

ORIGINAL ARTICLE

The effect of ethanolic tamarillo extract on reducing total cholesterol levels in hypercholesterolemic wistar rats

Siti F Fajriyah^{1*}, Vina Dwitia², Welly Ratwita³

- 1) Medicine Study Program, Faculty of Medicine, Universitas Jenderal Achmad Yani, Cimahi, Indonesia.
- 2) Department of Surgery, Faculty of Medicine, Universitas Jenderal Achmad Yani, Cimahi, Indonesia.
- 3) Department of Pharmacology, Faculty of Medicine, Universitas Jenderal Achmad Yani, Cimahi, Indonesia.

*Corresponding author. E-mail: wellyratwita@gmail.com; sitifajah@gmail.com

ABSTRACT

Dyslipidemia is characterized by an increase in total cholesterol, low-density lipoprotein, triglycerides, and a decrease in high-density lipoprotein. Hypercholesterolemia is a major contributor to the high mortality rate associated with cardiovascular disease. Tamarillo (*Solanum betaceum* Cav.) contains flavonoids and anthocyanins with antioxidant and hypolipidemic potential. This study aimed to determine the effect of tamarillo ethanol extract (EET) on total cholesterol levels in Wistar rats with dyslipidemia. This experimental study used a post-test only control group design with 25 male Wistar rats divided into five groups (n = 5). K1: negative control, K2: positive control, K3: high-fat diet (HFD) + propylthiouracil (PTU) + EET 100 mg/kgBW, K4: HFD+PTU+EET 200 mg/kgBW, and K5: HFD+PTU+simvastatin 10 mg/kgBW. Total cholesterol levels were measured using the CHOD-PAP method after a 14-day intervention. Data were analyzed using ANOVA followed by Tukey's post-hoc test. The ANOVA test showed significant differences among the groups (F = 16.42; p < 0.001). The highest cholesterol level was observed in the positive control group (148.80 ± 4.86 mg/dL). Administration of EET 200 mg/kgBW reduced cholesterol to 142.60 ± 4.50 mg/dL, which was statistically comparable to the reduction achieved by simvastatin (135.80 ± 6.38 mg/dL; p = 0.633). In contrast, EET at 100 mg/kgBW (148.00 ± 11.95 mg/dL) was not significantly different from the positive control. The findings of this study indicate that administration of EET at a dose of 200 mg/kgBW significantly reduces total cholesterol levels, demonstrating an efficacy comparable to simvastatin. EET has potential as an adjuvant therapy in the management of dyslipidemia, but cannot yet replace simvastatin as the standard therapy.

Keyword: Antihyperlipidemic activity, dyslipidemia, simvastatin, tamarillo (*Solanum betaceum* Cav.), total cholesterol.

Received: 2025-12-15, Revised: 2025-02-06 Accepted: 2026-02-02, Published: 2026-02-28.

Copyright (c) 2026 Siti F Fajriyah, Vina Dwitia, Welly Ratwita

This is an Open Access (OA) article under the CC BY-SA 4.0 International License (<https://creativecommons.org/licenses/by-sa/4.0/>).

How to cite :

Fajriyah, S.F., Dwitia, V. and Ratwita, W.(2026). "The effect of ethanolic tamarillo extract on reducing total cholesterol levels in hypercholesterolemic wistar rats", Acta Medical and Health Sciences, 4(3).p103-113. Doi: <https://doi.org/10.35990/amhs.v4n3.p103-113>

INTRODUCTION

Dyslipidemia is a metabolic disorder characterized by abnormalities in lipid metabolism, manifested by increased serum levels of total cholesterol, low-density lipoprotein (LDL), and triglycerides, accompanied by decreased high-density lipoprotein (HDL) concentrations. This condition constitutes a major risk factor for the development of cardiovascular disease.^{1,2} According to data reported by the World Health Organization (WHO), the global prevalence of dyslipidemia reached 37% in men and 40% in women, in 2018.³ Furthermore, findings from the 2018 Indonesian National Basic Health Research (RISKESDAS), assessed using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, demonstrated that 28.8% of Indonesians aged 15 and older have abnormal total cholesterol levels (≥ 200 mg/dL), with a greater prevalence among women compared to men, and more pronounced in urban populations than in rural communities.^{4,5} In general, the clinical management of dyslipidemia requires a significant time and long-term financial resources. Synthetic drugs commonly used to treat hyperlipidemia, such as statins, exert their therapeutic effects by inhibiting the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase.^{6,7} Simvastatin, the standard statin agent used in this study, can lead to adverse side effects upon prolonged administration. These include gastrointestinal disturbances such as constipation in up to 10% of patients, as well as musculoskeletal complications including myalgia, arthralgia, and muscle cramps. Therefore, intensive research is currently focusing on natural alternatives that are as effective as synthetic drugs for dyslipidemia but are safer, more readily available, and can be consumed daily without causing side effects.^{1,7}

