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THE EFFECT OF LANTANA CAMARA LEAF BOLING ON LDL-C AND HDL-C LEVELS IN WISTAR RATS FEED WITH A HIGH FAT DIET

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ABSTRACT

Background: Hypercholesterolemia, especially increased low-density lipoprotein cholesterol (LDL-C), is an important risk factor for cardiovascular disease. Lantana camara (komba-komba) contains bioactive compounds such as flavonoids and phenolics that have antioxidant activity and have the potential as hypolipidemic agents. Objective: This study aims to analyze the effect of Lantana camara leaf decoction on LDL-C and high-density lipoprotein cholesterol (HDL-C) levels in Wistar rats induced by a high-fat diet. Method: The study used a randomized pretest–posttest controlled pure experimental design. A total of 25 male Wistar rats were divided into five groups, namely negative control, positive control with simvastatin 10 mg/kgBW, and treatment groups with Lantana camara decoction doses of 250, 500, and 750 mg/kgBW. The intervention was given orally for three weeks. LDL-C and HDL-C levels were measured before and after the intervention using a colorimetric enzymatic method and analyzed using ANOVA and further tests with a significance level of $p<0.05$. Results: Lantana camara decoction showed a decrease in LDL-C, with the largest decrease at a dose of 750 mg/kgBW (Δ −86.6 mg/dL), followed by doses of 500 mg/kgBW (Δ −76.8 mg/dL) and 250 mg/kgBW (Δ −40.0 mg/dL). Significant differences compared to the negative control were found at doses of 500 and 750 mg/kgBW. However, there was no significant increase in HDL-C in the treatment group. Conclusion: Lantana camara leaf decoction has the potential to reduce LDL-C levels in rats with hyperlipidemia due to a high-fat diet, especially at doses of 500 and 750 mg/kgBW, but has not shown effectiveness in increasing HDL-C.

Kata Kunci:
Lantana Camara;
HDL-C;
LDL-C;
Hiperkolesterolemia

ABSTRAK

Latar Belakang: Hiperkolesterolemia, terutama peningkatan low-density lipoprotein cholesterol (LDL-C), merupakan faktor risiko penting penyakit kardiovaskular. *Lantana camara* (komba-komba) mengandung senyawa bioaktif seperti flavonoid dan fenolik yang memiliki aktivitas antioksidan dan berpotensi sebagai agen hipolipidemik. Tujuan: Penelitian ini bertujuan menganalisis pengaruh rebusan daun *Lantana camara* terhadap kadar LDL-C dan high-density lipoprotein cholesterol (HDL-C) pada tikus Wistar yang diinduksi diet tinggi lemak. Metode: Penelitian menggunakan desain eksperimen murni randomized pretest–posttest controlled. Sebanyak 25 ekor tikus Wistar jantan dibagi menjadi lima kelompok, yaitu kontrol negatif, kontrol positif dengan simvastatin 10 mg/kgBB, serta kelompok perlakuan rebusan *Lantana camara* dosis 250, 500, dan 750 mg/kgBB. Intervensi diberikan secara oral selama tiga minggu. Kadar LDL-C dan HDL-C diukur sebelum dan sesudah intervensi menggunakan metode enzimatik kolorimetrik dan dianalisis menggunakan ANOVA serta uji lanjut dengan tingkat kemaknaan $p<0,05$. Hasil: Pemberian rebusan *Lantana camara* menunjukkan penurunan LDL-C, dengan penurunan terbesar pada dosis 750 mg/kgBB (Δ −86,6 mg/dL), diikuti dosis 500 mg/kgBB (Δ −76,8 mg/dL) dan 250 mg/kgBB (Δ −40,0 mg/dL). Perbedaan signifikan terhadap kontrol negatif ditemukan pada dosis 500 dan 750 mg/kgBB. Namun, tidak terdapat peningkatan HDL-C yang signifikan pada kelompok perlakuan. Kesimpulan: Rebusan daun *Lantana camara* berpotensi menurunkan kadar LDL-C pada tikus dengan hiperlipidemia akibat diet tinggi lemak, terutama pada dosis 500 dan 750 mg/kgBB, tetapi belum menunjukkan efektivitas dalam meningkatkan HDL-C.

