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Research Paper

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Potential of Black Garlic (*Allium sativum*) as a Traditional Therapy for Dyslipidemia: A Systematic Review

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Abstract

Background: Dyslipidemia is a serious health problem with a high prevalence in Indonesia. It is a component of metabolic syndrome that increases the risk of other diseases such as obesity, diabetes mellitus, and hypertension. The treatment of dyslipidemia usually uses conventional therapies like statin drugs. Traditional remedies, such as black garlic, can also help treat dyslipidemia. However, further studies are needed to explore the potential of black garlic compounds to lower cholesterol and triglyceride levels in the blood. **Methods:** The study design is a literature review based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, which include population, intervention, comparators, and outcomes (PICO). The article search uses online databases, including Google Scholar, PubMed, Springer, Scopus, Cochrane Library, and ScienceDirect. The publication year is limited to 2014–2024, full-text, and experimental studies. The keywords used are "(black garlic OR *Allium sativum*) AND (dyslipidemia OR hypercholesterolemia OR LDL OR HDL OR hypertriglyceridemia) AND (clinical trial OR randomized control trial OR In vitro)". **Key findings:** Data are analyzed from 8 scientific journals that meet the inclusion and exclusion criteria**. Conclusions:** [Black garlic is effective in treating dyslipidemia due to its bioactive compounds such as flavonoids, S-allylcysteine, 5-HMF, pyruvate, thiosulfate, and alkaloids.

Keywords: *Allium sativum*, Herbs, Dyslipidemia, Hypercholesterolemia, and Hypertriglyceridemia.

Introduction

Dyslipidemia is one of the disorders that occurs as a result of disturbances in lipid metabolism and is recognized as a risk factor for cardiovascular disease, diabetes mellitus, obesity, and hypertension. Dyslipidemia is a disorder of lipid metabolism characterized by an increase or decrease in the levels of lipid fractions in plasma. The disorder may involve an increase in total cholesterol, LDL cholesterol, triglycerides, and a decrease in HDL cholesterol [1] . The Global Health Observatory (GHO) states that the prevalence of dyslipidemia is around 45% (WHO, 2018). Meanwhile, the prevalence rate of dyslipidemia in Southeast Asia is 30.3%. In Indonesia, the prevalence rate with total cholesterol levels >160 mg/dL in the ≥25 years age group is 36%. The province of Central Java has a rate of 51%, with an increasing prevalence rate of dyslipidemia in each of its districts or cities, indicating the need for further exploration into the medical management of dyslipidemia [2].

Non-pharmacological therapies that can be provided include recommendations to engage in physical activity for 30 minutes at moderate intensity 4 to 6 times per week, medical nutrition therapy with a low-calorie diet, and smoking cessation. Conventional pharmacological therapies that may be given include drugs from the statin group, bile acid sequestrants, fibrates, ezetimibe, PCSK9 inhibitors, omega-3 fatty acids (fish oil), and newer drug classes such as microsomal transfer protein (MTP) inhibitors, thyroid hormone mimetics, apo B antisense oligonucleotide (mipomersen), and LDL apheresis [3]. Other therapies that can be implemented for dyslipidemia include herbal treatments such as black garlic, starfruit, cerme, bay leaves, moringa leaves, and sambiloto [4].

Black garlic is preferred over regular garlic to treat dyslipidemia because during processing, the GSAC (Gamma-Glutamyl S-allylcysteine) compound is converted into the stable S-Allyl-L-cysteine sulfoxide (SAC) compound or breaks down into organosulfur compounds such as diallyl sulfide (DAS), diallyl disulphide (DADS), diallyl trisulfide (DATS), dithiins, and ajoene. In addition to SAC, black garlic contains other compounds such as phenols, flavonoids, thiosulfates,

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pyruvate, and S-Allylmercaptocysteine (SAMC) [5]. Black garlic (*Allium sativum*) is preferred over other herbal plants because the SAC and antioxidant content in black garlic is twice as high as that in other herbal medicines. Furthermore, when compared to conventional medications, the side effects of herbal medicines are much fewer [6].

