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Activity Test of Extract Edible Bird's Nest (*Aerodramus fuciphagus*) as a Natural Treatment to Lower LDL Levels

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Abstract: This study aimed to evaluate the effect of edible bird's nest (EBN) infusion (*Aerodramus fuciphagus*) on lowering low-density lipoprotein (LDL) levels in white rats (Rattus norvegicus) induced with hypercholesterolemia. Fifteen male Wistar rats were divided into five groups: negative control (distilled water), positive control (simvastatin 10 mg/kg BW), and three treatment groups receiving EBN infusion at doses of 10, 20, and 40 mg/200 g BW. LDL levels were measured before and after treatment using an enzymatic colorimetric method. The results showed that EBN infusion reduced LDL levels in all treatment groups, with the highest decrease at a dose of 40 mg/200 g BW (34.03%), followed by 20 mg (33.46%) and 10 mg (28.13%). Simvastatin, however, produced a greater LDL reduction (55.64%). In conclusion, EBN infusion can reduce LDL levels in hypercholesterolemic rats, particularly at doses of 20 mg/200 g BW, suggesting its potential as a natural lipid-lowering agent, although it is less effective than simvastatin.

Keywords: Edible Bird's Nest; Infusion; Low-density lipoprotein.

Introduction

Cardiovascular disease is one of the leading causes of death worldwide (Gaidai et al., 2023). In Indonesia, the prevalence of this health condition indicates that cardiovascular disease ranks second among the most commonly experienced illnesses by the population. This is based on a representative online survey conducted in 2024 involving 1,038 consumers in Indonesia.

Cardiovascular disease is closely associated with lipid metabolism disorders, particularly the increase of low-density lipoprotein (LDL) levels in the blood (Vural et al., 2021). Excess LDL can undergo oxidation into oxidized LDL (ox-LDL), which subsequently triggers the formation of atherosclerotic plaques on the blood vessel walls. This process progressively increases the risk of atherosclerosis, myocardial infarction (heart attack), and stroke (Hoogeveen, 2021). Currently, the management of elevated LDL levels is generally carried out using conventional therapy with statin-class drugs. Although proven effective, long-term use of statins is often associated with several side effects, such as myopathy, hepatotoxicity, and an increased risk of type 2 diabetes mellitus (Ruscica et al., 2022). In addition, the relatively high cost of treatment also poses a significant challenge, especially in developing countries (Tsushima & Hatipoglu, 2023).

With the growing public awareness of the importance of a healthy lifestyle and the increasing preference for natural-based products, therapies using natural and functional ingredients are gaining more attention. This approach is considered safer, has minimal side effects, and has the potential to provide long-term therapeutic benefits. One promising natural ingredient as a hypolipidemic agent is Edible Bird's Nest (EBN), which is a secretion from the sublingual glands of the swiftlet (*Aerodramus fuciphagus*), and has been traditionally used in Asian medicine for generations

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(Fan et al., 2022). EBN contains various bioactive compounds such as proteins, glycoproteins, and sialic acid, which are believed to have pharmacological activities, including antioxidant, immunomodulatory, anti-inflammatory, and cardiovascular protective effects (Ibrahim et al., 2021; Permatasari et al., 2023).

A study by Yida et al., 2022 demonstrated that EBN is capable of regulating cholesterol metabolism in the liver by modulating the transcription of key genes involved in cholesterol synthesis and clearance, such as HMGCR, LDLR, and CYP7A1. Administration of high-dose EBN for 12 weeks in rats fed a high-cholesterol diet (HCD) significantly reduced total cholesterol, LDL, and liver enzyme levels, even showing greater effectiveness than simvastatin. Additionally, Yida et al., 2015 also reported that EBN could alleviate hypercoagulation caused by a high-fat diet by reducing oxLDL levels, increasing prostacyclin, and regulating coagulation gene expression in the liver, indicating its protective effect against cardiovascular risk.

Furthermore, a study by Zhang et al., 2024 reinforced the evidence that EBN can improve glucose and lipid metabolic disorders in obese rats through the gut-liver axis mechanism. EBN intervention was shown to reduce LDL, oxLDL, and inflammatory markers such as IL-1β, IL-6, and TNF-α, while increasing HDL levels and metabolic activity. EBN also modulated gut microbiota, enhanced colonic bile acid production, and strengthened the intestinal barrier, ultimately reducing lipid absorption and systemic inflammation.