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INTRODUCTION

Lipid metabolism disorders are a key factor contributing to an increased risk of cardiovascular disease. Dyslipidemia is generally characterized by elevated levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides, or decreased levels of high-density lipoprotein cholesterol (HDL-C). These lipid abnormalities are closely linked to the formation and progression of atherosclerosis, the primary pathological process in various cardiovascular diseases, including coronary heart disease, myocardial infarction, and stroke (Wazir, M., 2023). High LDL-C can enter the intimal layer of blood vessels and undergo oxidation, then trigger an inflammatory response, the formation of foam cells, and the development of atherosclerotic plaques (Higashi, 2023).

Dyslipidemia is also associated with impaired endothelial function. Impaired endothelium exhibits decreased nitric oxide (NO) bioavailability, increased adhesion molecule expression, and increased oxidative stress and inflammation. LDL oxidation can inhibit the endothelial nitric oxide synthase/nitric oxide (eNOS/NO) pathway, thereby causing impaired vasodilation and accelerating atherogenesis (Higashi, 2023). Persistent endothelial damage can lead to structural changes in blood vessel walls, increased arterial stiffness, and impaired regulation of vascular tone. Therefore, lipid profile management is an important approach to reducing the risk of cardiovascular disease (Wazir, M., 2023; Higashi, 2023).

A high-fat diet, particularly one rich in saturated fatty acids and trans fats, is one factor that can affect lipid metabolism. This intake can increase LDL-C levels and worsen the atherogenic lipoprotein profile. Conversely, replacing saturated fat with unsaturated fat has the potential to improve lipid profiles and reduce cardiovascular risk (Maki, 2021; Christensen et al., 2024). Thus, a high-fat diet can be used as an experimental approach to induce changes in lipid metabolism in experimental animals, although the biological response may be influenced by diet composition, duration of administration, animal species, and metabolic condition.

In addition to causing changes in lipid profiles, a high-fat diet can also increase oxidative stress and trigger endothelial dysfunction. Animal models of high-fat diet-induced metabolic disorders have shown a link between dyslipidemia, increased vascular oxidative stress, inflammation, and impaired endothelial function (Ionică, 2021). Increased production of reactive oxygen species (ROS) can lead to lipid oxidation, activation of inflammatory pathways, decreased NO bioavailability, and altered vascular responses. Therefore, interventions that improve lipid profiles while also possessing antioxidant activity have the potential to provide benefits in preventing or managing cardiovascular disease risk.

The use of natural ingredients as sources of bioactive compounds to help control lipid metabolism disorders and oxidative stress is increasingly being researched. One plant with potential for development is the komba-komba plant (Lantana camara L.). This plant is known to contain various secondary metabolites, such as flavonoids, phenolic compounds, triterpenoids, terpenoids, phenolic acids, and iridoid glycosides (El-Din et al., 2022; Rincón-Ramos et al., 2025). The presence of this group of compounds is thought to contribute to various biological activities, including antioxidant and anti-inflammatory activities.

The antioxidant activity of L. camara extract has been reported through various testing methods . El-din et al., (2022) identified various compounds from the methanol extract of L. camara leaves, including terpenoids, flavonoids, iridoid glycosides, and phenolic compounds. The extract showed DPPH, ABTS, and superoxide anion scavenging activity with IC_{50} values of 34.01 ± 1.32 µg/mL, 30.73 ± 1.42 µg/mL, and 1.57 ± 0.19 µg/mL, respectively. These findings support the hypothesis that secondary metabolites, especially phenolic and flavonoid compounds, contribute to the antioxidant capacity of L. camara.

