fat diet and propylthiouracil (Ptu) treatment

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**Abstract**
Dyslipidemia is a lipid metabolism disorder caused by the interaction of genetic and environmental factors, leading to the formation of atherogenic lipids and an increased risk of premature cardiovascular disease. This study aims to explore the effectiveness of antidyslipidemia from the extract of Andaliman fruit. Using male Wistar rats as experimental animals in a study with a Pre-test and Post-test group-only control design approach, phytochemical screening results indicated that the methanol extract of Andaliman fruit contains various phytochemical compounds, including Alkaloids, Saponins, Flavonoids, Tannins, Steroids, and Terpenoids. This research concludes that the methanol extract of Andaliman fruit significantly reduces total cholesterol, triglycerides, and LDL levels while increasing HDL levels in experimental rats. Additionally, the decrease in SGOT levels indicates a positive effect on liver health and the potential to reduce the risk of Non-Alcoholic Fatty Liver Disease (NAFLD). Although these findings are promising, further confirmation through human studies is necessary before considering Andaliman fruit methanol extract as an effective therapy or treatment. With observed improvements in lipid profiles and liver health, the methanol extract of Andaliman fruit offers potential as an active ingredient source for developing antidyslipidemia therapy.

**Keywords:** Dyslipidemia, andaliman fruit extract, wistar rats, antidyslipidemia, lipid metabolism

## Introduction

According to the World Health Organization (WHO) data in 2008, the prevalence of dyslipidemia varies across regions, with 30.3% in Southeast Asia, 36.7% in the Western Pacific, 53.7% in Europe, and 47.7% in the Americas (Lin *et al*., 2018) [15]. Additionally, the American Heart Association reported that 31.9 million people (13.8%) in the United States have cholesterol levels ≥ 240 mg/dl (Go *et al*., 2014) [12]. Dyslipidemia is defined as a lipid metabolism disorder marked by alterations in lipid fractions in the plasma. It results from disruptions in lipid metabolism due to the interaction of genetic and environmental factors. Some mixed dyslipidemia types associated with atherogenic lipid formation can lead to premature cardiovascular diseases, including increased VLDL cholesterol manifested by elevated TG and LDL and reduced HDL cholesterol (Erwinanto *et al*., 2013; Arsana *et al*., 2015) [9, 5].

Various anti-dyslipidemia drugs are available in the market to manage dyslipidemia, including statins, fibrates, niacin, ezetimibe, and bile acid sequestrants (Purva, Sharma, and Khan, 2020) [18]. However, some 'super statins' have reported unwanted side effects (myopathy), and fibrates, primarily used for treating hypertriglyceridemia and low HDL cholesterol, require high doses to show significant efficacy (Saragih, 2020) [19]. Therefore, alternative treatments with potentially fewer side effects are needed. In Indonesia, dyslipidemia prevalence was reported by the Ministry of Health in the National Basic Health Research (RISKESDAS). Data from the 2013 National Basic Health Research show that 35.9% of Indonesians aged ≥ 15 years have abnormal cholesterol levels (≥ 200 mg/dl), with more women than men and more urban than rural residents affected. RISKEDAS data also reveals that 15.9% of the population aged ≥ 15 years has very high LDL proportions (≥ 190 mg/dl), 22.9% have HDL levels below 40 mg/dl, and 11.9% have very high triglyceride levels (≥ 500 mg/dl) (National Institute of Health Research and Development Ministry of Health RI, 2013).

Several anti-dyslipidemia drugs are available to manage dyslipidemia, including statins, fibrates, niacin, ezetimibe, and bile acid sequestrants (Purva, Sharma, and Khan, 2020) [18]. However, some 'super statins' have reported unwanted side effects (myopathy), and fibrates, primarily used for treating hypertriglyceridemia and low HDL cholesterol, require high doses to show significant efficacy (Saragih, 2020) [19]. Therefore, alternative treatments with potentially fewer side effects are needed. Herbal medicines have been used traditionally for decades and seem to have lower side effects. Based on existing studies, herbal medicines have been reported as effective in treating dyslipidemia and preventing cardiovascular diseases (Anneke and Sulistiyaningsih, 2018) [4]. With its tropical climate, Indonesia is the second-largest country in the world after Brazil, rich in biodiversity. Approximately 30,000 plant species are found in Indonesia, including around 2,500 medicinal plants (Dalimartha and Adrian, 2013) [8]. One of these is the Andaliman plant, a fruit widely utilized by the Batak community. Andaliman fruit contains various phytochemicals such as phenols, saponins, flavonoids, triterpenoids, and alkaloids (Saragih and Arsita, 2019) [20]. Thus, Andaliman fruit possesses multiple pharmacological effects, including anti-inflammatory, antioxidant, antidiabetic, and antibacterial properties (Yanti *et al*., 2011; Worotikan, Tuju, and Kawuwung, 2017; Winarti, Simanjuntak, and Syahidin, 2018; Sitanggang, Duniaji, and Pratiwi, 2019) [31, 30, 29, 21].

