JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI : 10.14710/dmj.v15i4.53955
JKD (DMJ), Volume 15, Number 4, July 2026 : 328-333

THE THERAPEUTIC POTENTIAL OF GALOBA (*HORNSTEDTIA* SP.) FRUIT EXTRACT: ELEVATION OF HDL-C IN HYPERCHOLESTEROLEMIC MICE (*MUS MUSCULUS*)

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Keywords:
Galoba Fruit Ethanol Extract, High density lipoprotein (HDL), High Fat Diet, Hypercholesterolemia, Mice (Mus musculus).

Received: 04 October 2025
Revised: 19 October 2025
Accepted: 29 October 2025
Available online: 01 July 2026

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ABSTRACT

Background: Hypercholesterolemia is a condition where total cholesterol levels exceed 200 mg/dL, often accompanied by decreased high-density lipoprotein (HDL) levels. This condition increases the risk of cerebrovascular disease, coronary heart disease, and peripheral artery disease. Non-pharmacological interventions using antioxidant-rich Galoba fruit (*Hornstedtia* sp.) have the potential to improve lipid profiles by modulating cholesterol metabolism. **Objective:** This study aimed to determine the effect of administering Galoba fruit (*Hornstedtia* sp.) ethanol extract on HDL-cholesterol levels in mice (*Mus musculus*) and explore its possible mechanistic pathways. **Methods:** This laboratory experimental study employed a post-test-only control group design. Twenty-five mice (*Mus musculus*) were randomly assigned to five groups: normal control (KN), negative control (K−), positive control (K+), treatment dose 1 (D1, 200 mg/kgBW), and treatment dose 2 (D2, 400 mg/kgBW). Hypercholesterolemia was induced through a high-fat diet (quail egg yolk, lard, and used cooking oil). HDL levels were measured after treatment and analyzed using ANOVA followed by a post hoc Tukey HSD test. **Results:** High-fat diet induction significantly increased total cholesterol levels. Administration of Galoba extract reduced total cholesterol and increased HDL levels. The D1 group (200 mg/kgBW) demonstrated the highest HDL increase of 35.20 mg/dL (81.86%), surpassing D2 (400 mg/kgBW) at 34.80 mg/dL (80.93%). Statistical analysis confirmed a significant increase in HDL levels (ANOVA, $p < 0.001$), with post hoc Tukey HSD showing significant differences between control and treatment groups. **Conclusion:** Ethanol extract of Galoba fruit (*Hornstedtia* sp.) effectively increased HDL levels in hypercholesterolemic mice, with the 200 mg/kgBW dose showing optimal effect. The potential mechanism involves inhibition of the HMG-CoA reductase pathway, which suppresses endogenous cholesterol synthesis, and antioxidant modulation, which reduces oxidative modification of lipoproteins and enhances reverse cholesterol transport. These findings support the therapeutic promise of *Hornstedtia* sp. as a natural lipid-modulating agent.

BACKGROUND

Cholesterol is a lipid compound found in plasma and tissues in both free and stored forms. It is synthesized endogenously from acetyl coenzyme A (Acetyl-CoA) in various tissues. Excessive cholesterol accumulation can lead to hypercholesterolemia, a major risk factor for atherosclerosis in vital arteries, which may result in cerebrovascular disease, coronary heart disease, and peripheral arterial disorders. Hypercholesterolemia is

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often asymptomatic in its early stages but can manifest with nonspecific symptoms such as fatigue, paresthesia, and headaches. Diagnosis typically involves elevated total cholesterol, low-density lipoprotein (LDL), triglycerides, and low levels of high-density lipoprotein (HDL), with normal HDL levels ranging from 40–60 mg/dL[1,2] In Indonesia, hypercholesterolemia remains a significant public health problem. According to the Kementerian Kesehatan Republik Indonesia through the Riset Kesehatan Dasar (Riskesdas) 2018 survey, the national prevalence of hypercholesterolemia was 35%, increasing from 39.4% in individuals aged 15–34 years to 52.9% in those aged 35–59 years. Certain provinces, such as West Papua and Maluku, recorded higher rates, up to 70% and 40%, respectively surpassing the national average.[3-7] These data underscore the urgent need for effective, accessible, and well-tolerated interventions to manage hypercholesterolemia.