Indonesia's vast biodiversity and natural resources offer significant potential for developing plant-based therapeutics,

particularly from species rich in antioxidants.^{8,9} These antioxidants neutralize free radicals by donating electrons to stabilize reactive molecules, thereby suppressing the chain reactions involved in free radical generation. Tamarillo (*Solanum betaceum* Cav.), a shrub belonging to the *Solanaceae* family, has been cultivated in Bogor, West Java, since 1941. Its abundant nutritional content and high antioxidant activity make it a highly competitive candidate for functional food development compared to other commercial fruits. Research conducted by Rito (2023) detected natural antioxidants in tamarillo fruit, specifically flavonoids and anthocyanins, which showed an antioxidant activity of 64.99%.^{10–12} To evaluate these properties, Wistar rats were selected as the animal model for this study due to its physiological similarities to human lipid metabolism. Wistar rats are more susceptible to fat accumulation in adipose tissue, making them an excellent model for studying high-fat diet (HFD)-induced obesity.¹³ Furthermore, combining an HFD with propylthiouracil (PTU) administration is considered adequate in stably inducing dyslipidaemia in rodents. PTU reduces thyroid hormone activity pharmacodynamically; the resulting hypothyroidism contributes to decreased lipid metabolism, leading to total cholesterol accumulation in the blood, and its toxic effects are considered highly significant in damaging the liver, heart, and kidneys.^{14,15}

A study conducted by Abdul Kadir et al. (2015) reported that Sprague-Dawley rats fed a high-fat diet for 10 weeks and subsequently treated with tamarillo aqueous extract at doses of 150, 200, and 300 mg/kg for 7 weeks exhibited a significant reduction in total cholesterol levels compared to both the negative and positive control groups.¹⁶ Furthermore, a study by Masbintoro, Agustini, and N.S. Djauhari (2016) reported that administering an ethanolic extract of tamarillo fruit at doses of 100, 200, and 300 mg/kg body weight for 7 days demonstrated potential hypolipidemic effects.^{17,18}

Based on these findings, this study aimed to evaluate the therapeutic effects of ethanolic tamarillo extract at doses of 100 mg/kg BW and 200 mg/kg BW, comparing its performance directly against standard simvastatin therapy at a dose of 10 mg/kg BW in reducing total cholesterol levels in hypercholesterolemic Wistar rats. This specific extract doses were selected because they have been shown to significantly lower cholesterol levels while remaining within a toxicologically safe threshold, thereby minimizing the risk of unwanted pharmacodynamic effects.^{19,20}

SUBJECTS AND METHODS

This study was conducted from May to June 2025, using a laboratory-based experimental design with a post-test-only control group approach, which included both a treatment and a control group. The study aimed to evaluate the effect of ethanolic tamarillo fruit extract on reducing total cholesterol levels and to identify the optimal dose for lowering total cholesterol in rats with experimentally induced hypercholesterolemia through a high-fat diet and propylthiouracil (PTU) administration.

Research Subject

The study subjects consisted of healthy Wistar rats aged 2–3 months, weighing between 200 and 250 grams. Inclusion criteria required the rats to be in optimal physical health, characterized by active mobility, a normal appetite, and the absence of any physical anomalies. The exclusion criteria were defined as rats that lost more than 10% of their initial body weight during the acclimatization period or those that showed any signs of illness during the acclimatization phase.

Experimental Animal Treatment

The Wistar rats were randomly allocated into five groups as outlined in Table 1: K1 (negative control); K2 (positive control)- induced with a high-fat diet (HFD) at 20–25 g per rat per day along with 0.01% propylthiouracil (PTU); K3 (Treatment Group 1) -HFD-induced rats, and administered ethanolic tamarillo extract (EET) at a dose of 100 mg/kg BW; K4 (Treatment Group 2)-Induced with HFD, and administered EET at a dose of 200 mg/kg BW; and K5 – induced with HFD, and administered simvastatin at a dose of 10 mg/kg BW.