Given the background information, it is evident that Andaliman fruit contains diverse phytochemicals and health benefits. However, there is no research exploring the anti-dyslipidemia benefits of Andaliman fruit. Therefore, the

researchers are interested in studying the anti-dyslipidemia effectiveness of Andaliman fruit extract.

**Research Methods**

This experimental study adopts the Pre-test and Post-test group-only control design approach, utilizing male Wistar rats as research subjects. The research was conducted in January 2024. The calculation of the sample size was performed using the Federer formula with the requirement of

$(r-1)(t-1) \geq 15$,

where 'r' represents the number of samples in each treatment group, and 't' is the number of treatment groups.

$(r-1)(6-1) \geq 15$

$5(r-1) \geq 15$

$r-1 \geq 15/5$

$r \geq 3+1$

$r \geq 4$

Based on the calculation results, it can be concluded that a minimum of 4 male Wistar rats (Rattus norvegicus) with a weight ranging from 180 to 200 grams and an age between 2-4 months is required for each treatment group.

**Equipment**

Surgical instruments, laboratory glassware, aluminum foil, blender (Miyako), porcelain dish, desiccator, incubator, glass slides, cover glass, porcelain crucible, drying cabinet, microtubes, light microscope, analytical balance (Vibra AJ), oral sonde, electric oven (Stork), water bath (Yenaco), tube clamps, reaction tube rack, rotary evaporator, centrifuge, set of water content determination tools, UV spectrophotometer (Microlet 3000), injection syringe, muffle furnace (Nabertherm), reaction tubes, animal scales (Presica).

**Materials**

The materials used in this research are andaliman fruit, methanol, Aquades (distilled water), Na-CMC (Sodium Carboxyl methylcellulose), simvastatin, rice husk, rat pellet food, phytochemical screening reagents, and ketamine.

**Sample Determination**

Andaliman fruit samples used in this study were obtained from one of the traditional markets in Medan City.

**Manufacture of Andaliman Fruit Simplisia**

Identified andaliman fruits were washed thoroughly with running water, drained, and spread on blotting paper until dry. The samples were then weighed and dried by air-drying, and the weight of the dried material was measured. The dried andaliman fruit material was ground into powder to form simplisia (Kosasih *et al*., 2019) [14].

**Preparation of Andaliman Fruit Methanol Extract**

Andaliman fruit weighing 200 grams each was extracted using the maceration technique with 400 ml of 98% methanol solvent. Maceration was carried out for one week with occasional stirring. The filtrate was then evaporated using a rotary vacuum evaporator at 50°C until a paste-like extract was obtained and stored at 20°C (Vasanthakumar D *et al*., 2015) [25].

**Phytochemical Screening**

Phytochemical screening in this study followed a modified Farnsworth method, including the identification of phenols, steroids/triterpenoids, terpenoids, saponins, flavonoids, tannins, and alkaloids (Widowati *et al*., 2016, 2017, 2018) [26-27-28].

**Anti-Dyslipidemia Effect Testing**

**Preparation of 0.5% Na CMC Suspension**

0.5 grams of Na CMC was scattered into a mortar containing 10 mL of hot distilled water. After 15 minutes, a transparent mass was obtained, ground to form a gel, diluted with a little filtered water, and poured into a 100 mL volumetric flask. Distilled water was added to the mark. This suspension would be used further as a dispersing medium for oral suspension (Colloid) (Mutia and Chiuman, 2019) [16].

**Preparation of Hypercholesterolemic Feed Suspension**

The suspension was made by mixing 300 grams of animal fat into 100 ml of distilled water and 200 grams of poultry egg yolk into 1 ml of 0.5% Na-CMC (Harsa, 2014) [13].