Research conducted in Indonesia also shows the antioxidant potential of L. camara leaves. Khairan, K., (2024) reported that the ethanol extract of L. camara leaves has DPPH and ABTS radical scavenging activity with IC_{50} values of 140 ppm and 163 ppm, respectively. The study also showed the presence of metabolites from the terpenoid and fatty acid groups and potential activities related to inflammation and oxidoreductase processes. However, it should be noted that the results of antioxidant activity are highly dependent on the plant part, growing location, extraction method, type of solvent, extract concentration, and testing method used.

Although the antioxidant activity of L. camara has been reported, most previous studies used extracts or fractions obtained through extraction processes with specific solvents, such as methanol or ethanol. Evidence regarding the effect of L. camara leaf decoction using water as a simple solvent on lipid profiles, especially in conditions of lipid metabolism disorders due to a high-fat diet, is still limited. Differences in preparation methods can affect the type and amount of bioactive compounds extracted.

Therefore, the antioxidant activity obtained from L. camara organic extracts or fractions cannot be directly assumed to have the same effect as water decoctions of L. camara leaves. Research using water decoctions is needed to obtain more relevant evidence for simple preparations that have the potential to be used in traditional medicine.

In addition to its biological activity, the use of L. camara as an interventional agent requires consideration of safety aspects. This plant contains various secondary metabolites, including the pentacyclic triterpenoids lantadene A and lantadene B, which have been associated with toxic effects in livestock. Exposure to L. camara in herbivorous animals has been reported to cause liver disorders, jaundice, photosensitization, and damage to certain organs (Ramírez et al., 2025). Therefore, the use of L. camara leaves as a herbal ingredient needs to be done carefully by considering the dose, plant part, preparation method, duration of administration, and available toxicological evidence.

On the other hand, the results of toxicological evaluations of certain extracts do not always indicate the same level of risk. Khairan, K., (2024) reported that the ethanol extract of L. camara leaves had an LC_{50} value of 574 ppm in the brine shrimp lethality assay and was predicted to be inactive against several toxicological parameters, such as hepatotoxicity, carcinogenicity, mutagenicity, and cytotoxicity. However, these results are an initial evaluation of the ethanol extract and cannot yet be used to conclude the safety of L. camara leaf water decoction in experimental animals or humans. Thus, the use of water decoction in this study is a relevant approach to explore the potential traditional uses of the plant, but does not eliminate the need for further evaluation of toxicity, organ safety, and effective doses.

Based on the description above, there is a research gap in the form of limited experimental evidence regarding the effect of Lantana camara leaf water decoction on lipid profiles under high-fat diet conditions. This study was conducted to evaluate the effect of L. camara leaf water decoction on lipid profile parameters, especially total cholesterol, LDL-C, HDL-C, and triglyceride levels in experimental animals fed a high-fat diet. The hypothesis of this study is that L. camara leaf water decoction can improve lipid profiles under high-fat diet conditions. The results of this study are expected to provide initial evidence regarding the potential of L. camara leaf water decoction as a source of natural ingredients that have the potential to support the control of lipid metabolism disorders, as well as serve as a basis for further research regarding the mechanism of action, effective dosage, preparation standardization, and safety aspects.

METHOD

Type of Research

This study was a controlled experimental study with a randomized pretest–posttest controlled experimental design involving five parallel groups of Wistar rats. The study was conducted to evaluate the effect of Lantana camara leaf decoction on lipid profiles, specifically LDL and HDL levels, in Wistar rats induced by a high-fat diet. The research was conducted at the Biomedical Laboratory of the Faculty of Medicine, Halu Oleo University. The experimental unit was a single Wistar rat, with LDL and HDL levels measured in the serum of each rat.