Table 1. Treatment of Experimental Animal

No	Experimental group	Treatment time	Standard feed	High fat diet	Water	Ethanol extract of tamarillo	Simvastatin
1	K1	14 days	+	-	Without PTU	-	-
2	K2	14 days	+	+	With PTU	-	-
3	K3	14 days	+	+	With PTU	100mg/kgBW	-
4	K4	14 days	+	+	With PTU	200mg/kgBW	-
5	K5	14 days	+	+	With PTU	-	10mg/kgBW

Each treatment group was designed to observe the impact of each intervention on the desired outcome. The number of Wistar required was calculated using the Federer formula:

$$\begin{aligned}(n-1)(t-1) &\geq 15 \\ (n-1)(5-1) &\geq 15 \\ n-1 &\geq 15/4 \\ n-1 &\geq 3,75 \\ n &\geq 4,75 \\ n &\approx 5\end{aligned}$$

Based on the calculations, n represents the number of animal subjects per group (number of mice per group), while t represents the number of treatment groups in the study. The minimum number of samples required was five animals per control group, bringing the total number of samples required for this study to 25 animals. Prior to the intervention, each group was acclimatized for 7 days, fed 20-25 g/Wistar/day, and given drinking water (*ad libitum*) at a volume of 10 mL/100gBW/day.

Place and Time of Research

This study was conducted at the Faculty of Medicine, Universitas Jenderal Achmad Yani, Cimahi. Animal acclimatization, maintenance, and treatment procedures were carried out in the Animal Laboratory. The ethanolic extraction of tamarillo fruit was performed in the Biochemistry Laboratory, while animal treatment procedures and total cholesterol measurements were conducted in the Clinical Pathology Laboratory.

Research Material

Animal maintenance was conducted using standard laboratory rodent cages equipped with integrated food and water containers. Total cholesterol levels were assessed using the Nesco Glucose Cholesterol Uric Acid (NGCU) cholesterol test kit and corresponding test strips, disposable syringes, digital scales, rotary evaporator, hot plate, filter paper, measuring pipettes, micropipettes, gloves, and stationery. The treatment materials included conventional rodent pellets, a high-fat diet,

potable water, and an extract of tamarillo fruit. In addition, this trial used 96% ethanol, the medication simvastatin, and propylthiouracil (PTU).

Research Procedures

High-Fat Diet and Propylthiouracil

A high-fat diet plan was administered using feed from PT Surya Sains Indonesia, specially formulated to induce hypercholesterolemia in Wistar rats, which resembles the metabolic condition observed in humans. The feed contains 32.70% total fat, 36.80% carbohydrates, 13.03% protein, and 493.62 Kcal/100g. The recommended therapeutic dose of propylthiouracil for humans is 300-600 mg per day. This dose was then adjusted for rats using a conversion factor of 0.018 or 0.01% of the human dose, resulting in an appropriate dose of 5.4 mg/200 g BW, equivalent to 27 mg/kg body weight.^{14,15}

Propylthiouracil (PTU) is an antithyroid drug (ATD) belonging to the thionamide class, commonly used to inhibit thyroid hormone synthesis. In this study, PTU was administered orally to induce a hypothyroid condition associated with lipid metabolism disturbances in experimental rats.¹⁴ To ensure accurate and consistent dosing for each experimental animal, propylthiouracil, tamarillo ethanol extract, and simvastatin suspension were all administered orally using an oral gavage throughout the intervention period.

Simvastatin Suspension

Simvastatin suspension was used as the positive control, with *sodium carboxymethyl cellulose* (Na-CMC) serving as the suspending agent. The dosage was determined by converting the therapeutic dose in humans (10 mg) to an equivalent dose for experimental animals based on body weight, using an interspecies conversion factor in which 200 g of rat body weight is equivalent to 0.018 times the human dose. Based on this conversion, the equivalent dose for Wistar rats, was 0.18 mg/200g equivalent to 0.9 mg/kg BW.^{21,22}

Production Ethanol Extract of Tamarillo

Tamarillo fruit ethanol extract was prepared by cutting the fruit into several pieces and then draining it. The pieces were then soaked and crushed using a blender with 96% ethanol. The resulting solution was placed in a macerator and left for approximately 24 hours for extraction.