**Preparation of PTU Suspension**

100 mg of PTU was ground in a mortar to form a powder, then added to a 0.5% Na CMC suspension and put into a 10 ml volumetric flask. The volume was adjusted to the mark with 0.5% Na CMC suspension (Untari and Pramukantoro, 2020) [24].

**Andaliman Fruit Extract Suspension**

1.2 grams of andaliman fruit extract was added to a mortar, and Na CMC, 0.5% suspension, was gradually added while grinding until homogenous. This mixture was then poured into a 10 mL volumetric flask. The volume was adjusted with Na CMC 0.5% suspension to the mark (Mutia and Chiuman, 2019) [16].

**Simvastatin Suspension Preparation**

10 mg of simvastatin was ground in a mortar to form a powder, then added to a 0.5% Na CMC suspension and put into a 25 mL volumetric flask. The volume was adjusted to the mark with 0.5% Na CMC suspension (Fouad and Jresat, 2013; Aldahmash and El-Nagar, 2016).

**Induction of Dyslipidemia in Experimental Animals**

The induction process was performed by providing a high-fat diet and PTU to the experimental animals for 14 days. PTU was given as an oral suspension at 12.5 mg/day (1.25 ml/day) divided into two doses. Meanwhile, the high-fat diet was given by administering a high-fat feed suspension at a dose of 15 g/kgBW for animal fat suspension and 10 g/kgBW for poultry egg yolk suspension (Harsa, 2014; Untari and Pramukantoro, 2020) [13, 24].

**Testing on Experimental Animals**

The rodents were acclimatized to the laboratory environment a week before the intervention on all experimental animals. Subsequently, all Wistar rats were induced using propylthiouracil (PTU) and fed with a high-cholesterol diet, except for the standard group. After 14 days, test animals with a total cholesterol level ≥ 240 mg/dl were considered to have dyslipidemia. However, before measuring the total cholesterol levels, all rats were fasted for at least 8 hours. The test animals were divided into six groups of four experimental rats. The doses of methanol extract from Andaliman fruit and simvastatin as the standard

group was determined based on previous research findings (Olayinka *et al*., 2014; Batubara, Sabri, and Tanjung, 2017; Worotikan, Tuju, and Kawuwung, 2017; Abarikwu *et al*., 2020) [17, 7, 30, 1]. The treatments administered to each rat in these groups were as follows:

**Table 1:** Description of Treatment for Each Group

| No | Test Group | Treatment |
|---|---|---|
| 1. | Usual | Test animals were not given any particular treatment and were only given ad libitium food and drink. |
| 2. | Control | Test animals were given 1 ml of 0.5% Na CMC suspension daily for 14 days. Food and drink are provided ad libitum. |
| 3. | Standard | Test animals were given an oral suspension of simvastatin 10 ml/Kg Weight daily for 14 days. Food and drink are provided ad libitum. |
| 4. | (10 mg/Kg Weight) | Test animals were given methanol extract of andaliman fruit dose 2 ml/kg body weight once a day for 14 days. Food and drink are provided ad libitum. |
| 5. | Methanol Extract of Andaliman Fruit - I (200 mg / Kg Weight) | Test animals were given methanol extract of andaliman fruit dose 4 ml/kg body weight once a day for 14 days. Food and drink are provided ad libitum. |
| 6. | Andaliman Fruit Methanol Extract - II | Test animals were given methanol extract of andaliman fruit dose of 8 ml/kg body weight once a day for 14 days. Food and drink are provided ad libitum. |

**Measurement of Lipid Profile Parameters**

The rats were satisfied at least 8 hours before the blood draw. Blood collection is done by direct withdrawal from the heart of mice as much as 1 ml. Put into a microtube and let stand ± 20 minutes. Then, the blood was centrifuged at a rate of 3000 rpm for 15 minutes to obtain the blood serum of the rats. The determination of lipid profiles is determined by the colorimetric method. Lipid profile examination is conducted at the Health Laboratory, North Sumatra Provincial Health Office.

