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ORIGINAL ARTICLE

The effect of tamarillo (Solanum betaceum Cav.) ethanol extract on the reduction of triglyceride levels in dyslipidemia wistar rats

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ABSTRACT

Dyslipidemia, an abnormality in lipid metabolism marked by elevated triglycerides, cholesterol, or LDL and low HDL, increases cardiovascular risk. Tamarillo (Solanum betaceum Cav.) contains flavonoids and anthocyanins with potential lipid-lowering effects. This study evaluated the effect of ethanol extract of Tamarillo fruit (ETB) at doses of 100 mg/kg body weight (BW)/day and 200 mg/kg BW/day on triglyceride levels in Wistar rats with dyslipidemia, compared with simvastatin at 10 mg/kg BW/day. A posttest-only control group design was used with 25 male Wistar rats divided into five groups: negative control, positive control, ETB 100, ETB 200, and simvastatin. Dyslipidemia was induced with a high-fat diet and propylthiouracil for 14 days, followed by 14 days of treatment. Triglyceride levels were measured using the GPO-PAP method. Data were analyzed using the Shapiro–Wilk test, Levene's test, and the Kruskal–Wallis test. The results showed no statistically significant differences between groups ($p > 0.05$). However, ETB at 200 mg/kg BW/day demonstrated a 22.6% reduction in triglyceride levels compared with the positive control, although the effect was slightly less than that of simvastatin. In conclusion, Tamarillo ethanol extract did not significantly reduce triglyceride levels but showed a favorable trend at higher doses, indicating potential for further research with dose optimization, longer duration, and standardized active compounds.

Keyword: Anthocyanins, dyslipidemia, ethanol extract, flavonoids, tamarillo, triglycerides

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INTRODUCTION

Dyslipidemia is a common health issue that hinders efforts to prevent non-communicable chronic diseases. It results from abnormalities in lipid metabolism, which manifest as changes in total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride levels in the bloodstream.[1] This condition is a major risk factor for cardiovascular disorders, which remain the leading cause of global mortality. A high-fat diet, insufficient fiber intake, and sedentary lifestyle contribute to the high prevalence of dyslipidemia in Indonesia and many other countries. Therefore, early prevention through lifestyle interventions and health education is essential.[2,3] Cardiovascular disease triggered by dyslipidemia develops through a complex process of atherosclerosis. Among lipid parameters, triglycerides play a particularly important role. Triglycerides are the body's primary energy storage molecules, composed of glycerol and three fatty acids. Their circulating levels are influenced by diet, hepatic metabolism, and physical activity.[4] Elevated triglyceride levels can accelerate the formation of atherosclerotic plaques in blood vessels, thereby increasing the risk of coronary heart disease. Maintaining stable triglyceride levels is therefore a crucial indicator of cardiovascular health.[5] Several factors contribute to high triglyceride levels. Primary causes are related to inherited lipid metabolism disorders, while secondary factors include obesity, diabetes mellitus, hypothyroidism, and alcohol consumption. Even in individuals with normal cholesterol levels, hypertriglyceridemia remains an independent predictor of cardiovascular risk.[6] If the level is very high, this condition can trigger acute pancreatitis, which is life-threatening.[7] This shows that monitoring triglyceride levels is important, both in healthy individuals and in those at risk. The management of hypertriglyceridemia requires an integrated approach between lifestyle changes and pharmacological therapy. Dietary modifications, such as reducing saturated fat intake and increasing soluble fiber intake, can help lower blood lipid levels.[8] Regular physical activity helps increase triglyceride breakdown and improve the overall lipid profile. If lifestyle changes are not sufficiently effective, medications such as statins or fibrates can be used to regulate lipid metabolism.[9] However, long-term use often causes side effects, including liver dysfunction or myalgia.