Experimental Animals

The experimental animals used were 25 Wistar rats aged 6–8 weeks with a body weight of 250–300 g. The rats were male. The rats were obtained from the Animal Care Section of the Biomedical Laboratory of Haluoleo University. Inclusion criteria included Wistar rats aged 6–8 weeks, weighing 250–300 g, in good health, active, and showing no signs of disease during the acclimatization period. Exclusion criteria included rats experiencing illness, injury, severe decline in general condition, or death before the start of the intervention. The termination criteria (humane endpoint) were determined based on a decline in general condition, severe weight loss, and impaired mobility. Prior to treatment, all rats underwent a 14-day acclimatization period. During this period, the rats were fed standard feed and their health was monitored.

Cage Maintanance and Condition

Mice were kept in laboratory conditions at a room temperature of 20°C–24°C, relative humidity ranging from 45%–65%, and a light-dark cycle of 12 hours of light (06.00–18.00) and 12 hours of darkness (18.00–06.00). The mice were placed in cages at a density of 5 adults per cage to prevent stress due to overcrowding, with access to standard feed provided *ad libitum* (always available). Drinking water using reverse osmosis (RO) water was provided through a special drinking bottle *ad libitum*.

A standard diet was provided during the acclimatization period. After the acclimatization period, the mice were fed a high-fat diet for seven weeks according to the hyperlipidemia induction protocol used in the study. The composition of the high-fat diet consisted of 25% coconut oil, 1% pure (endogenous) cholesterol, and duck egg yolk, with an energy content of 3.8–4.2 kcal/g and a proportion of energy derived from fat of 35%–45%. The diet was prepared by the UHO Biomedical Laboratory, with the amount of food given at 20 grams per head per day for 14 days.

Determination and Distribution of Samples

A total of 25 Wistar rats were divided into five groups, each consisting of five rats. The group division used a simple block method with the help of Excel or a randomization website, taking into account initial body weight to reduce potential bias in the placement of animals into study groups.

The five research groups consist of:

1. Simvastatin control group (KS): 5 mice were given a high-fat diet and the appropriate dose of simvastatin10 mg/kgBW.
2. Negative control group (KN): 5 mice were given a high-fat diet without pharmacological intervention or Lantana camara decoction.
3. Treatment group 1 (KP-1): 5 mice were given a high-fat diet and boiled Lantana camara leaves at a dose of 250 mg/kgBW.
4. Treatment group 2 (KP-2): 5 mice were given a high-fat diet and boiled Lantana camara leaves at a dose of 500 mg/kgBW.
5. Treatment group 3 (KP-3): 5 mice were given a high-fat diet and boiled Lantana camara leaves at a dose of 750 mg/kgBW.

The intervention was administered for three weeks after the hyperlipidemia model was established. The intervention was administered daily (in the morning) at 9:00 a.m., via oral tube, with a volume of 1–2 mL/day (based on body weight and dosage for each group). It was administered 1–2 hours after feeding.

Sample Size Calculation

A total of five mice were used in each research group, so the total number of animals was 25. The basis for determining the sample size was the Resource Equation Method, with error degrees of freedom (DF) of 20.

Preparation of Lantana Camara Decoctio

Lantana camara (komba-komba) leaves were obtained from the Kendari region of Southeast Sulawesi. The collected leaves were cleaned to remove dirt, then dried and cut into smaller pieces. One kilogram of fresh, chopped Lantana camara leaves was then boiled in a 1:10 ratio of water to plant material for 15–30 minutes. After the boiling process was complete, the solution was allowed to cool to room temperature and then filtered. Fresh decoction or stock solution was prepared weekly and stored in the refrigerator at 4°C. The resulting decoction was used as an intervention material according to the treatment doses, namely 250, 500, and 750 mg/kgBW. The dosage was calculated based on the concentration of the final solution prepared.

Lipid Profile Measurement

LDL and HDL levels were used as the primary parameters of the study. Initial measurements were taken on day 14 after the high-fat diet was administered to evaluate the success of the hyperlipidemia model. A second measurement was taken on day 32 after three weeks of Lantana camara leaf decoction.