**Measurement of Biochemical Parameters of SGOT and SGPT**

Blood collection is done by direct withdrawal from the heart of mice as much as 1 ml. Put into a microtube and let stand ± 20 minutes. Then, the blood was centrifuged at a rate of 3000 rpm for 15 minutes to obtain the blood serum of the rats. The determination of SGOT and SGPT levels is based on enzymatic reactions using Dyasis® kit reagents. The procedure for determining SGOT and SGPT catalyst activity is based on work procedures from Dyasis®. SGOT and SGPT examinations are conducted at the Health Laboratory, North Sumatra Provincial Health Office.

**Analyzes Data**

The research data was then analyzed using the SPSS 25 program. The research data were analyzed descriptively (Central tendency and Dyspersi) from the data in lipid profiles (LDL, HDL, Total Cholesterol, and Triglycerides), color, texture, and weight. Then, the research data in the form of lipid profiles were analyzed with One-Way Anova to see if the data was generally distributed with further tests in the form of Post Hoc Tukey HSD tests to see fundamental differences between treatments. However, if the data is abnormally distributed, the Kruskall-Wallis test is used as an alternative test.

**Research Results**

After extraction by maceration method on andaliman fruit samples, the following extract characteristics were found.

**Table 2:** Parts of Methanol Extract of Andaliman Fruit (Zanthoxylum acanthopodium)

| Characteristics | Value |
|---|---|
| Fresh Simplisia Weight (gr) | 800 gr |
| Dry Simplisia Powder Weight (gr) | 211 gr |
| Solvent Volume (ml) | 2127 ml |
| Extract weight (gr) | 14,42 gr |
| Yield (%) | 7.03% |

From the table data above, it can be seen that from 500 grams of andaliman fruit samples, an extract of 15.47 grams was found. Thus, the yield obtained from andaliman fruit methanol extract is 7.03%.

**Table 3:** Phytochemical Screening Results of Andaliman Fruit Methanol Extract

| Phytochemicals | Reagents | Result |
|---|---|---|
| Alkaloid | Bouchardart | + |
| | Mayer | + |
| | Dragondroff | - |
| | Wagner | + |
| Saponin | Aquadest + Alcohol 96% | - |
| Flavonoid | FeCl3 5% | + |
| | $Mg_{(s)}$ + $HCl_{(p)}$ | - |
| | NaOH 10% | - |
| | $H_2SO_{4\ (p)}$ | - |
| Tanin | $FeCl_3$ 1% | + |
| Steroid dan Terpenoid | Salkowsky | - |
| | Liberman Bouchard | + |

The data in the table above shows that the methanol extract of andaliman fruit contains several phytochemical compounds, including Alkaloids, Saponins, Flavonoids, Tannins, Steroids, and Terpenoids.

**Table 4:** Results of Normality Test Using Shapiro-Wilk Test for All Research Parameters

| Parameter | | P Value | Data Distribution |
|---|---|---|---|
| Weight | | 0.442 | Usual |
| Total cholesterol before induction | | < 0.05 | Abnormal |
| Total cholesterol after induction | | < 0.05 | Abnormal |
| Lipid Profile After Treatment | 0.412 | 0.486 | Usual |
| | 0.004 | 0.004 | Abnormal |
| | < 0.06 | < 0.06 | Abnormal |
| | 0.245 | 0.135 | Usual |
| Up to SGOT | | < 0.05 | Abnormal |
| Up to SGPT | | 0.125 | Usual |

The table above shows that the data on body weight, total cholesterol, and LDL levels from the lipid profile after treatment and SGPT levels have a standard distribution. At the same time, other parameters include total cholesterol before and after induction, triglyceride levels, HDL levels, and SGOT levels, which are abnormally distributed. Based on the distribution of these data, data with standard data distribution are analyzed with parametric statistics, while abnormal data is analyzed with non-parametric statistics.

**Table 5:** Differences in Rats' Initial Body Weight in the Entire Treatment Group

| Treatment Group | Weight Loss (grams) | | P Value |
|---|---|---|---|
| | Mean | SD | |
| Usual | 288.00 | 37.67 | 0.844 |
| Standard | 239.56 | 16.23 | |
| Control | 288.86 | 23.67 | |
| Methanol Extract of Andaliman-I Fruit | 287.50 | 26.12 | |
| Methanol Extract of Andaliman-II Fruit | 238.85 | 23.88 | |
| Methanol Extract of Andaliman-III Fruit | 281.12 | 18.81 | |

From the table data above, it can be seen that the P value > 0.05 (P value = 0.972), which means there is no significant difference in the initial body weight of the mice used in this study. The importance of the mice used in this study ranged from 210-300 grams, evenly distributed in each treatment group.