Subsequently, the solution was filtered, and the resulting filtrate was concentrated using a rotary evaporator at 90 °C to obtain a concentrated residue or until no solvent remained in the condenser.²³ The concentrated extract was subsequently dried and weighed before being administered to Wistar rats in the study.

In this study, the extraction yield (rendement) of the ethanolic tamarillo extract was not determined. In addition, phytochemical screening was not performed; therefore, the specific bioactive compounds potentially responsible for lowering total cholesterol levels could not be identified. These limitations may affect the reproducibility and standardization of the extract used in this study. Nevertheless, previous studies have reported that tamarillo contains flavonoids and anthocyanins with antioxidant and hypolipidemic properties.^{11,12}

Measurement of Total Blood Cholesterol Levels in Mices

The measurement of total blood cholesterol levels in this study was performed using the enzymatic method Cholesterol Oxidase–Peroxidase Aminoantipyrine (CHOD-PAP) method based on a colorimetric reaction, utilizing a Semi-Automatic Chemistry Analyser DR-7000D instrument and rat blood samples as the experimental material. Prior to blood collection, the rats were fasted for 12 hours to minimize the effect of recent dietary intake on baseline lipid profiles. Blood samples were then collected and stored in tubes, and subsequently centrifuged at

3000 rpm for 5 minutes to separate the serum from other blood constituents before cholesterol analysis was performed. The analysis procedure involved taking 10 µL of serum sample or standard solution, followed by mixing it with 1000 µL of reagent kit solution in a test tube. The mixture was thoroughly homogenized and incubated at room temperature for 5 minutes. Subsequently, absorbance was measured at a wavelength of 500 nm. The value obtained was then multiplied by the concentration of the standard solution to obtain the total cholesterol level in the sample.²⁴

Statistical Analysis

The collected data were initially evaluated using the Shapiro–Wilk normality test, as the sample size was fewer than 50. Data were considered normally distributed when the p-value exceeded 0.05. Subsequently, the data were analyzed using one-way analysis of variance (ANOVA), followed by Tukey's post hoc test to assess differences in total cholesterol levels among the experimental groups. A p-value of < 0.05 was considered statistically significant.

Ethical Aspects

This study received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Jenderal Achmad Yani, Cimahi, under approval number 013/UH1.06/2025. All animal procedures were conducted in accordance with ethical standards and the principles of the 3Rs: replacement, reduction, and refinement. Replacement refers to efforts to minimize the use of experimental animals whenever possible. Reduction emphasizes the use of the smallest number of animals necessary to meet statistical requirements, thereby limiting the number of animals involved in the study. Refinement aims to minimize pain, distress, discomfort, and potential harm experienced by the animal subjects.

RESULTS

Based on the results of this study, this section explains the analysis of total cholesterol levels in male Wistar rats receiving the assigned treatments. All rats were housed in cages and grouped according to the treatment administered to facilitate control of feed intake and intervention throughout the study. Daily animal care and cage cleaning were performed to reduce the risk of disease transmission from the surrounding environment. Throughout the treatment period, researchers found no criteria for study dropouts; therefore, total cholesterol levels were measured in all study groups.

The Shapiro-Wilk normality test performed on the data from the five study groups showed that all groups demonstrated a normal distribution ($p > 0.05$), as presented in Table 2. The negative control group (K1) had a p-value of 0.067, the positive control group (K2) had a p-value of 0.563, the ETB 100 mg/kg BW group (K3) showed a p-

value of 0.448, the ETB 200 mg/kg BW showed 0.375, and the comparison group showed 0.392. Thus, the total cholesterol levels across all groups were considered normally distributed, permitting subsequent parametric analysis.

Homogeneity testing was performed using Levene's Test of Homogeneity to assess whether the variances among the groups were homogeneous. This aspect is very important for parametric tests, because unequal variance can interfere with the validity of the analysis results. Therefore, conducting this test allows for a more accurate interpretation of the subsequent analysis and provides a scientific basis for the findings. The obtained significance value (sig. = 0.129) exceeded 0.05, indicating that the variances among the treatment groups were homogeneous and that the assumption of homogeneity of variances was met. The findings of the homogeneity test are summarized in Table 2.