The limitations of the effectiveness and potential side effects of synthetic drug therapy have driven increased interest in research based on natural ingredients. Natural sources rich in bioactive compounds, particularly antioxidants, are believed to have the ability to lower lipid levels through various mechanisms, including inhibiting cholesterol absorption in the digestive tract and increasing bile acid excretion.[10,11] In addition, antioxidants play an important role in protecting lipids from oxidation, the initial stage of atherosclerotic plaque formation.[12] This natural ingredient-based approach is considered relatively safer for long-term consumption and has the potential to serve as a complementary therapy to support conventional medical treatment. Tamarillo (*Solanum betaceum Cav*.) is a natural ingredient that shows significant potential. This fruit contains various phytochemical compounds, including flavonoids, anthocyanins, and vitamins C and E.[13] Flavonoids play a role in inhibiting cholesterol synthesis in the liver, while anthocyanins help maintain the integrity and health of blood vessels. Vitamins C and E function as potent antioxidants that inhibit lipid peroxidation, thereby protecting cells and body tissues from oxidative degradation.[14] The combination of these bioactive compounds confirms the potential of Tamarillo as a promising natural lipid-lowering agent, and opens up opportunities for further development in natural medicines or supplements.[10]

Previous research has shown that administering ethanolic Tamarillo extract effectively reduces cholesterol and triglyceride levels in dyslipidemic animal models.[15] A concentration of 96% ethanol is used as a solvent medium because it optimally extracts both polar and non-polar compounds. The mechanism of lipid reduction involves inhibiting lipid metabolism enzymes and increasing lipid excretion through bile. These findings reinforce the potential of Tamarillo as an alternative therapy for hypertriglyceridemia.[16] The present study uses a validated dyslipidemia model induced by propylthiouracil (PTU) and a high-fat diet, which closely mimics lipid metabolism disturbances in humans. Male Wistar rats were used to minimize the hormonal influence from estrogen. This model allows for a more stable and representative condition of dyslipidemia, thereby providing a reliable basis for testing the efficacy of natural ingredient-based interventions.[17,18] The novelty of this research lies in evaluating two different doses of ethanolic Tamarillo extract (100 mg/kgBW/day and 200 mg/kgBW/day) while directly comparing their effects on triglyceride levels with simvastatin, a standard lipid-lowering drug. This comparative approach is expected to clarify the relative efficacy of Tamarillo extract and provide a stronger scientific foundation for its potential development as a safe and effective alternative therapy in dyslipidemia management.

METHODS AND SUBJECT

Research Design

This study adopted a proper experimental design with in vivo methods in a laboratory setting. The design applied was a posttest control group with randomization of the control and treatment groups. This method was chosen to enable researchers to compare treatment effects objectively across different groups. The study was conducted with five treatment groups: a negative control group, a positive control group, two groups receiving Tamarillo extract at different doses, and one simvastatin group as a favorable control comparison.

Research Location and Time

The study was conducted in several laboratories at the Faculty of Medicine, Universitas Jenderal Achmad Yani, including animal, pharmacology, and biochemistry. The animal laboratory was used to maintain the test rats and administer treatments, the pharmacology laboratory to prepare extracts and suspensions, and the biochemistry laboratory to analyze triglyceride levels. The study was conducted from July to August 2025, with all stages conducted following systematically designed procedures to ensure data accuracy.

Population and Research Sample

a. Population

This population in this study consisted of male Wistar rats obtained from the Animal Laboratory of Universitas Jenderal Achmad Yani. The rats were selected based on uniformity of age and body weight to minimize biological variability that could affect the results.

b. Inclusion and Exclusion Criteria

Inclusion criteria included male Wistar rats aged 3–5 months with a body weight of 200–250 grams, in good health, active, smooth, shiny fur, no defects, and no prior treatment. Exclusion criteria included rats that experienced a weight loss of more than 10% after adaptation and rats that died during maintenance or research.

c. Sample Size and Calculation

The sample size was determined using Federer's formula, with a minimum of five rats per group. A total of 25 test animals were used, divided into five treatment groups. Each group consisted of one negative control, one positive control, two groups receiving Tamarillo extract at different doses (100 mg/kgBW and 200 mg/kgBW), and one group with simvastatin at 10 mg/kgBW.

Research Materials and Equipment

a. Materials

The primary materials used were ripe Tamarillo (*Solanum betaceum Cav*.), simvastatin, a high-fat diet, and propylthiouracil (PTU). Laboratory chemicals include 96% ethanol, GPO-PAP kit (AIM,Indonesia), $FeCl_3$ reagent, standard buffer solutions, and standard feed for the animal adaptation phase.

b. Equipment

The equipment used included an analytical balance, oven, rotary evaporator, measuring cup, test tubes, filter paper, syringe, individual cages, microcapillaries, vacutainer tubes, centrifuge, spectrophotometer, micropipette, test tube rack, stopwatch, and spatula.