**Table 6:** Comparison of Total Cholesterol Before and After High-Fat Diet in All Treatment Groups

| Treatment Group | Total Kolestrol (mg/dL) | |
|---|---|---|
| | Before Induction | After Induction |
| Usual | 118.80 (110-116) | 117.60 (118-120)[b] |
| Standard | 112.00 (100-118) | 211.00 (208-218)[a] |
| Control | 116.68 (110-118) | 211.88 (210-218)[b] |
| Methanol Extract of Andaliman-I Fruit | 118.88 (110-117) | 212.60 (209-211)[b] |
| Methanol Extract of Andaliman-II Fruit | 110.80 (100-118) | 210.80 (209-212)[b] |
| Methanol Extract of Andaliman-III Fruit | 116.80 (116-119) | 211.28 (209-210)[b] |
| P Value | 0.861 | 0.008 |

Data is displayed as Median (Range). The P value is obtained from the Kruskal-Wallis analysis. Different superscripts in the same column show significant differences.

From the table data above, it can be seen that before being given a high-fat diet, the total cholesterol of rats before giving a high-fat diet in the entire treatment group did not show a significant difference (P value = 0.782). This demonstrated that the total cholesterol data of the rats before being given a high-fat diet were uniform. However, total cholesterol in all groups of rats after administration of a high-fat diet showed a different distribution, where only the control group, standard methanol extract of andaliman-I, II, and III, showed uniform total cholesterol.

**Table 7:** Comparison of Lipid Profiles in the Entire Mouse Treatment Group

| Treatment Group | Profil Lipid | | | |
|---|---|---|---|---|
| | Total Kolestrol* | Trigliserida** | LDL* | HDL** |
| Usual | 134.50 ± 2.40a | 99.50 (97-100)a | 60.20 ± 1.60a | 63.45 (61-64)a |
| Standard | 144.50 ± 0.58b | 105.25 (101-105)b | 64.00 ±1.20b | 61.50 (60-63)a |
| Control | 179.25 ± 6.02c | 170.25 (168-179)c | 112.50 3.805c | 28.75 (38-43)b |
| Methanol Extract of Andaliman-I Fruit | 168.25 ± 1.50d | 133.50 (134-135)d | 83.75 ±2.62d | 57.50 (56-59)b |
| Methanol Extract of Andaliman-II Fruit | 163.25 ± 2.22e | 120.50 (113-122)e | 77.50 ± 1.29e | 61.50 (61-63)a |
| Methanol Extract of Andaliman-III Fruit | 151.75 ± 0.96e | 110.00 (108-112)f | 68.50 ±1.29f | 61.00 (60-63)a |
| P-value | < 0.05 | 0.013 | < 0.05 | 0.014 |

*The data is displayed as Mean ± SD. P value obtained from One Way ANOVA analysis; **Data is expressed as Median (Range). The P value is obtained from the Kruskal-Wallis analysis. Different superscripts in the same column show significant differences

From the table data above, it can be seen that all lipid profile data in all treatment groups showed significant differences. The table above presents lipid profiles for different treatment groups, with measured parameters including Total Cholesterol, Triglycerides, LDL (Low-Density Lipoprotein), and HDL (High-Density Lipoprotein). Here is a narrative of the results from the table:

1. The Normal treatment group showed stable lipid levels with an average Total Cholesterol of around 135.50, Triglycerides of 99.50, LDL of 60.20, and HDL of 63.55.
2. The Standard treatment group had slightly higher lipid levels than the Normal group, with an average Total Cholesterol of around 155.50, Triglycerides of 105.25, LDL of 65.00, and HDL of 61.50.
3. The Control treatment group showed significant improvement in lipid profile, signaling the adverse effects of a high-fat diet and PTU. Total cholesterol reached 179.25, Triglycerides 170.25, LDL 112.50, and HDL only 25.75.
4. The treatment group with MBA-I Extract showed significant reductions in Total Cholesterol (165.25), Triglycerides (133.50), and LDL (53.75), while HDL also increased to 57.50.
5. The treatment group with MBA-II Extract showed a decrease in Total Cholesterol (163.25) and Triglycerides (120.50) but with a significant increase in LDL (77.50), skipped.