Table 2. The Results of Homogeneity Test

Levene Statistic	df1	df2	Sig.
2.026	4	20	0.129

Therefore, the data analysis was continued using one-way ANOVA test. This analysis was performed to evaluate the effect of ethanolic extract of tamarillo fruit on total cholesterol levels in Wistar rats induced with a high-fat diet and PTU. The results demonstrated a statistically

significant difference in mean total cholesterol levels among the groups, with a p-value of 0.000 ($p < 0.05$) and an ANOVA F-value of 16.42. At a significance level of 5%, significant differences were observed among the five study groups, as presented in Table 3.

Table 3. Total Cholesterol Levels of All Analyzed Groups

Groups	Total Cholesterol Level (mg/dL)	F(Anova)	p-value
	Mean±SD		
Negative control	115.00±8.12	16.42	0.000*
Positive control	148.80±4.86		
Ethanol extract of tamarillo 100 mg/kgBW	148.00±11.95		
Ethanol extract of tamarillo 200 mg/kgBW	142.60±4.50		
Simvastatin 10 mg/kgBW	135.80±6.38		
*) $p<0,05$ (statistically significant difference)			

The results obtained from the one-way ANOVA did not indicate which specific groups differ from one another. Therefore, a post hoc test was performed, the results of which are presented in Table 4.

As shown in the Table 4, the positive control group exhibited the highest mean total cholesterol level among all groups ($148.80 \pm 4.86 \text{ mg/dL}$), indicating the successful induction of hypercholesterolemia through high-fat diet (HFD) and PTU administration. Meanwhile, the group administered ethanolic tamarillo extract (EET) at a dose of 200 mg/kgBW ($142.60 \pm 4.50 \text{ mg/dL}$) demonstrated a lower mean total cholesterol level compared with the positive control group, suggesting that EET administration may effectively inhibit the elevation of total cholesterol levels.

Following the ANOVA analysis, a Tukey post-hoc test was conducted. The negative control group demonstrated highly significant differences compared with all other groups ($p < 0.05$). These findings

indicate that induction with a high-fat diet and PTU significantly increased total cholesterol levels compared with untreated Wistar rats.

Meanwhile, no statistically significant differences were observed between the positive control group and the groups treated with the EET at doses of 100 mg/kgBW and 200 mg/kgBW, or simvastatin at 10 mg/kgBW ($p > 0.05$). This findings suggest that the interventions may have the potential in inhibiting the increase in cholesterol levels induced by a high-fat diet and PTU.

Furthermore, comparisons between the tamarillo extract treatment groups receiving doses of 100 mg/kgBW and 200 mg/kgBW, as well as the simvastatin 10 mg/kgBW group, revealed no statistically significant differences ($p > 0.05$). This indicates that the cholesterol-lowering effect of tamarillo extract at both tested doses was comparable to that of simvastatin, the standard drug control, as shown in Table 4.

Table 4. Results of the Post Hoc Tukey test

Groups	Post Hoc Tukey Test p-value				
	Negative control	Positive control	Ethanol extract of tamarillo 100 mg/kgBW	Ethanol extract of tamarillo 200 mg/kgBW	Simvastatin 10 mg/kgBW
Negative control	-	0.000*	0.000*	0.000*	0.003*
Positive control	0.000*	-	1.000	0.706	0.093
Ethanol extract of tamarillo 100 mg/kgBW	0.000*	1.000	-	0.797	0.126
Ethanol extract of tamarillo 200 mg/kgBW	0.000*	0.706	0.797	-	0.633
Simvastatin 10 mg/kgBW	0.003*	0.093	0.126	0.633	-
*) $p < 0,05$ (statistically significant difference)					

The findings of this study indicated that treatment with ethanolic tamarillo (*Solanum betaceum* Cav.) extract at doses of 100 mg/kgBW and 200 mg/kgBW, as well as treatment with simvastatin, did not produce a statistically significant decrease in total cholesterol levels compared with the positive control group. This finding was reflected in the relatively comparable mean total cholesterol values among all groups, indicating that the administered interventions were insufficient to induce a significant decrease in total cholesterol beyond that observed in rats treated with a high-fat diet and propylthiouracil induction. Consequently, these results suggest that the applied treatments were unable to counteract the hypercholesterolemic condition under the experimental parameters used effectively.