Based on these findings, edible bird's nest extract holds promise as an effective and safe natural therapeutic agent for lowering LDL levels and improving lipid balance through multi-target mechanisms involving gene regulation, the immune system, and gut microbiota. Therefore, further research is needed to evaluate the in vivo lipid-lowering activity of EBN extract and support its use as a natural alternative therapy in the prevention and management of cardiovascular diseases.

Method

Sample Processing

Swiftlet nests come from Pangkep Regency, South Sulawesi. EBN was cleaned manually using tweezers to remove dirt such as feathers, then washed under clean water. After the washing process, the EBN was dried at room temperature, then ground using a blender and sieved through a 40-mesh sieve to increase the surface area and facilitate the extraction process (Zam Zam & Musdalifah, 2022). The procedure for preparing the edible bird's nest (EBN) infusion begins by weighing the EBN powder according to the required concentration: 50 mg for 0.05%, 100 mg for 0.1%, and 200 mg for 0.2%. The powder is then moistened with distilled water in an amount equivalent to twice its weight (for example, 2 drops for 50 mg) and left to stand for 10–15 minutes. Afterward, 100 mL of distilled water is added, and the mixture is heated in a water bath for 15 minutes, starting from when the temperature reaches 90°C, with occasional stirring. The infusion is then filtered while still hot using flannel cloth, and hot water is added through the residue until the final volume reaches 100 mL (Marlina & Syafitri, 2023).

The Preparation PTU 0,1%

The preparation of 0.1% propylthiouracil (PTU) solution is intended to induce elevated cholesterol levels. PTU functions by inhibiting thyroid hormone synthesis, which indirectly stimulates the liver and leads to an increase in blood lipid and cholesterol metabolites. To prepare the solution, 10 mg of PTU is dissolved in distilled water to a final volume of 100 mL (Sasmita et al., 2023).

The preparation of a high-fat diet

The preparation of a high-fat diet feed is carried out by mixing all the ingredients, which include 15 grams of corn, 15 grams of wheat bran, 25 grams of corn starch, 3 grams of tapioca flour, 2 grams of calcium carbonate ($CaCO_3$), 0.2 grams of table salt, 0.3 grams of premix, and 39 grams of beef fat. The entire mixture is then ground using a specialized grinder until pellets are formed, followed by a drying process before use (Hasanuddin et al., 2022).

The Preparation of Positive Control (Simvastatin Suspension)

A total of 1 gram of Na-CMC is weighed and gradually added into an Erlenmeyer flask containing 50 mL of hot water at approximately 70°C, while stirring until fully dissolved and forming a homogeneous solution. This solution is then transferred into a volumetric flask, and distilled water is added until the total volume reaches 100 mL, followed by thorough mixing to ensure homogeneity. Next, the simvastatin suspension is prepared by first arranging the necessary tools and materials. Simvastatin is weighed at 10 mg and then suspended in the 1% Na-CMC solution until the final volume reaches 100 mL. The resulting simvastatin suspension is used as a positive control and administered orally to the test animals (Hikmah et al., 2022).

Treatment of Experimental Animals

Before the experiment began, all test animals were acclimatized to the laboratory environment for 7 days. The animals used were healthy white rats (*Rattus norvegicus*), each weighing approximately 200 grams, with a total of 15 rats (Alim et al., 2023). After the acclimatization period, the rats were weighed and randomly divided into five treatment groups, with each group consisting of three rats. Prior to treatment, all rats were fasted for 8 hours while still having access to drinking water. Initial LDL cholesterol levels were then measured. From day 8 to day 14, the rats were fed a high-fat diet (HFD) and given drinking water containing 0.1% propylthiouracil (PTU) solution to induce elevated LDL cholesterol levels. After the induction period, LDL levels were measured again to confirm that the rats had developed hypercholesterolemia.

On day 15, the induced rats were then orally administered the treatments for 7 consecutive days as follows: Group 1**:** Given distilled water (negative control); Group 2**:** Given simvastatin suspension (positive control); Group 3**:** Given edible bird's nest (EBN) infusion at a dose of 10 mg/kg body weight; Group 4**:** Given EBN infusion at a dose of 20 mg/kg body weight; and Group 5**:** Given EBN infusion at a dose of 40 mg/kg body weight

On day 21, the LDL cholesterol levels in the rats were measured again. Blood samples were collected through the retro-orbital vein using a hematocrit pipette. The blood samples were allowed to clot for 1–2 hours and then centrifuged to obtain serum. This serum was then analyzed to measure LDL levels using a Humalyzer (Thermo Scientific Indico).