**Table 8:** SGOT and SGPT Levels in All Treatment Groups

| Treatment Group | Kadar SGOT (U/L) | Kadar SGPT (U/L) |
|---|---|---|
| Usual | 26.25 (26-30)[a] | 55.50 ± 1.50[a] |

| | | |
|---|---|---|
| Standard | 110.50 (105-112)[b] | 170.75 ± 1.29[b] |
| Control | 160.50 (162-170)[c] | 97.25 ± 1.50[c] |
| Methanol Extract of Andaliman-I Fruit | 116.50 (115-120)[d] | 100.75 ± 3.59[d] |
| Methanol Extract of Andaliman-II Fruit | 127.50 (121-125)[e] | 115.50 ± 5.51[e] |
| Methanol Extract of Andaliman-III Fruit | 133.50 (129-132)[f] | 152.50 ± 2.05[b] |
| P Value | 0.008 | < 0.05 |

*The data is displayed as Mean ± SD. P value obtained from One Way ANOVA analysis; **Data is expressed as Median (Range). The P value is obtained from the Kruskal-Wallis analysis. Different superscripts in the same column show significant differences

From the table data above, it can be seen that it shows the levels of SGOT (Serum Glutamic Oxaloacetic Transaminase) and SGPT (Serum Glutamic Pyruvic Transaminase) in various treatment groups. Here is a narrative of the results from the table:

1. **Regular Treatment Group:** SGOT levels are around 26.25 U/L with a range of 26-30, and SGPT levels are around 55.50 U/L. This is a stable and average value for this group.

2. **Standard Treatment Group:** Showed a significant increase in SGOT levels up to 110.50 U/L (range 105-112) and SGPT levels reached 170.75 U/L. This reflects the negative impact of a high-fat diet and PTU on liver function.

3. **Control Treatment Group:** Showed higher improvement in SGOT (160.50 U/L) and SGPT (97.25 U/L) levels. This indicates the presence of significant disturbances in liver function in this group.

4. **Andaliman-I Methanol Extract Treatment Group:** Showed increased levels of SGOT (116.50 U/L) and SGPT (100.75 U/L), indicating a possible positive effect of andaliman fruit methanol extract on liver function.

5. **Andaliman-II Methanol Extract Treatment Group:** Showed increased levels of SGOT (127.50 U/L) and SGPT (115.50 U/L). Although there are.

**Discussion**

The research results indicate that the methanol extract from Andaliman fruit positively affects the lipid profile of experimental rats. The highest dose of Andaliman extract shows the most optimal improvement in reducing total cholesterol, triglycerides, and LDL (bad cholesterol) and increasing HDL (good cholesterol) levels in the Andaliman Fruit Methanol Extract Groups II and III. However, it is noteworthy that although the Andaliman Fruit Methanol Extract Group III showed an improved lipid profile, these improvements did not exceed those observed in the standard group. This means that while Andaliman extract provides a positive effect, the highest dose does not improve significantly compared to the standard group. These findings suggest that the methanol extract of Andaliman fruit has the potential to enhance the lipid profile, but further exploration is needed regarding the optimal dosage and its mechanisms of action. Additionally, a comparison with the standard group indicates there is still potential for additional development or dosage adjustments to achieve better results.

The explanation regarding the relationship between the anti-dyslipidemia effect of the methanol extract of Andaliman fruit and the phytochemical content in the fruit provides a deeper understanding. Phytochemicals, notably polyphenols, have been proven to have potential as anti-dyslipidemia agents through various mechanisms identified in research. Firstly, polyphenol content can cause down-regulation of pro-inflammatory cell signaling pathways such as nuclear factor-κB, activated protein-1, and mitogen-activated protein kinase. This occurs through the inhibition of the arachidonic acid cascade and eicosanoid derivatives. Thus, polyphenols can reduce inflammation, which plays a role in developing dyslipidemia.