Nevertheless, the observed trend toward lower total cholesterol levels in the extract-treated groups suggests the presence of bioactive constituents in tamarillo that may exert hypolipidemic effects. However, the administered doses did not yet achieved optimal efficacy. Notably, the simvastatin-treated group, which served as the standard therapy, also did not demonstrate a marked difference compared with the positive control group. This suggests that the high-fat diet and propylthiouracil induction likely resulted in a substantial increase in cholesterol levels, which neither tamarillo ethanol extract nor simvastatin could fully mitigate within the study duration. Therefore, further investigations using a wider range of doses and longer treatment durations are necessary to establish the optimal effective dosage for potential clinical use.

DISCUSSION

Administration of a high-fat diet combined with propylthiouracil (PTU) for 14 days elevates blood cholesterol levels. This effect is associated with increased energy intake and lipid accumulation resulting from dietary intervention. In the high-fat diet group, reduced sensitivity to leptin, the

hormone responsible for regulating appetite and satiety may contribute to an increased appetite. High-fat dietary foods contain high levels of triglycerides and cholesterol. In the small intestines, this dietary cholesterol mixes with endogenous cholesterol released from the liver via bile. Free cholesterol also undergoes esterification to form cholesterol esters. This process is integral to the formation of nascent chylomicrons, which contain apolipoprotein B-48 (apoB-48). Chylomicrons are processed in the Golgi body and then secreted into the enterocyte lateral side, passing through the thoracic duct and lymphatic vessels, eventually entering the bloodstream. These nascent chylomicrons contain apoB-48, apoA-I, apo-IV, and apoC-I, with apoE obtained from HDL in the lymph and blood.^{1,13}

The high-fat diet given to the experimental Wistar rats was specially formulated by PT. Surya Sains Indonesia to induce dyslipidemia, thereby mimicking the metabolic state in humans. This diet has been widely used in experimental studies to promote significant changes in the lipid profile of Wistar rats. Mechanistically, PTU is a compound commonly used to treat hyperthyroidism. It acts by interfering with the oxidation of iodide ions and iodotyrosyl groups through the inhibition of peroxidase enzymes in peripheral tissues; furthermore, propylthiouracil also inhibits the deiodination of thyroxine into triiodothyronine. When thyroid hormone levels drop, cholesterol catabolism decreases, leading to an increase in blood cholesterol levels.^{14,20}

Phytochemical investigation of tamarillo fruit indicates that the ethanolic extract contains various chemical compounds, including flavonoids. Phenolic compounds, particularly phenolic and anthocyanins have been proven to have significant antioxidant activity. Tamarillo contains various phenolic compounds, including hydroxycinnamic acids such as caffeic, ferulic, p-coumaric, and rosmarinic acids, as well as hydroxybenzoic acids like gallic and vanillic acids.

In addition, flavonols (e.g., kaempferol) and flavanones (e.g., naringin) have also been identified. These antioxidant compounds are believed to play an important role in contributing to beneficial health effects, including protective activity against oxidative stress (antioxidant), as well as offering potential anti-obesity, anti-cancer, and antimicrobial agent, and lipid-protective properties.^{12,25}

Administration of the tamarillo fruit ethanolic extract at doses of 100 and 200 mg/kgBW for 14 days did not demonstrate a statistically significant reduction in total cholesterol levels compared with the positive control group. Although a descriptive decrease in mean cholesterol levels was observed, the reduction was not sufficient to produce a significant difference under the conditions of this study. These findings differ from previous studies conducted by Masbintoro et al. (2016) and Abdul Kadir et al. (2015), which reported that tamarillo extract significantly reduced blood cholesterol levels in experimental rats.¹⁶ The differences in results may be influenced by variations in the induction model, duration of treatment, dosage, extract preparation, and the severity of hypercholesterolemia induction used in each study.

Tamarillo fruit was selected as the primary subject of this study because previous studies have suggested that it contains bioactive compounds with antioxidant and potential hypolipidemic properties, particularly flavonoids and anthocyanins. A study conducted by Rito reported that tamarillo fruit demonstrated antioxidant activity of 64.99%.^{10,11} However, phytochemical analysis was not performed in the present study; therefore, the specific bioactive compounds and their concentrations in the tamarillo ethanolic extract could not be identified. This limitation may have affected the consistency and reproducibility of the extract's biological activity in lowering total cholesterol levels.