Result and Discussion

This study was conducted to determine the effect of administering an infusion of Edible Bird's Nest (*Aerodramus fuciphagus*) on the reduction of blood Low-Density Lipoprotein (LDL) levels in male white rats (Rattus norvegicus). The extraction process was carried out by infusion, aiming to extract water-soluble active compounds such as sialic acid, proteins, and otheantioxidant compounds found in edible bird's nest (Ardo, 2017; Farsani et al., 2016). The study used 15 male Wistar strain white rats that had been acclimatized for seven days. Male white rats were chosen because they have a fast metabolism, are easy to handle, and produce consistent biological data, as they are not influenced by hormonal cycles like female rats (Alim et al., 2023).

The measurement of blood LDL levels was carried out using an enzymatic colorimetric chemical method based on spectrophotometry. The fundamental principle of this method involves a series of enzymatic reactions, starting with the hydrolysis of cholesterol esters by the enzyme cholesterol esterase into free cholesterol and fatty acids:

Cholesterol ester + H_2O → (cholesterol esterase) → Free cholesterol + Fatty acids

The free cholesterol is then oxidized by the enzyme cholesterol oxidase, producing 4-cholesten-3-one and hydrogen peroxide (H_2O_2):

Free cholesterol + O_2 → (cholesterol oxidase) → 4-cholesten-3-one + H_2O_2

The resulting hydrogen peroxide then reacts with a chromogen in a reaction catalyzed by peroxidase, forming a colored complex:

H_2O_2 + Chromogen → (peroxidase) → Colored complex + H_2O

The intensity of the color formed is directly proportional to the LDL level in the sample (figure 1), which is then read using a Humalyzer device. This device operates on the principle of light absorbance at a specific wavelength to quantitatively measure blood chemistry parameters (Shrestha et al., 2022).

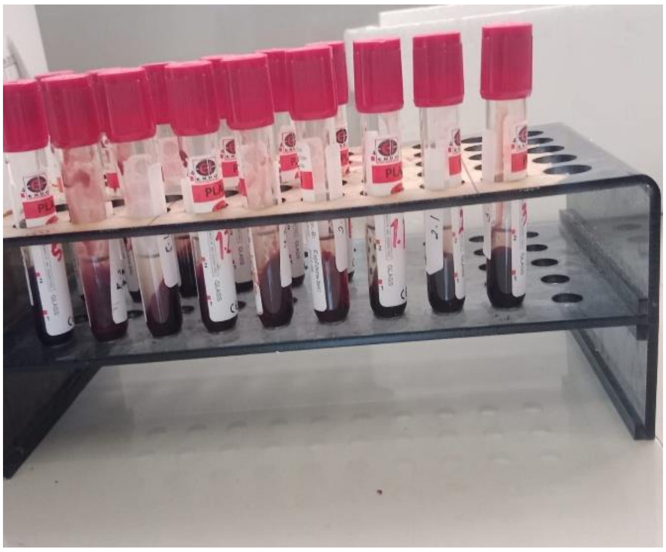

Figure 1. Blood Serum

In this study, the rats were induced with 0.1% propylthiouracil (PTU) orally to trigger hyperlipidemia. PTU is known to suppress thyroid hormone activity, which indirectly decreases the expression of LDL receptors in the liver, leading to increased cholesterol levels, including LDL, in the blood (Katsumata et al., 1991). After 7 days of PTU induction, blood LDL levels increased beyond the normal threshold, indicating a state of hypercholesterolemia (Abdolhosseinipoor et al., 2018).

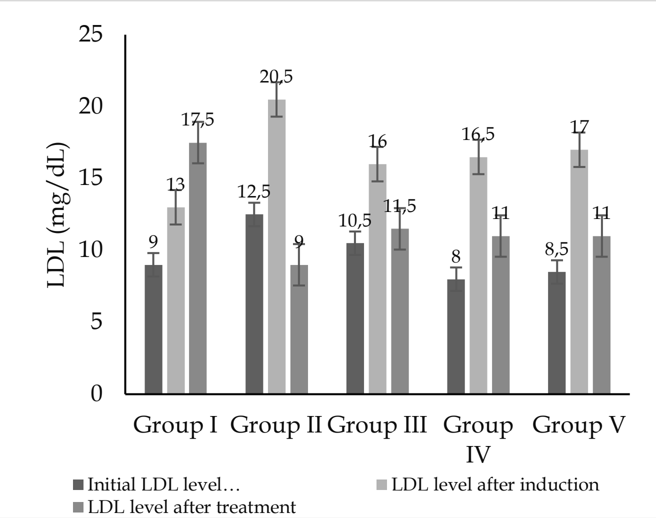

Figure 2. Results of LDL Blood Level Reduction in White Rats (*Rattus norvegicus*)