Not only Indonesia uses this traditional medicine; many cultures around the world such as Babylon, China, Egypt, Greece, Phoenicia, Rome, and the Vikings have also made use of it. Black garlic is a natural remedy that has been evidenced in several studies to have therapeutic effects, including anticancer, antibacterial, antiviral, antidiabetic, antihypertensive, cardioprotective, hepatoprotective, hypolipidemic, and antioxidant effects due to its organosulfur compounds. This garlic is characterized by a single clove that is black in color. This trait distinguishes it from other types of garlic. The black color results from spontaneous fermentation for 40 days at a temperature of 60–70°C. This garlic does not smell as pungent as other types. The taste of black garlic is unique due to its high lactic acid content, giving it a sour flavor. The taxonomy of black garlic is as follows: Division: Magnoliophyta; Class: Liliopsida; Order: Asparagales; Family: Alliaceae; Subfamily: Allioideae; Tribe: Allieae; Genus: Allium; Species: A. sativum [3,6].

Excess fat in the body leads to the production of triglyceride precursors, namely acetyl co-A and malonyl co-A, in large amounts in the liver. As a result of the high production of these two compounds, lipid levels can increase, which ultimately leads to increased triglyceride synthesis. In addition, elevated levels of these two compounds inhibit the function of CPT-1, which is responsible for degrading lipids. Black garlic can increase the expression of CPT-1 mRNA to perform its main function, namely degrading lipids, thereby reducing their levels in the blood. The flavonoid content in black garlic can reduce oxidative stress through the mechanism of inhibiting the conversion chain reaction from superoxide to hydrogen peroxide, thereby suppressing oxidative stress [7,8]. Although the potential of black garlic as a hypolipidemic therapy has been explored in several studies, systematic studies summarizing the specific bioactive mechanisms of compounds in black garlic against dyslipidemia are still limited. Therefore, in this systematic review-based research article, we summarize the current knowledge regarding the effectiveness of black garlic's bioactive compounds in lowering lipid levels as a traditional therapy for dyslipidemia.

Materials and Methods

Search Strategy

The research was conducted by identifying, evaluating, and interpreting all findings on a topic relevant to the research title. The journal search for writing this systematic review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guideline, which includes determining the Population, Intervention, Comparators, and Outcome (PICO) as follows: Population (P): In vivo subjects in the form of rats. Intervention (I): Administration of extract or cloves of black garlic (Black *Allium Sativum*). Comparators (C): The comparator is a disease control group or a group before treatment. Outcome (O): There are active compounds in black garlic that potentially have effects on total cholesterol, LDL, HDL, and triglycerides, which influence dyslipidemia.

Studies on animals (rats) were chosen because the rat model has lipid metabolism similar to humans, thus providing a preliminary overview of the effectiveness of black garlic before clinical trials in humans, as well as due to limitations in in vivo research on human subjects. The article search strategy in this literature review used online databases including Google Scholar, PubMed, Springer, Scopus, Cochrane Library, and ScienceDirect. Databases like Scopus and PubMed were chosen for their high publication standards, while Google Scholar, Cochrane Library, and ScienceDirect were used to broaden the research scope. The search strategy used keywords and Boolean operators AND, OR NOT or AND NOT to broaden or make the search more specific, thereby facilitating the selection of relevant articles. The keywords used to find articles were black garlic, *Allium Sativum*, Hypercholesterolemia, Hypertriglyceridemia, and Dyslipidemia, while the keywords in vitro, clinical trial, and randomized controlled trial were used to filter for in-depth experimental studies. The publication year restriction applied was 2014–2024 to focus on data recency.

Inclusion and Exclusion Criteria

The inclusion criteria in this study are as follows: (1) studies with an experimental research design; (2) original articles from primary sources; (3) research articles published within the last 10 years (2014-2024); (4) full-text articles in either English or Indonesian; (5) articles with research samples using comparators or placebo; and (6) articles that examine black garlic extract or cloves. Meanwhile, the exclusion criteria for this study include: (1) duplicate articles; (2) articles without a complete structure; (3) articles that do not discuss black garlic; and (4) articles that are inaccessible or restricted.