Prior to blood sampling, mice were fasted for 10–12 hours with continued access to drinking water. Blood samples were taken from the retro-orbital plexus (posterior orbital sinus) using a lateral approach. The blood was then processed to obtain serum by centrifugation at 4,000 × g for 15 minutes. The serum was stored at −20°C until analysis.

Serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels were measured using a colorimetric enzymatic method. The test was performed using the commercial HDL-c direct FS and LDL-c direct FS kits (Glory Diagnostics). The absorbance of the sample was read using a Jenway UV-Vis spectrophotometer at a wavelength of 500 nm. All measurement procedures were performed according to the protocol recommended by the kit manufacturer. Lipid levels are expressed in mg/dL.

Randomization and Building

The division of mice into research groups was done randomly using a randomization website with the help of Excel. LDL and HDL levels were measured blindly.

Endpoint and Euthanasia

The endpoint of the study was the change in LDL and HDL levels between before and after the intervention in each group. Throughout the study, the animals' general condition and health were monitored periodically. After all research procedures were completed, the mice were euthanized using the inhalation anesthesia overdose method. This method has received Ethical Approval with No. DP.04.03/e-KEPK.1/636/2024.

Data Analysis

Data were analyzed using IBM SPSS Statistics 25 software. Continuous variables are presented as mean ± standard deviation (SD) if they meet the normal distribution assumption or as median and interquartile range (IQR) if they do not meet the assumption.

Data distribution was tested using the Shapiro–Wilk test, while homogeneity of variance was evaluated using Levene's test. Because LDL and HDL levels were measured in the same animals at two time points, before and after the intervention, the effects of treatment group, measurement time, and the interaction between group and time were analyzed using two-way repeated-measures ANOVA if the analysis assumptions were met. If significant main effects or interactions were found, the analysis was continued with Bonferroni-adjusted pairwise comparison tests. Effect sizes and 95% confidence intervals were reported when calculated based on the available data. A two-sided p-value <0.05 was set as the limit for statistical significance.

RESULT

Level Low Density Lipoprotein- Cholesterol (LDL-C)and and High Dnsity Lipoprotein Cholesterol (HDL-C)

LDL measurements in this study aimed to determine cholesterol levels between groups. The sample consisted of five groups: the Negative Control Group (NC), the Simvastatin Group (CS), the Treatment Group (KP-1), KP-2, and KP-3. Measurements were conducted twice: before the intervention and on the 21st day of the intervention.

Table 1. Mean + SEM Level *LDL-C* And HDL- Cexperimental animals based on the measurement day for each group.

Group	LDL Measurement I (mg/dL)	LDL Measurement II (mg/dL)	Δ LDL (mg/dL)	HDL Measurement I (mg/dL)	HDL Measurement II (mg/dL)	Δ HDL (mg/dL)
KN	156.8 ± 2.8	203.4 ± 2.7	**46.6**	44.6 ± 17.90	15.6 ± 1.5	**-29**
KS	170.4 ± 3.0	91.0 ± 10.6	**-79.4**	43.8 ± 22.97	85.2 ± 2.2	**41.4**
KP-1	166.6 ± 3.5	126.6 ± 7.1	**-40**	45.6 ± 19.58	20.2 ± 4.4	**-25.4**
KP-2	164.8 ± 3.7	88.0 ± 4.0	**-76.8**	44.0 ± 25.51	22.6 ± 2.8	**-21.4**
KP-3	170.4 ± 3.9	83.8 ± 6.6	**-86.6**	43.2 ± 26.61	18.8 ± 1.39	**-24.4**

Based on Table 1, in measurement II, all treatment groups (KP-1, KP-2, KP-3) and the positive control group (KS) showed a decrease in LDL levels compared to measurement I, with the largest decrease in KP-3 (Δ = -86.6 mg/dL). In contrast, the negative control group (KN) experienced an increase in LDL levels (Δ = +46.6 mg/dL). Description of HDL levels: The KS group showed the most striking increase in HDL levels (Δ = +41.4 mg/dL). The KN group and all treatment groups (KP-1, KP-2, KP-3) actually experienced a decrease in HDL levels, with the smallest decrease in KP-2 (Δ = -21.4 mg/dL) and the largest in KN (Δ = -29.0 mg/dL). In general, the treatment group showed an LDL-lowering effect that was close to the effect of Simvastatin (KS), but the effect on HDL was still variable and tended to decrease, except for KS, which increased.