Research Procedure

a. Material Collection

Material collection was structured to ensure the quality of the samples used in the study. Fresh Tamarillo fruits (*Solanum betaceum Cav*.) were collected from Ciwidey Farm at optimal ripeness and free from physical defects. Male Wistar rats (age 3–5 months, weight 200–250 g) were obtained from the Animal Laboratory of .

b. Extract Preparation

The extract preparation process began with drying the Tamarillo fruit to obtain dry simplicia, which was then ground into a fine powder. This powder was extracted using 96% ethanol through a four-day maceration process accompanied by periodic stirring to maximize the dissolution of bioactive compounds. The resulting solution was filtered to separate the solid residue from the filtrate, and then evaporated using a rotary evaporator at 50 °C to remove residual solvent. This process yields a concentrated extract ready for animal experiments as a treatment agent.19,20

d. Preparation of Simvastatin Suspension

Simvastatin suspension was made at a dose of 0.18 mg per rat. The simvastatin was first dissolved in 0.2 mL of distilled water to form a homogeneous suspension. The suspension was then administered orally with care to ensure each rat received the dose according to the calculation.

e. Preparation of High-Fat Diet and PTU

High-fat diet (HFD) feed in the form of pellets was obtained from PT. Surya Sains Indonesia. The pellets were prepared by mixing fat, carbohydrate, and protein source materials, then molded and dried to a stable moisture content of 12.25% to maintain quality and shelf life. The formulation contained 32.70% fat and 36.80% carbohydrates, with a total energy of 493.62 Kcal/100 g and 294.30 Kcal/100 g derived from fat. In this study, 25 male Wistar rats were fed with HFD pellets at 25 g/rat/day to ensure consistent energy intake. To induce dyslipidemia, propylthiouracil (PTU) was incorporated into the diet to trigger hypothyroidism, which affects lipid metabolism. The HFD mixed with PTU was presented as a homogeneous emulsion with a total volume of 120 mL per administration. PTU was administered at a dose of 27 mg/kgBW (equivalent to 5.4 mg/rat), dissolved in 0.2 mL of distilled water, and delivered via oral gavage once daily for 14 consecutive days to all 24 test rats to ensure consistent induction of dyslipidemia.

f. Preparation of Animals Experiment

Animal Experiment were housed individually in clean, comfortable, and safe cages to minimize stress levels that could affect research results. During the seven-day adaptation period, each rat was given 25 grams of standard feed daily, with ad libitum access to drinking water. The cage environment was regulated to maintain stable lighting, temperature, and humidity, ensuring optimal physiological conditions for the test animals. After the adaptation period, the rats were randomly divided into five treatment groups, considering body weight and age consistency, to ensure more accurate measurements of dependent variables and valid comparisons between groups.

g.Treatment of Test Animals

Test animals were treated for 14 days, with groups divided according to the research design. The negative control group received only standard feed without additional treatment, while the other groups were exposed to dyslipidemia induction through a high-fat diet. The positive control group was given simvastatin at a dose of 10 mg/kg body weight, a standard dose previously reported to be effective in rat models. In contrast, the treatment groups received ethanolic extract of Tamarillo (ETB) at doses of 100 mg/kg body weight or 200 mg/kg body weight.

The selection of ETB doses was based on previous literature reporting that Tamarillo ethanol extract within these ranges showed hypolipidemic and antioxidant effects in rodent models, while still within the safe tolerance limits. The 100 mg/kg BW dose was chosen to represent a lower effective dose, while 200 mg/kg BW was selected to evaluate a higher dose response and to assess whether a dose–response relationship could be observed. The daily diet was administered in the morning, while ETB and simvastatin administration were scheduled in the afternoon to maximize absorption of active compounds in the digestive tract and minimize potential interactions with dietary components.

h.Triglyceride Level Measurement

Triglyceride concentration was measured using the GPO-PAP kit (AIM, Indonesia) based on a colorimetric enzymatic method according to the manufacturer's protocol. Blood was collected through the retroorbital plexus using a microcapillary after the rats were fasted for approximately 12 hours to minimize postprandial variation. Each blood sample was placed in a tube, allowed to clot for one hour, and centrifuged at 3,000 rpm for 10 minutes to obtain serum. From each rat, one serum sample was obtained, resulting in a total of 25 serum samples from all groups. Each serum sample was measured in duplicate to ensure accuracy and reproducibility. The serum was reacted with the enzymatic reagent, incubated at a controlled temperature, and its absorbance was measured using a spectrophotometer at a wavelength of 500 nm. Triglyceride levels were then determined by comparing sample absorbance values with standard solutions, yielding quantitative results.[21]