The study selection process was carried out through several stages designed to ensure that only relevant and high-quality literature was included in this review. The selection stages consisted of: Initial Screening: This process began with screening the titles and abstracts of all literature identified based on the search results. Articles that were not relevant to the topic or did not meet the inclusion criteria were excluded at this stage. For example, studies that only discussed regular garlic without fermenta-

tion or were not related to metabolic syndrome would be eliminated. Full Text Evaluation: Articles that passed the initial stage were then further evaluated by reading the full text. At this stage, researchers ensured that each article met all inclusion criteria, such as using black garlic as the main intervention, having extractable data, and being published in English or Indonesian. Articles that did not meet the exclusion criteria, such as those that were only reviews or editorials, were also removed. Consensus: If there were differences of opinion among researchers in determining the eligibility of an article, the issue was resolved through joint discussion. This approach was used to ensure that all selected literature had relevant scientific value and was aligned with the objectives of the research.

After the selection process was complete, the next step was data extraction using a standard form. The data extracted included:

General information about the study, such as the author's name, year of publication, and study location. Study characteristics, including research design (e.g., in vitro or animal trials), subject population (e.g., rats or cell cultures), and the type of black garlic used. Relevant research outcomes, such as the content of active compounds in black garlic (e.g., S-allyl cysteine or flavonoids) and its pharmacological effects on metabolic syndrome, such as improved lipid levels. The data extraction process was carried out carefully to ensure that all relevant information was accurately recorded. The successfully extracted data was then analyzed for further synthesis.

Data Analysis

Data analysis in this study was carried out by considering the characteristics and results of each article that passed the selection process. Due to methodological differences or heterogeneity among the studies found, such as differences in the types of rats used, the methods of administering black garlic, or the outcome measurement techniques, a quantitative meta-analysis could not be conducted. Therefore, a narrative synthesis approach was used to interpret the data descriptively.

Findings Classification: The first step in narrative synthesis is grouping the results based on specific themes or categories. For example, research findings can be grouped according to the mechanisms of action of black garlic, such as antioxidant, anti-inflammatory, or antidiabetic effects. In addition, the primary bioactive compounds identified, such as S-allyl cysteine, polyphenols, and flavonoids, are also classified to illustrate their relevance to metabolic syndrome.

Descriptive Synthesis: After findings regarding how black garlic works to alleviate metabolic syndrome are classified, each data group is summarized descriptively. This process involves explaining the antioxidant effects of black garlic by referring to its mechanism in reducing oxidative stress in the body, while its antidiabetic effects are explained by emphasizing increased insulin sensitivity and lowered blood sugar levels.

Integration of Findings: The final stage is the integration of results from various studies to provide a holistic view of the potential of black garlic as a traditional therapy for dyslipidemia. The researcher compares the findings across studies and identifies gaps or inconsistencies in the literature. For example, some studies may show significant results in rats with dyslipidemia but not in healthy rats. This forms the basis for making recommendations for future research.

Preliminary Conclusions: The results of this synthesis are then used to draw preliminary conclusions regarding the effectiveness of black garlic. These conclusions provide guidance for traditional therapeutic practices as well as implications for further research, particularly in the development of more specific and tested black garlic-based medicines.

Results

Based on the search strategy using keywords, a total of 6,172 journals were found from PubMed, Sciencedirect, Cochrane Library, and Google Scholar. After that, 10 duplicate journals were identified and excluded. Next, 6,903 journals were removed through screening because they did not meet the keywords ("black garlic" or "*Allium sativum*") and ("dyslipidemia" or "hypercholesterolemia" or "LDL" or "HDL" or "hypertriglyceridemia"). Afterwards, 71 journals were briefly reviewed through their abstracts and it was found that 55 journals did not meet the criteria, as they were classified as "systematic review" and "meta-analysis" studies. Thirteen journals were then read in full to determine their eligibility. Five journals were excluded because they could not be accessed or were restricted. As a result, the final number of journals that met all the criteria was eight. These findings were then presented in the PRISMA 2020 figure 1.

Based on a literature review, nine studies were identified with different populations and interventions to demonstrate the effectiveness of black garlic extract in reducing total cholesterol, LDL cholesterol, triglycerides, and increasing HDL. These studies used various strains of rats, including Wistar, Sprague-Dawley, and Swiss albino rats. The rat models in these studies also varied. In all research findings, the rats were subjected to certain treatments, such as a high-fat diet, diabetes mellitus models, NAFLD (non-alcoholic fatty liver disease) models, and carbon tetrachloride intoxication. The duration of treatment in these studies ranged from 2 weeks to 6 months. A commonality across all studies was the experimental design and the use of One-way ANOVA for data analysis.