Based on the results of the study on the effect of *Collocalia fuciphaga* (edible bird's nest) infusion on lowering blood LDL levels in white rats (*Rattus norvegicus*), Figure 2 shows an increase in LDL levels following induction, followed by a decrease after treatment. In Figure 3, the findings indicate that the negative control group (distilled water) experienced an increase in LDL levels, with an average percentage change of -37.27%, suggesting that without treatment, LDL levels tend to remain elevated or fluctuate due to the body's homeostatic processes. Meanwhile, the positive control group that received simvastatin showed a decrease in LDL levels by 55.64%. Simvastatin is a first-line statin drug that works by inhibiting the HMG-CoA reductase enzyme involved in hepatic cholesterol synthesis, thereby reducing LDL levels by 20–50%, while also increasing HDL levels and lowering triglycerides (Murphy et al., 2016; Nishio et al., 2005).

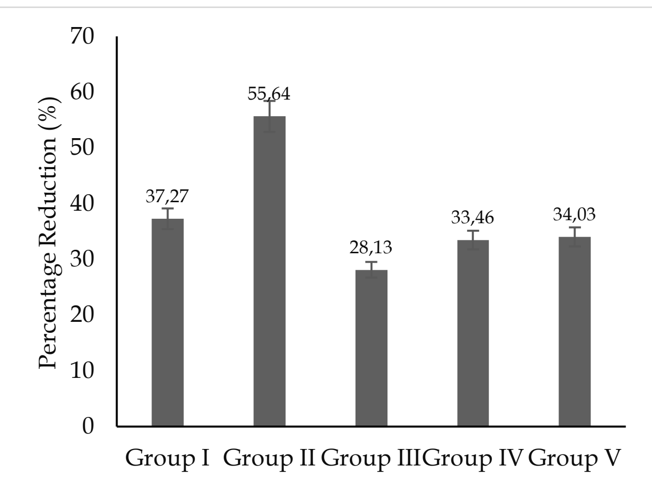

Figure 3. Percentage Reduction (%) LDL

In the treatment groups that received edible bird's nest infusion, the dose of 10 mg/200 g BW resulted in a 28.13% reduction in LDL, the 20 mg/200 g BW dose resulted in a 33.46% reduction, and the 40 mg/200 g BW dose led to a 34.03% reduction. These results indicate that the infusion of edible bird's nest can significantly reduce LDL levels, although not as effectively as simvastatin. The most optimal reduction appeared at doses between 20–40 mg/200 g BW, suggesting a potential effective dose range within this interval. However, there was no significant difference between the 20 mg and 40 mg doses, which may indicate a plateau effect or a threshold of efficacy.

The mechanism by which edible bird's nest lowers LDL is strongly believed to be related to its sialic acid content and antioxidant compounds, which can prevent LDL oxidation and inhibit atherosclerotic plaque formation. Additionally, bioactive compounds in the bird's nest are also known to enhance the activity of endogenous antioxidant enzymes and improve lipid metabolism (Al-Khaldi et al., 2022; Zhang et al., 2024).

Overall, the findings of this study strengthen the potential of edible bird's nest as a natural agent in lowering blood LDL levels, particularly in hypercholesterolemic conditions induced by propylthiouracil. Although its effects are not equivalent to simvastatin, the bird's nest infusion still demonstrated biologically significant results and is worth further development as a potential supplement for hyperlipidemia therapy.

Conclusion

Based on the results of the study, the infusion of edible bird's nest (*Aerodramus fuciphagus*) was able to reduce blood LDL levels in white rats (Rattus norvegicus) induced with hypercholesterolemia. The most optimal reduction occurred at a dose of 20 mg/200 g body weight, although it was not as effective as simvastatin.

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This article was written by three authors, namely M, AN. ZZ., and A. DA. All authors worked together in carrying out each stage of the article writing.

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The authors declare no conflict of interest.

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