Pharmacological treatments, particularly HMG-CoA (3-hydroxy-3-methyl-glutaryl-coenzyme A) reductase inhibitors (statins), are effective but associated with adverse effects such as myopathy, elevated liver enzymes, and gastrointestinal disturbances.[2,8] Consequently, complementary therapies derived from medicinal plants with antioxidant properties are increasingly explored as safer alternatives. Plant-derived antioxidants can neutralize reactive oxygen species (ROS), reduce LDL oxidation, and improve lipid profiles.[9]

Galoba fruit (*Hornstedtia* sp.), an endemic Zingiberaceae species from Maluku, contains flavonoids, alkaloids, polyphenols, tannins, and saponins with reported antioxidant, anti-inflammatory, anticoagulant, and antihypertensive properties .[10] Previous studies demonstrated flavonoids' ability to lower cholesterol by inhibiting HMG-CoA reductase, thereby decreasing endogenous cholesterol synthesis, upregulating LDL receptors, and enhancing reverse cholesterol transport, which increases HDL levels.[11,12]

Therefore, alternative treatments in the form of complementary therapy utilizing phytopharmaceuticals are recommended to treat hypercholesterolemia. Medicinal plants have been shown to contain antioxidant compounds that prevent oxidation, thus protecting the body from Reactive Oxygen Species (ROS). Free radicals circulating in the body are pathogenic and can cause several diseases, such as hypercholesterolemia.[13] This is supported by literature that shows that Moringa leaves and starfruit contain antioxidants that can lower high cholesterol levels.[11,12]

The mechanism by which flavonoids lower cholesterol levels is by inhibiting HMG-CoA reductase. This process decreases cholesterol synthesis and increases LDL receptors in the liver cell membrane and extrahepatic tissue. This process can also increase HDL levels in the blood, which absorb cholesterol from macrophages. This can lower total cholesterol levels, thereby reducing blood lipid levels.[13]

Despite the well-documented antioxidant profile of Galoba, no prior in vivo study has specifically evaluated its effect on lipid profile modulation, particularly HDL elevation, in hypercholesterolemic models**.** This study aimed to determine the effect of *Hornstedtia* sp. ethanol extract on HDL-cholesterol levels in hypercholesterolemic mice and identify the optimal effective dose.

METHODS

This study was a laboratory experimental research with a post-test-only control group design. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Universitas Pattimura (No. 002/FK-KOM.ETIK/I/2025). The research was conducted from May to August 2024, encompassing proposal development, extraction, animal experimentation, and data analysis. Experimental work was carried out in the Biochemistry and Physiology Laboratory, Faculty of Medicine. HDL measurements were performed in the Clinical Pathology Laboratory, Faculty of Medicine, and the Regional Special Hospital Laboratory of Provinsi Maluku.

Fresh Galoba fruit (*Hornstedtia* sp.) was collected from Maluku Province, washed, dried, and powdered. The extraction process was conducted at UPT Laboratorium Herbal Materia Medica Batu. The fruit powder was macerated using 96% ethanol in a 1:10 (w/v) ratio for 72 hours at room temperature. The macerate was filtered and concentrated with a rotary evaporator to obtain a viscous extract, with an average yield of 12.5% (w/w) of the dried material. The extract was stored at 4 °C until use.[10]

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A total of 25 male BALB/c mice, aged two months and weighing 20–30 g, were obtained from Gold Mice Farm, South Sulawesi. Hypercholesterolemia was induced by a high-fat diet (quail egg yolk, lard, and used cooking oil) for 14 days. The condition was confirmed when total cholesterol levels exceeded 200 mg/dL, measured using an enzymatic colorimetric method (Enzymatic colorimetric assay).[14,15]

The mice were randomly assigned into five groups (n = 6 per group):

- KN: Normal control (standard diet, no treatment)
- K−: High-fat diet only
- K+: High-fat diet + Simvastatin 0.9 mg/kgBW
- D1: High-fat diet + Galoba fruit ethanol extract 200 mg/kgBW
- D2: High-fat diet + Galoba fruit ethanol extract 400 mg/kgBW

After 14 days of treatment, blood samples were collected via retro-orbital puncture under anesthesia. HDL cholesterol levels were measured using an enzymatic colorimetric method with a spectrophotometer at 546 nm.[16]

Data were analyzed using SPSS version 26. Normality and homogeneity were assessed using the Shapiro–Wilk and Levene tests. If data met parametric assumptions ($p > 0.05$), one-way ANOVA followed by Tukey HSD post hoc analysis was performed to determine group differences.