Research Variables

The variables in this study were divided into independent and dependent variables. The independent variables consisted of the administration of ethanolic extract of Tamarillo (*Solanum betaceum Cav.*) at two different doses, namely 100 mg/kgBW and 200 mg/kgBW, as well as the administration of simvastatin at a dose of 10 mg/kgBW. Additionally, a dyslipidemia induction model was performed using a combination of propylthiouracil (PTU) and a high-fat diet (HFD). The dependent variable measured was the blood triglyceride levels in male Wistar rats with dyslipidemia induced by PTU and HFD. The selection of these variables was intended to evaluate and compare the extent to which each treatment can reduce triglyceride levels in test animals, thereby providing an overview of the relative effectiveness of Tamarillo extract compared to conventional therapy. Additionally, this study is expected to provide a scientific basis for developing safe and potentially alternative therapies based on natural ingredients for controlling blood lipid levels.

Operational Definition

Operational definitions clarify the boundaries and measurements of each research variable. The Wistar strain rats were aged 3–5 months with a body weight of 200–250 grams, and were weighed using digital scales. Blood triglyceride levels were measured using the GPO-PAP enzymatic method and expressed in mg/dL. Dyslipidemia in this study was defined as increased triglyceride levels after induction with a combination of propylthiouracil (PTU) and a high-fat diet (HFD) compared to baseline conditions. Tamarillo fruit extract and simvastatin were administered orally via oral gavage at predetermined doses. Propylthiouracil was used as an additional inducer to influence lipid metabolism in the rats.

Data Analysis

The research data were analyzed using the Shapiro-Wilk normality test because the sample size was less than 50, to ensure normal data distribution. Next, a homogeneity of variance test was conducted to determine the similarity of variances between groups. If the data were normally distributed and homogeneous, the differences between groups were analyzed using one-way ANOVA, followed by Tukey's post hoc test to see for significant differences. However, if the data did not meet the assumptions of normality or homogeneity, the non-parametric Kruskal-Wallis test was used. A p-value < 0.05 is considered to indicate a statistically significant difference. All analyses were performed at a 95% confidence level using SPSS software.

Research Ethics

This study was approved by the Ethics Committee of the Faculty of Medicine, (Number: [013/UH1.06/2025]) and the relevant animal laboratory. All research procedures followed the 3R (Replacement, Reduction, and Refinement) principles, ensuring that experimental animals were treated humanely. The Replacement principle was applied by considering alternative methods to replace live animals whenever possible. The Reduction principle is implemented through careful research planning to minimize the number of test animals used while maintaining statistical adequacy. The Refinement principle ensures that test animals are free from hunger, thirst, pain, discomfort, and stress, and had the opportunity to express their normal behavior.

RESULTS AND DISCUSSION

Results

The Shapiro–Wilk test indicated that all groups had p-values > 0.05, confirming that the triglyceride level data were normally distributed (Table 1).

Table 1. Results of the Shapiro–Wilk Normality Test and Means

Group	Mean±SD (mg/dL)	p-value
Negative group	110,20 ± 14,55	0,722
Positive group	117.80 ± 38,09	0,302
ETB 100 group	116,20 ± 13,72	0,055
ETB 200 group	95,20 ± 6,76	0,274
Control group	115,00 ± 12,02	0,104

Negative Control: standard feed
Positive Control: standard feed, DTL, and PTU
ETB 100: standard feed, DTL, and PTU, ethanol extract of Tamarillo at a dose of 100 mg/kgBW/day
ETB 200: standard diet, DTL, and PTU, ethanol extract of Tamarillo fruit at a dose of 200 mg/kgBW/day
Comparative Control: standard diet, DTL, and PTU, plus simvastatin at a dose of 10 mg/kgBW/day

The next step is to test the variance homogeneity. This test aims to confirm whether the data groups being analyzed have the same variance. Variance homogeneity is an important requirement in parametric tests, as variance heterogeneity can affect the validity of the analysis results. Thus, this test is conducted so that the results of the subsequent analysis can be interpreted more accurately and scientifically justified. The results of the homogeneity test using Levene's Test of Equality of Error Variances are shown in Table 2.