Overall, the findings from all the presented studies

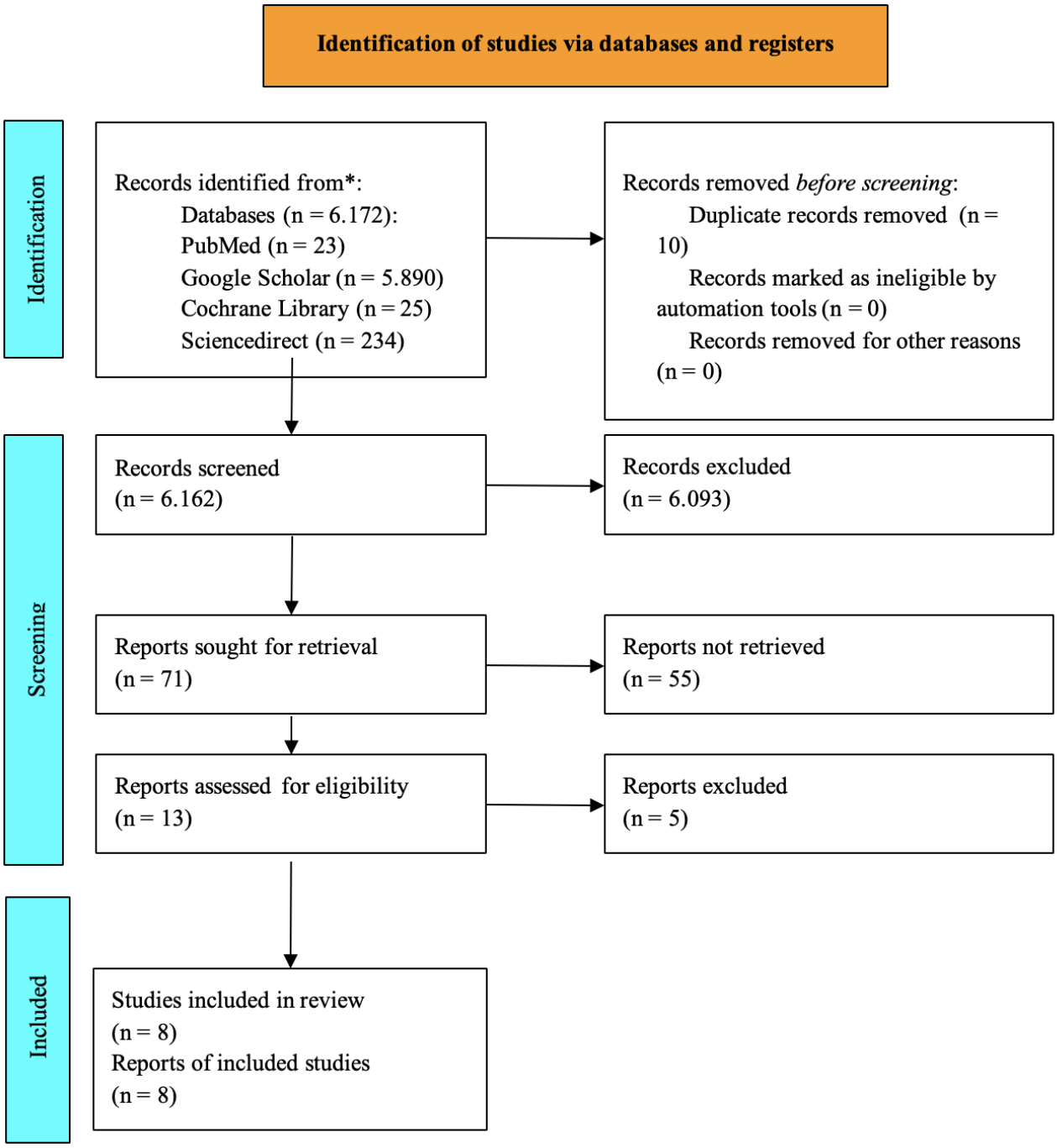


Figure 1 PRISMA Flow Diagram of the study selection process

indicate the effectiveness of black garlic extract and cloves in reducing blood cholesterol and triglyceride levels. The study by Prihanti et al. (2019) stated that black garlic extract at an effective dose of 7.5 mg/kgBW can significantly reduce LDL and triglyceride levels [8]. Ha et al. (2015) reported that black garlic extract at an effective dose of 0.5% can significantly lower total cholesterol and triglyceride levels [7]. Susanti et al. (2024) found that administering black garlic extract at doses of 30 mg/kgBW and 45 mg/kgBW can significantly reduce LDL and total cholesterol levels as well as significantly increase HDL levels [9]. Chang et al. (2017) also stated that administering black garlic at doses of 0%, 0.2%, 0.6%, and 1.2% in feed can significantly reduce body weight, triglycerides, and total cholesterol levels, and increase HDL significantly in the treatment groups [10]. Nurmawati et al. (2021) demonstrated that administering black garlic cloves at an effective dose of 1350 mg/200gBW can significantly decrease triglyceride, LDL, and total cholesterol levels [11]. Tran et al. (2018) stated that black garlic extract can significantly decrease total cholesterol, triglycerides, and LDL, and significantly increase HDL at a dose of 200 mg/kgBW in test animals [12]. Amor et al. (2017) stated that administering black garlic at a dose of 250 mg/kgBW can reduce LDL and triglyceride levels in rats [13].

The results from several of these studies suggest that

Table 1 Study characteristics

No.	Title	Author	Type of Research	Population and Sample	Intervention	Result
1.	*Effect of Black Garlic Extract on Blood Glucose, Lipid Profile, and SGPT-SGOT of Wistar Rats Diabetes Mellitus Model.*	Prihanti, G. S., Isnaini, F., Yudistia, R., Faradilla, A., Rahman, M. 2019.	*Study in vivo*	Wistar white rats aged 2-3 months with a body weight of 150-200 grams, divided into 4 groups (n=6).	Administration of black garlic extract at doses of 7.5 mg/kgBW, 15 mg/kgBW, and 30 mg/kgBW after induction with alloxan at a dose of 160 mg/kgBW was then compared with the disease control group.	There was a significant decrease ($p<0.001$) in blood glucose levels, LDL, triglycerides, SGOT, and SGPT depending on the administered dosage..
2.	*The Effects of Black Garlic (Allium sativum) Extracts on Lipid Metabolism in Rats Fed a High Fat Diet.*	Ha, A. W., Ying, T., Kim, W. K. 2015.	*Study in vivo*	One-month-old Sprague-Dawley rats divided into 4 groups (n=8).	Feeding with a high-fat content and black garlic extract at doses of 0.5% (5 grams extract/kg feed) and 1.5% (15 grams extract/kg feed) for 5 weeks. Compared to the disease control group.	There was a significant decrease in SREBP-1C mRNA expression ($p<0.05$), which led to a reduction in total cholesterol and triglyceride levels..