RESULTS

Cholesterol levels were measured using the point-of-care testing (POCT) method at baseline (Day 0), after high-fat diet (HFD) induction (Day 15), and after treatment (Day 29). As shown in Table 1, HFD induction successfully increased total cholesterol levels in all groups except the normal control (KN). Following treatment, both the simvastatin group (K^+) and the treatment groups (D1 and D2) demonstrated a decrease in total cholesterol levels, with the D1 group showing the most pronounced reduction.

Table 1. Total cholesterol levels (mg/dL) measured using POCT on Days 0, 15, and 29 (mean ± SD, n = 6)

Groups	Day-0 before treatment (mg/dL)	Day-15 after HFD-induction (mg/dL)	Day-29 after treatment (mg/dL)
KN	<100	101.00 ± 1.30	101.20 ± 1.30
K-	<100	132.10 ± 1.92	139.80 ± 5.07
K+	<100	134,80 ± 2.05	103.80 ± 3.03
D1	<100	134.20 ± 3.96	106.60 ± 9.24
D2	<100	135.20 ± 3.49	113.60 ± 7.60

* KN = Normal control; K^- = Negative control; K^+ = Positive control (simvastatin); D1 = Galoba extract 200 mg/kgBW; D2 = Galoba extract 400 mg/kgBW.

Serum lipid analysis was performed using a photometer at a wavelength of 500 nm to determine total cholesterol, LDL, HDL, and triglyceride concentrations. The absorbance values obtained were converted to corresponding concentration units. Statistical analysis (mean, minimum, and maximum values) was performed for HDL levels across the five groups (n = 6 per group). Figure 1 shows a boxplot of HDL levels in each group. The treatment group receiving 200 mg/kgBW galoba fruit ethanol extract (D1) demonstrated the highest increase in HDL levels compared to the 400 mg/kgBW group (D2), indicating that the lower dose was more effective in elevating HDL levels.

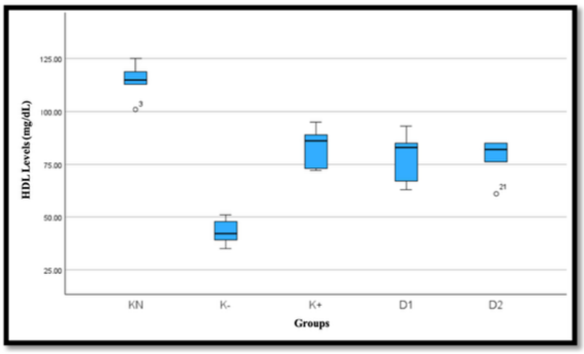

Figure 1. Boxplot graph of HDL levels (mg/dL) in each group, n = 6. Bars represent minimum–maximum values, boxes represent interquartile range, and lines indicate median values

A one-way ANOVA test revealed a statistically significant difference in HDL levels between groups ($p < 0.001$). Further analysis using Tukey's HSD post hoc test confirmed that the D1 group had significantly higher HDL levels than the negative control group and was comparable to the positive control group (simvastatin).

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DISCUSSION

This study showed that a high-fat diet (HFD) composed of lard, quail egg yolk, and repeatedly used cooking oil successfully induced hypercholesterolemia in mice, as reflected by a significant decrease in HDL levels compared to the normal control (KN). These findings are consistent with previous studies demonstrating that saturated fat and oxidized oil intake can increase total cholesterol and lower HDL.[17] Quail egg yolk contains approximately 2138 mg cholesterol/100 g, lard contains 38–43% saturated fatty acids, and repeated use of cooking oil is known to elevate lipid levels significantly.[18,19] These findings align with previous studies reporting that saturated fats and oxidized oils can increase total cholesterol and lower HDL levels.[17]