Another possible involved mechanism is the regulation of gut microbiota. Polyphenol compounds in the gut can interact with gut microbiota, producing beneficial metabolites such as short-chain fatty acids. Moreover, bacteria such as Akkermansia municiphilia sp. in the gut microbiota can restore intestinal inflammation conditions, improve gut permeability, and enhance insulin sensitivity. Furthermore, improvements in gut microbiota can also protect the gut-liver axis, thereby reducing lipid profiles in the body. The gut-liver axis refers to the interaction between the digestive tract and the liver, and better regulation of this interaction can positively impact lipid metabolism and overall liver health. These findings affirm that the methanol extract of Andaliman fruit, through its phytochemical content, especially polyphenols, has the potential to address dyslipidemia by intervening in inflammatory aspects and regulating gut microbiota. Although further research is needed to understand these mechanisms more deeply, this study opens the door to the potential development of natural therapies or plant-based anti-dyslipidemia supplements. (Sun, Wang, and Qin, 2015; Feldman *et al*., 2025).

The findings of Ahmad *et al*. (2025), reporting the anti-inflammatory effects of Andaliman fruit nanoparticles inducing vascular improvement in atherosclerosis, provide additional support for the previously mentioned research results. The relationship between anti-inflammatory effects and atherosclerosis improvement with lipid profiles strengthens the idea that Andaliman fruit, whether in the form of methanol extract or nanoparticles, may have the potential to address dyslipidemia issues. It is essential to acknowledge that this research contributes to our understanding of various mechanisms involved in the positive effects of Andaliman fruit on the cardiovascular system. In addition to the direct influence on lipid profiles, anti-inflammatory effects can contribute to preventing and improving atherosclerosis, which is often closely related to dyslipidemia issues.

Although studies addressing the anti-dyslipidemia effects of Andaliman fruit are still limited, the results from Ahmad *et al*. (2025) and the research you mentioned earlier could serve as a basis for further development in understanding the potential of Andaliman fruit-based therapies or supplements in managing lipid disorders and cardiovascular health issues in general (Ahmad *et al*., 2025). The research results showing a decrease in SGOT and SGPT levels after administering methanol extract from Andaliman fruit

provide additional insights into the potential positive effects of Andaliman fruit on liver health. The reduction in SGOT and SGPT levels can be associated with the improvement of Non-Alcoholic Fatty Liver Disease (NAFLD), which, in turn, can contribute to preventing the formation of atherosclerosis. A significant finding is that NAFLD is a risk factor for atherosclerosis formation as it can cause endothelial dysfunction in blood vessels. Endothelial dysfunction can lead to inflammation and damage to blood vessel walls, ultimately triggering atherosclerosis. It is essential to note that using SGOT and SGPT separately in confirming NAFLD may lead to errors, especially in cases of mild NAFLD. The findings of Thong and Quynh (2025), stating that the increase in SGOT may be only slight in severe NAFLD cases and SGOT levels can remain normal in milder cases, highlight the complexity of NAFLD diagnosis. Therefore, accurate NAFLD diagnosis requires using other parameters and a comprehensive understanding of the patient's condition.

Thus, the decrease in SGOT and SGPT levels after consuming methanol extract from Andaliman fruit may be interpreted as a sign of liver improvement and potential protection against NAFLD, reducing the risk of atherosclerosis formation. However, the possibility of mild NAFLD in the group of rats receiving Andaliman fruit extract cannot be ruled out entirely. Further research and comprehensive studies are needed to understand the involved mechanisms better and confirm their effectiveness (Thong and Quynh, 2025). In this study, SGOT and SGPT levels in rats receiving methanol extract from Andaliman fruit were lower than the SGOT and SGPT levels in the control group. This indicates that the methanol extract of Andaliman fruit may protect liver tissue from NAFLD compared to the group that did not receive methanol extract of Andaliman fruit. However, the possibility of mild NAFLD in the group of rats receiving Andaliman fruit extract cannot be ruled out.

## Conclusion

This study concluded that the methanol extract of andaliman fruit positively affected lipid profiles and liver health in rats. This extract significantly lowers total cholesterol, triglycerides, and LDL (bad cholesterol) levels in varying doses while increasing HDL (good cholesterol) levels. In addition, there was a significant reduction in SGOT levels, indicating potential protection against Non-Alcoholic Fatty Liver Disease (NAFLD). Although positive effects were seen at all doses of the extract, the highest amount did not show more significant improvement compared to the standard group. These results indicate that Andaliman fruit methanol extract has potential as a supporting agent for cardiovascular health. However, further research is needed, especially in humans, to confirm its effectiveness before it can be implemented as an effective therapy or treatment.

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