Table 2. Homogeneity Test Results

Levene Statistic	df1	df2	Sig.
4,697	4	20	0,008

Based on Table 2, a significance value of 0.008 was obtained, which is smaller than 0.05. This indicates that the variance between treatment groups is not homogeneous; in other words, there are differences in data distribution between groups. This condition indicates that the assumption of variance homogeneity in parametric tests is unmet. Therefore, data analysis cannot be continued using a one-way ANOVA test, and an alternative approach is required. Therefore, this study utilizes the non-parametric Kruskal–Wallis test as a follow-up approach to examine the differences in triglyceride levels between treatment groups.

After determining that the variances between groups were not homogeneous, the non-parametric Kruskal–Wallis test was used to analyze differences in triglyceride levels. This test is used as an alternative to one-way ANOVA when the assumption of homogeneity of variance is not met. The purpose of using the Kruskal–Wallis test is to determine whether there are differences between more than two independent groups in their medians. With this approach, the data analysis results can still describe significant and non-significant differences between groups, even though the data does not meet the requirements for parametric tests. The results of the Kruskal–Wallis test are shown in Table 3.

Table 3. Results of the Kruskal–Wallis Test

Test Statistics	Value
Kruskal-Wallis H	7,515
df	4
Asymp. Sig.	0,111

Based on the results of the Kruskal-Wallis test in the table above, the Asymp. Sig. Value was 0.111, which is greater than 0.05. This indicates no statistically significant difference in triglyceride levels between treatment groups. Thus, the analysis results indicate that the variations in values observed in each group are not statistically significant enough to be considered different. In other words, although each group has an average value that is not the same, the differences remain within the statistically homogeneous limits. Therefore, all groups are in a relatively comparable condition without any significant differences.

Discussion

The statistical analysis indicated that although the data were normally distributed, variance heterogeneity required the use of a non-parametric test. This ensured that the analysis remained valid and accurately reflected the biological variability inherent in animal studies. The Kruskal–Wallis test showed no statistically significant differences in triglyceride levels among groups, indicating that the effects of Tamarillo ethanol extract (ETB) at the tested doses were modest.[17,18] Several factors may explain the lack of significant effects. The small sample size and high variability within some groups reduced the statistical power needed to detect differences.[18–20] In addition, previous studies have reported that dyslipidemia induction using a high-fat diet combined with propylthiouracil (PTU) produces moderate lipid disturbances rather than severe dyslipidemia, which may limit the magnitude of treatment responses.[21,22] Biological variation among animals, including baseline physiology and metabolic differences, may also have influenced individual responses to ETB.[23] Pharmacological and Methodological considerations are equally important. The bioavailability of flavonoids and anthocyanins in ETB may have been limited. Furthermore, the relatively short treatment period may have been insufficient, as similar studies have shown that plant-based therapies often require longer intervention periods or higher doses to achieve significant results.[24] Moreover, extraction and storage conditions could affect the concentration of active compounds, and possible synergistic or antagonistic interactions between constituents may alter efficacy.[25]

Despite these limitations, a downward trend in triglyceride levels was observed, particularly at the 200 mg/kgBW dose, suggesting biological activity. Nevertheless, the efficacy of ETB, even at the highest dose, did not match the effect of simvastatin.[26] The observed trend indicates, however, potential therapeutic value. Flavonoids and anthocyanins in Tamarillo are known to influence lipid metabolism by stimulating lipoprotein lipase activity, inhibiting hepatic triglyceride biosynthesis, and enhancing fatty acid oxidation.[27] These mechanisms support the plausibility of ETB as a lipid-lowering agent, though its impact remains weaker and less consistent compared to standard pharmacological therapy.[28]

Overall, the findings highlight the need for optimization of ETB through higher or standardized doses, improved formulations to enhance bioavailability, and longer treatment durations. Future studies with larger sample sizes and more robust dyslipidemia induction models are warranted to better clarify the therapeutic potential of Tamarillo extract in dyslipidemia management.[29]

CONCLUSION

Administration of Tamarillo (ETB) extract has shown potential in reducing triglyceride levels in dyslipidemic rats, especially at a dose of 200 mg/kg/day. However, this effect was not statistically significant and was not comparable to simvastatin. Nonetheless, this positive trend makes ETB a promising candidate for further research as an alternative therapy.

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DECLARATION OF CONFLICT OF INTEREST

The authors declare that there are no potential conflicts of interest related to this article's research, writing, and/or publication.

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