Table 2. Significance between groups in changes in LDL levels in the treatment group and control group in measurement I

GROUP	KN	KS	KP-1	KP-2	KP-3
KN		0.11	0.57	1.0	0.11
KS	0.11		1.00	1.00	1.00
KP-1	0.57	1.00		1.00	1.00
KP-2	1.00	1.00	1.00		1.00
KP-3	0.11	1.00	1.00	1.00	

* p= <0.05

Table 3. Significance between groups in changes in LDL levels in the treatment group and control group in measurement II.

GROUP	KN	KS	KP-1	KP-2	KP-3
KN		0.001*	1.00	0.002*	0.001*
KS	0.001*		0.00*	1.00	1.00
KP-1	1.00	0.00*		0.001*	0.001*
KP-2	0.002*	1.00	0.001*		1.00
KP-3	0.001*	1.00	0.001*	1.00	

* p= <0.05

Table 4. Significance between groups in changes in HDL levels in the treatment group and control group in measurement I

GROUP	KN	KS	KP-1	KP-2	KP-3
KN		1.00	1.00	1.00	1.00
KS	1.00		1.00	1.00	1.00
KP-1	1.00	1.00		1.00	1.00
KP-2	1.00	1.00	1.00		1.00
KP-3	1.00	1.00	1.00	1.00	

* p= <0.05

Table 5. Significance between groups on changes in levelsHDL in the treatment group and control group in measurement II.

GROUP	KN	KS	KP-1	KP-2	KP-3
KN		0.00*1	1.00	1.00	1.00
KS	0.001*		0.001*	0.001*	0.001*
KP-1	1.00	0.001*		1.00	1.00
KP-2	1.00	0.001*	1,000		1.00
KP-3	1.00	0.001*	1.00	1.00	

* p= <0.05

The table above shows that there are differences in the KS group (Simvastatin control) with KN and all treatment groups.

DISCUSSION

This study used five treatment groups, namely negative control (KN), positive control/simvastatin (KS), and three Lantana camara extract dose groups (KP-1, KP-2, KP-3), with LDL and HDL levels measured at two time points (Measurement I and Measurement II). The results in Table 1 show a fairly consistent pattern: all groups receiving the intervention (KS, KP-1, KP-2, KP-3) experienced a decrease in LDL levels at measurement II compared to measurement I, while the negative control group (KN) actually showed a sharp increase in LDL (Δ = +46.6 mg/dL). The opposite pattern occurred in the HDL parameter, where only the KS group showed an increase (Δ = +41.4 mg/dL), while the KN and all extract treatment groups actually experienced a decrease in HDL.

The progressive and dose-dependent reduction in LDL levels in groups KP-1 (Δ = -40 mg/dL), KP-2 (Δ = -76.8 mg/dL), and KP-3 (Δ = -86.6 mg/dL) indicates a dose-dependent relationship between Lantana camara extract administration and LDL reduction. Even at the highest dose (KP-3), the effect exceeded that of the simvastatin group (KS, Δ = -79.4 mg/dL). The inter-group significance test in measurement II (Table 3) confirmed this finding: KN was significantly different from KS, KP-2, and KP-3 ($p < 0.05$), while KP-1 was not significantly different from KN, indicating that the hypolipidemic effect of the extract only appeared significantly at medium and high doses. The absence of significant differences between groups in measurement I (Table 2) confirmed that the initial conditions of all groups were relatively homogeneous before the intervention, so that changes in measurement II could be attributed to the treatment effect.