3.	*Lipid Profile and Blood Glucose Levels of Wistar Rats Fed a Non-High Fat Nutriment Supplemented with Black Garlic Extract*	Susanti, R., Kristamtini, K., 2024	*Study in vivo*	24 rats were divided into 4 groups, each consisting of 6 rats (n=24).	Administration of black garlic extract at doses of 15 mg/kgBW, 30 mg/kgBW, and 45 mg/kgBW for 14 days, then compared with the disease control group.	There was a significant decrease ($p<0.05$) in total cholesterol, triglycerides, and LDL levels in the group given black garlic. There was a significant increase ($p<0.05$) in HDL in the group given black garlic. The effective dose in this study was 45 mg/kgBW.
4.	*Methanolic extract of black garlic ameliorates diet-induced obesity via regulating adipogenesis, adipokine biosynthesis, and lipolysis*	Chen, Y. C., Kao, T.H., Tseng, C.Y., Chang, W.T., Hsu, C.L. 2014	*Study in vivo*	Eight-week-old Wistar rats were divided into 4 groups.	Administration of black garlic methanol extract for 8 weeks at doses of 0.1%, 0.3%, and 0.6%. Compared to the disease control group.	Administration of black garlic methanol extract significantly reduced body weight and triglyceride levels ($p<0.05$), as well as increased HDL levels and fecal lipids in rats ($p<0.05$).
5.	*Black Garlic Ameliorates Obesity Induced by a High-fat Diet in Rats*	Chang, W., Shiau, D., Cheng, M., Tseng, C., Chen, C., Wu, M *et al*. 2017	*Study in vivo*	Ten-week-old male Wistar rats were divided into 4 groups (n=8)	Feeding with a high-fat content and black garlic at concentrations of 0%, 0.2%, 0.6%, and 1.2% for 6 weeks, then compared to the diseased control group.	There was a significant decrease in body weight, triglyceride levels, and total cholesterol in the blood, as well as a significant increase in HDL ($p<0.05$).
6.	*The effect of single clove Black garlic on the hemostasis status and lipid profile in male Sprague Dawley rats with non-alcoholic fatty liver disease*	Nurmawati, L., Sulchan, M., Muis, S. F., Purnomo, H. D., Djamiatun, K., Ardiaria, M *et al.* 2021.	*Study in vivo*	Male Sprague-Dawley rats were divided into 7 groups (n=6).	Feeding with a high-fat content and black garlic cloves at doses of 450 mg/200 gBW, 900 mg/200 gBW, and 1350 mg/200 gBW for 8 weeks. Compared to the sick control group.	There was a significant decrease in triglyceride, LDL, and total cholesterol levels ($p<0.001$) with an effective dose of 1350 mg/200 gBW.
7.	*Beneficial Effects of an Aged Black Garlic Extract in the Metabolic and Vascular Alterations Induced by a High Fat/Sucrose Diet in Male Rats.*	Amor, S., Hedström, D. G., Carro, B. M., García, A. M. I., Almodóvar, P., Prodanov, M *et al.* 2018.	*Study in vivo*	Three-month-old Sprague-Dawley rats were divided into 3 groups (n=8).	Feeding a high-fat diet for 12 weeks was followed by administration of black garlic extract at a dose of 250 mg/kg from week 12 up to 6 months. This was compared to the disease control group.	There was a significant decrease in LDL cholesterol and triglyceride levels ($p<0.05$), and a significant increase in HDL levels ($p<0.01$).