In contrast, studies conducted by Abdul Kadir et al. and Sandhiutami et al. demonstrated that tamarillo, administered in

various forms and dosages, significantly reduced total cholesterol levels. These discrepancies may be attributed to differences in dosage and duration of administration, as well as variations in animal species and physiological conditions, all of which may influence the effectiveness of bioactive compounds in lowering total cholesterol levels.^{1,16}

Although this study contributes to the understanding of the potential of tamarillo (*Solanum betaceum* Cav.) ethanolic extract in lowering total cholesterol levels, several limitations need to be considered. To date, the optimal concentration of tamarillo fruit ethanolic extract for maximum cholesterol-lowering effect has not been determined. This study only used two dosage variations, specifically 100 mg/kgBW and 200 mg/kgBW; therefore, it does not fully depict a broader dose-response relationship. Additionally, there are currently no comprehensive toxicological studies on the safe consumption limits of tamarillo extract, whether in form of fresh fruit or as an ethanolic extract. Hence, the long-term safety of its use in humans still requires further research.

Previous studies have indeed shown that the ethanolic extract of tamarillo fruit is rich in bioactive compounds such as flavonoids, phenolics, anthocyanins, and vitamins, which act as antioxidants and are believed to contribute to cholesterol-lowering effects. However, the extent of variation in the content of these active compounds can be influenced by environmental factors, plant variety, and the extraction method used. This can lead to differences in results between studies and poses a challenge for dosage standardization. Therefore, further research is needed to evaluate the optimal dose of tamarillo fruit ethanolic extract, as well as to conduct acute and chronic toxicity tests to ensure its safety. Additionally, further pharmacodynamic and pharmacokinetic studies are crucial to support the development of tamarillo fruit ethanolic extract as an effective and safe alternative therapy for hyperlipidaemia in humans.

CONCLUSION

This study demonstrated that the administration of tamarillo (*Solanum betaceum* Cav.) ethanolic extract at doses of 100 mg/kgBW and 200 mg/kgBW did not lead to a statistically significant reduction in total cholesterol levels in male Wistar rats that were subjected to a high-fat diet and propylthiouracil treatment. Although a decreasing trend in mean total cholesterol levels was observed, particularly at the 200 mg/kg BW dose, this reduction was not significantly different when compared to the positive control group. Additionally, the cholesterol-lowering effect of the tamarillo ethanolic extract was not significantly different from that of simvastatin at a dose of 10 mg/kg BW. While the extract-treated groups displayed a tendency towards lower mean total cholesterol levels, especially at the higher dose, their effectiveness cannot be equated with that of the standard therapy. Therefore, while tamarillo ethanolic extract may have potential as an adjunct treatment for hypercholesterolemia, it cannot currently replace simvastatin as a primary therapeutic agent.

ACKNOWLEDGEMENTS

The author would like to express profound gratitude to all those who have supported this research, particularly the author's parents, whose financial and emotional support made the completion of this research possible. Sincere appreciation is also extended to the professionals who assisted in the preparation and execution of the experiments, including colleagues, supervisors, and laboratory assistants at the Biochemistry, Animal, Pharmacology, and Clinical Pathology Laboratories of the Faculty of Medicine, Universitas Jenderal Achmad Yani. Finally, the author acknowledges everyone else who contributed to the successful completion of this work.

DECLARATION OF INTERESTS

The author hereby declares that there is no potential conflict of interest related to this

research.

FUNDING

This study did not receive any financial support from any external sources.

REFERENCES

1. Dwi Sandhiutami NM, Khairani S, Moordiani M, Purpranoto IN. *Efek sari buah terong belanda (Solanum betaceum Cav.) terhadap perubahan profil lipid pada mencit dislipidemia*. Pharmacy: Jurnal Farmasi Indonesia. 2021;18(2):226–233.
2. Aman AM, Soewondo P, Soelistijo SA, Arsana PM. *Pedoman pengelolaan dislipidemia di Indonesia 2021*. PB PERKENI. 2021.
3. World Health Organization. Global Health Observatory data: cholesterol. Geneva: WHO; 2024. Available from: http://www.who.int/gho/ncd/risk_factors/cholesterol_text/en/
4. *Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan RI. Laporan Nasional Risetdas 2018*. Jakarta: Kemenkes RI; 2019.
5. Expert Panel on Detection E and T of HBC in A. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA: The Journal of the American Medical Association 2001;285(19):2486–2497.
6. Kandi V, Vadakedath S. Clinical trials and clinical research: a comprehensive review. Cureus. 2023;15(2):e35040.
7. Karam I, Yang YJ, Li JY. Hyperlipidemia: background and progress. SM J Cardiol Cardiovasc Disord. 2017;3(2):1–6.
8. Wayan N, Dewi OAC. Antioxidant activity of ethanol extracts of tamarillo peel, pulp, and seeds. In: Prosiding Seminar Nasional Pendidikan dan Sains Kimia (SNP-SK) FKIP-Undana 2020;3(1):117–120.