These findings are consistent with the mechanisms of action of flavonoids and phenolic compounds that have been widely reported in Lantana camara plants. Recent phytochemical studies confirm that L. camara flowers and leaves are rich in polyphenolic compounds, especially flavonoids and phenolic acid derivatives, with strong antioxidant activity, demonstrated by the high percentage of DPPH radical inhibition in methanolic extracts (da Fonseca, AM, 2023). The flavonoid, triterpenoid, and phenolic compounds in L. camara have also been reported to play an important role in antioxidant activity by scavenging free radicals and reducing oxidative stress (Shehzadi & Noreen, 2025; Ramírez et al., 2025). Mechanistically, flavonoids are known to reduce LDL levels through at least three pathways: (1) inhibition of the HMG-CoA reductase enzyme, thereby suppressing endogenous cholesterol biosynthesis, (2) inhibition of VLDL synthesis at the transcriptional level, which helps stabilize plasma LDL levels, and (3) activation of the lecithin-cholesterol acyltransferase (LCAT) enzyme, which accelerates serum cholesterol clearance (Laka et al., 2022).

Inhibition of HMG-CoA reductase by plant phenolic and flavonoid compounds also leads to increased expression of LDL receptors in hepatocytes, accelerating the uptake of LDL from the circulation, a mechanism that is principally similar to the mode of action of statins, including simvastatin, which was used as a positive control in this study (Laka et al., 2022). Similar dose-dependent effect patterns were also reported for various other plant extracts on high-fat diet-induced rats, for example Cassia fistula fruit extract significantly reduced LDL and increased HDL in hyperlipidemic rats (Tariq et al., 2024), as well as methanolic extract of Averrhoa carambola which lowers serum lipids in a dose-dependent manner through inhibition of HMG-CoA reductase and pancreatic lipase activity.

In contrast to the pattern on LDL, the effect of Lantana camara extract on HDL did not show the expected results. All treatment groups (KP-1, KP-2, KP-3) actually experienced a decrease in HDL in the second measurement, although the decrease was relatively smaller compared to the negative control group (KN, Δ = -29 mg/dL), with the smallest decrease in KP-2 (Δ = -21.4 mg/dL). Only the simvastatin (KS) group managed to increase HDL significantly. The significance test in the second measurement (Table 6) showed that significant differences occurred mainly between KS and all other groups (KN, KP-1, KP-2, KP-3; $p < 0.05$), while there were no significant differences between the extract treatment groups and KN itself, indicating that L. camara extract at the tested dose range was not able to produce an HDL-increasing effect equivalent to simvastatin.

These findings align with several reports in the literature that the effects of phytochemicals on HDL tend to be more variable and inconsistent than their effects on LDL. For example, naringin—a flavonoid glycoside—has been reported to significantly lower plasma cholesterol, LDL, and triglycerides, but without significantly altering HDL levels in animal models (Laka et al., 2022). This indicates that the metabolic pathways that influence LDL catabolism (through HMG-CoA reductase inhibition and LDL receptor up-regulation) are not always identical to the pathways that regulate HDL biogenesis and maturation, which involve more of the enzymes lecithin-cholesterol acyltransferase (LCAT), cholesteryl ester transfer protein

(CETP), and ATP-binding cassette transporter A1 (ABCA1). Alternatively, the decrease in HDL in the treatment group may also be related to the effects of a high-fat diet that persisted during the intervention period, so that the lipoprotein remodeling process in the liver had not fully recovered even though LDL levels had improved. Variations in HDL responses to plant extracts in a high-fat diet model have also been reported in studies of andaliman (Zanthoxylum acanthopodium) fruit extract, which significantly reduced total cholesterol, triglycerides, and LDL, but its effect on HDL was inconsistent across all test doses.