8.	*Amelioration of Single Clove Black Garlic Aqueous Extract on Dyslipidemia and Hepatitis in Chronic Carbon Tetrachloride Intoxicated Swiss Albino Mice*	Tran, G. B., Dam, S. M., Le, N. T. N. 2018.	*Study in vivo*	Eight-week-old male Swiss albino mice weighing 30-32 grams were divided into 4 groups (n=5).	Administration of black garlic extract at a dose of 200 mg/kgBW orally for 30 days. After 1 hour, the rats were given CCl4 at a dose of 1 ml/kg. This was compared to the disease control rats, which were given CCl4 at a dose of 1 ml/kg twice a week for 28 days.	There was a significant decrease in triglyceride and LDL cholesterol levels ($p<0.05$) with an effective dose of 200 mg/kgBW..

both extracts and cloves of black garlic have considerable effectiveness in lowering LDL, triglycerides, and total cholesterol, as well as increasing HDL levels through various mechanisms. Essentially, various compounds in black garlic such as flavonoids, SAC, SAMC, and other metabolic compounds each contribute to lowering blood lipid levels, although with different dosages. The limitation of this research is that there are still some journals which state that not all doses of black garlic extract can significantly reduce LDL levels. The study by Chen et al. (2014) found that administering methanolic black garlic extract at the given dose did not significantly decrease LDL, triglyceride, and total cholesterol levels in the blood ($p>0.05$) [14]. This indicates that further studies are needed to determine the optimal dosage of black garlic extract for lowering LDL and total cholesterol levels. Another limitation in these studies is the variation in rat strains, which may result in different responses to each treatment. However, in general, administering black garlic extract to rats at various doses has a fairly good and effective effect in reducing triglycerides and cholesterol. Another limitation lies in the selection of the method, as the studies focused solely on in vivo research with rats as subjects. Therefore, further studies in humans using randomized controlled trial designs are needed to confirm its clinical effectiveness.