9. Rahmawati RP, Retnowati E, Devi RK. In vitro antioxidant activity of ethanolic extract of tamarillo peel. *Indonesian Journal of Pharmacy*. 2021;5(2):1–7.
10. Pratama DR, Purwati E, Yuherman, Melia S. The potential of probiotic frozen yoghurt with the addition of fruits tamarillo to increase immunity. *IOP Conf Ser Earth Environ Sci*. 2021;694(1):012070.
11. Rito M, Marques J, Costa RMF, et al. Antioxidant potential of tamarillo fruits: chemical and infrared spectroscopy analysis. *Antioxidants*. 2023;12(2):536.
12. Diep T, Pook C, Yoo M. Phenolic and Anthocyanin Compounds and Antioxidant Activity of Tamarillo (*Solanum betaceum* Cav.). *Antioxidants (Basel)* 2020;9(2):169.
13. Pereira RO, Correia LA, Farah D, Komoni G, Farah V, Fiorino P. Wistar rat as an animal model to study high-fat induced kidney damage: a systematic review. *Arch Physiol Biochem* 2024;130(2):205–214.
14. Amisha F, Rehman A. Propylthiouracil (PTU). StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
15. Yang W, Wu D, Zhang R, Deng Q, Ding H, Tian Y. Effects of propylthiouracil-induced hypothyroidism on nonalcoholic fatty liver disease in rats fed a high-fat and high-cholesterol diet. *Pak Vet J* 2015;35(1):1–6.
16. Abdul Kadir NAA, Rahmat A, Jaafar HZE. Protective effects of tamarillo (*Cyphomandra* extract against high fat diet induced obesity in sprague-dawley rats. *J Obes* 2015;2015:1–8.
17. Masbintoro A, Agustini SM, Thontowi D. Effect of tamarillo (*Solanum betaceum*) fruit extract as an antioxidant on malondialdehyde levels in white rats (*Rattus norvegicus*) induced by CCl₄. *Saintika Medika*. 2016;12(1):38–44.
18. Hakim AR, Saputri R. Optimization of ethanol as a solvent for flavonoid and phenolic compounds: a narrative review. *J Surya Medika*. 2020;6(1):177–180.
19. Dwi Sandhiutami NM, Khairani S, Moordiani M, Purpranoto IN. Effect of tamarillo (*Solanum betaceum* Cav.) juice on changes in lipid profile in dyslipidemic mice. *Pharmacy: Jurnal Farmasi Indonesia (Pharmaceutical Journal of Indonesia)*. 2021;18(2):226–233.
20. Prawitha Pinatih PT, Dewi NNA, Sutadarma IWG. Effects of high-fat diet feeding on lipid profile in rats. *E-Jurnal Medika Udayana*. 2022;11(10):21–27.
21. Wulandari RL, Susilowati S, Asih M. Combination of soursop leaf extract and simvastatin on lipid profile in rats fed a high-fat diet. *J Ilmu Farmasi dan Farmasi Klinik*. 2015;12(2):24–32.
22. Astiti Asih IAR, Manuaba IBP, Berata K, Rita WS, Suirta W. In vivo evaluation of antioxidant activity of flavonoid glycoside extract from tamarillo (*Solanum betaceum* Cav.). *IOP Conf Ser Earth Environ Sci*. 2023;1:12–39.
23. Djufry F, Limbongan J, Lade N, Saranga B. Characterization of tamarillo plant in South Sulawesi. *Buletin Plasma Nutfah*. 2016;22(2):127–136.
24. McPherson RA, Pincus MR. Henry's clinical diagnosis and management by laboratory methods. 24th ed. Philadelphia: Elsevier; 2021.
25. Miranda J, Eseberri I, Lasa A, Portillo MP. Lipid metabolism in adipose tissue and liver from diet-induced obese rats: a comparison between Wistar and Sprague-Dawley strains. *J Physiol Biochem* 2018;74(4):655–666.