Comparison with the KS group provides important insights into the position of Lantana camara extract as a potential hypolipidemic agent. For LDL parameters, the highest dose of the extract (KP-3) demonstrated numerically equivalent or even slightly superior efficacy compared to simvastatin, and was not statistically significantly different from KS (Table 3). However, for HDL parameters, simvastatin remained significantly superior compared to all extract groups (Table 6). This pattern suggests that the mechanism of action of L. camara extract is likely more dominant in the inhibition of cholesterol biosynthesis and reduced absorption pathway (affecting LDL) than in the enhancement of reverse cholesterol transport, which underlies the HDL increase induced by statins. Statins such as simvastatin are known to increase HDL, among other things, by increasing apolipoprotein A1 expression and LCAT activity, a pleiotropic effect not always shared by single flavonoid compounds or plant extracts (Laka et al., 2022).

The hypolipidemic effect observed in this study is consistent with the phytochemical profile of L. camara, which has been widely confirmed in recent studies. The flavonoid and total phenolic compounds in L. camara leaf and flower extracts were reported to be quite high and correlated with strong antioxidant capacity, both through DPPH and ABTS assays (El-din et al., 2022). This antioxidant activity is important in the context of dyslipidemia caused by a high-fat diet, because oxidative stress plays a major role in the oxidation of LDL to oxidized-LDL (ox-LDL), which is atherogenic. By suppressing lipid peroxidation and stabilizing lipoprotein membranes, the antioxidant compounds in L. camara extract have the potential to not only reduce LDL levels quantitatively but also improve the quality of circulating LDL particles (Laka et al., 2022). TA recent comprehensive review of the ethnobotany and pharmacology of L. camara also confirmed that the triterpenoids, flavonoids, and iridoid glycosides of this plant possess a broad spectrum of biological activities, including metabolic potential relevant to lipid regulation, although specific studies on their direct effects on lipid profiles in high-fat diet animal models—as conducted in this study—are still limited and constitute an important novelty of this study (Ramírez et al., 2025).

Limitations and Implications

Several points need to be considered when interpreting these results. First, the consistent reduction in HDL across all treatment groups indicates that the duration or dosage of the extract used may not be optimal for producing an effect on the HDL metabolic pathway. Therefore, further studies with varying durations or dose combinations are needed. Second, the exact molecular mechanism of the effect of L. camara extract on key lipid metabolism enzymes (HMG-CoA reductase, LCAT, LPL) in this study has not been directly tested and is only interpreted based on correlation with the literature; further biomolecular testing (e.g., gene expression or enzyme activity) is needed to confirm the proposed pathway. Third, given that L. camara has also been reported to contain compounds with potential toxicity at high doses (da Fonseca et al., 2022), safety studies (subchronic toxicity testing) are still needed before this extract is considered for further development as a natural hypolipidemic agent.

Overall, the results of this study provide preliminary evidence that Lantana camara extract has promising effectiveness in lowering LDL levels in a high-fat diet-induced rat model, with a dose-dependent effect and at the highest dose (KP-3) comparable to simvastatin. However, the effect on increasing HDL levels has not been optimally achieved, so this extract is more appropriately positioned as a potential LDL-lowering (hypolipidemic) agent rather than an agent that improves the overall lipid profile.

CONCLUSION AND SUGGESTION

Lantana camara leaf decoction at doses of 500 and 750 mg/kg body weight was associated with lower LDL-C levels compared to the negative control condition. However, the decoction did not significantly increase HDL-C levels. Therefore, these findings support a potential LDL-C-lowering effect but do not indicate an improvement in the overall lipid profile.

Further studies should use larger sample sizes, include a control group with a normal diet, standardize the ingredients according to their active compounds, and evaluate total cholesterol, triglycerides, liver function markers, histopathology, and toxicity. Future studies should also use repeated-measures statistical models and report effect sizes and confidence intervals.

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