Treatment with both simvastatin and Galoba fruit ethanol extract significantly increased HDL levels compared to the negative control. Post hoc Tukey HSD analysis showed no significant difference between the simvastatin group (K^+) and the Galoba treatment groups (D1 and D2), indicating that Galoba extract demonstrated comparable efficacy to simvastatin in raising HDL levels. The optimal effect was observed at the 200 mg/kgBW dose, whereas the 400 mg/kgBW dose did not produce an additional increase. The HDL-elevating effect of Galoba is likely attributed to its bioactive compounds, particularly flavonoids and phenolics. These compounds possess antioxidant activity, inhibit HMG-CoA reductase, and enhance ATP-binding cassette transporter A1 (ABCA1) expression, thereby promoting reverse cholesterol transport and elevating circulating HDL levels. This mechanism is consistent with previous studies showing the lipid-modulating effects of phytochemicals in hyperlipidemic models.[20,21]

The lower efficacy at higher doses may be explained by metabolic saturation, reduced bioavailability, or accumulation of active substances in the gastrointestinal tract, as suggested by Rabiei et al. (2014) and Rohmani et al. (2015).[22,23] Although simvastatin remains the standard therapy for dyslipidemia, Galoba extract offers potential advantages in tolerability and could serve as an adjunct or alternative therapy for patients who experience adverse effects from statins. This is in line with Sari et al. (2020), who demonstrated that combining herbal and pharmacological agents can enhance lipid profile outcomes.[21]

The translational relevance of these findings can be further explored through dose conversion. Using the body surface area method proposed by Reagan-Shaw et al. (2008), the 200 mg/kgBW dose in mice corresponds to approximately 16.2 mg/kgBW in humans. For an adult weighing 60 kg, this equals an estimated 972 mg/day of galoba fruit ethanol extract.[24] This calculated human equivalent dose provides an initial reference point for clinical trial design, although further studies on pharmacokinetics and pharmacodynamics are necessary before clinical application.[25]

This study has some limitations, only HDL levels were assessed, without measurements of LDL, triglycerides, or inflammatory biomarkers that could provide a more comprehensive understanding of lipid modulation. Additionally, histopathological and molecular analyses were not performed to verify the underlying mechanisms.[25] These limitations should be addressed in future studies to strengthen the translational potential of Galoba extract.

In conclusion, Galoba fruit ethanol extract at a dose of 200 mg/kgBW significantly increased HDL-C levels in hypercholesterolemic mice, demonstrating efficacy comparable to simvastatin. Dose translation suggests that a human equivalent dose of approximately 972 mg/day may be feasible. Galoba has the potential to serve as a natural adjunct or alternative therapy for dyslipidemia, but further clinical studies are needed to establish its safety, formulation, and efficacy in humans.

CONCLUSION

Ethanol extract of Galoba fruit (*Hornstedtia* sp.) was proven to significantly increase HDL cholesterol levels in hypercholesterolemic mice induced by a high-fat diet, with the 200 mg/kgBW dose showing optimal effectiveness compared to the 400 mg/kgBW dose. This effect is likely related to the flavonoid content acting as antioxidants that modulate lipid metabolism and counteract oxidative stress. These findings indicate that Galoba fruit extract has promising potential as a complementary therapy for hypercholesterolemia, although further clinical studies

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in humans are required to confirm its efficacy, optimal dosage, and safety profile.

ETHICAL APPROVAL

All experimental protocols were approved by the Ethics Committee of the Faculty of Medicine, Universitas Pattimura, under the number 002/FK-KOM.ETIK/I/2025.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING

All research funding comes through internal grant of PNBP 2024 from Faculty of Medicine of Universitas Pattimura, Ambon, Indonesia.

AUTHOR CONTRIBUTIONS

Conceptualization, MZAS, RDA, and DQ; methodology, MZAS and RDA; data analysis, MZAS, RDA; data collection, MZAS; wrote the original draft, MZAS; review and edit, RDA and DQ; supervision, RDA and DQ.

ACKNOWLEDGMENTS

We sincerely thank the Faculty of Medicine of Universitas Pattimura, Ambon, Indonesia for funding this research through internal grant of PNBP 2024 funds.

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