Discussion

Dyslipidemia

Dyslipidemia is a lipid metabolism disorder characterized by an imbalance of lipid levels in the blood, which may involve an increase or decrease in one or more lipid fractions. The lipid fractions that are commonly affected include increased total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, as well as decreased high-density lipoprotein (HDL) cholesterol [15]. Dyslipidemia results from disturbances in lipoprotein metabolism and can be classified into two categories based on its cause: primary dyslipidemia and secondary dyslipidemia. Primary dyslipidemia is caused by genetic or hereditary factors, while secondary dyslipidemia is due to a high-fat diet, certain medications, or underlying health conditions such as diabetes, metabolic syndrome, nephrotic syndrome, or hypothyroidism [16].

Dyslipidemia is a common cause of cardiovascular diseases and can worsen the process of atherosclerosis. According to WHO data, the prevalence of dyslipidemia among adults over the age of 25 is 36%. Meanwhile, data from the American Heart Association (AHA) reveal that in the United States, more than 100 million people have a total cholesterol level greater than 200 mg/dl. In Indonesia, data from the 2018 Basic Health Research (Riskesdas) shows that more than half of the population over the age of 15 has abnormal cholesterol levels, with a higher prevalence in women than in men [17].

Dyslipidemia typically does not present with specific symptoms or clinical complaints, and therefore often goes undetected. Symptoms usually relate to complications caused by dyslipidemia itself, such as coronary heart disease and stroke. In patients with extremely high triglyceride levels, dyslipidemia can cause several complications such as acute pancreatitis, hepatosplenomegaly, paresthesia or tingling sensations, breathing difficulties, and impaired consciousness. Elevated triglyceride levels can also affect the appearance of retinal blood vessels, and cause blood plasma to appear white and milky. Individuals with high LDL levels often develop characteristic signs such as corneal arcus, xanthelasma, and xanthomas, which typically accumulate in the Achilles tendon, elbows, and knees [18].

Black Garlic

Phytochemical components of black garlic

Black garlic (*Allium sativum*) is the result of fermenting garlic processed at high temperatures for a period of time. This fermentation process leads to changes in chemical contents and creates new formulas that are more stable than before. The main change occurring during heating is the conversion of alliin (S-Allyl-L-cysteine sulfoxide), which is unstable in fresh garlic, into the more stable S-Allyl-cysteine (SAC). Apart from SAC, black garlic contains other compounds such as flavonoids, thiosulfate, pyruvate, alkaloids, and hydroxymethylfurfural. Black garlic extract is known to provide various health benefits, acting as an antioxidant, anti-inflammatory, and antibacterial agent [5,19].

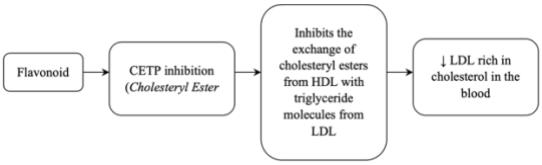
Pharmacology

Black garlic is highly beneficial for health. Every 100 grams of black garlic contains 143 kcal of energy, 3.57

grams of protein, 7.14 grams of fat, 14.29 grams of carbohydrates, 3.6 grams of fiber, 71 mg of calcium, 1.29 mg of iron, 571 mg of sodium, and 4.3 mg of vitamin C [20]. The S-Allyl-cysteine (SAC) content in black garlic exhibits antioxidant and hypolipidemic effects [11]. The antioxidant activity of polyphenols and SAC plays a key role in increasing the activity of enzymes such as glutathione (GSH), glutathione peroxidase (GPx), and glutathione reductase (GRd), as well as scavenging free radicals and helping to reduce oxidative stress [10]. SAC also has anti-inflammatory effects by inhibiting NF-κB activation and reducing the production of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β. The organosulfur compounds in black garlic can modulate signaling pathways such as PI3K/Akt and MAPK to inhibit cancer cell proliferation and induce apoptosis [21]. Research by Nurmawati et al. (2021) confirms that the compounds found in garlic can be used as medication for dyslipidemia, as they help balance plasma lipids through the action of allicin on PAI-1 levels [11].

Flavonoids

Flavonoids are derivatives of 2-phenyl-benzyl-γ-pyrone and have a variety of benefits, such as antioxidant, antifungal, antibacterial, anti-inflammatory, and antiviral activities. The flavonoid content in black garlic can reduce oxidative stress by inhibiting the chain reaction that converts superoxide into hydrogen peroxide, thereby suppressing oxidative stress. In addition, flavonoids also inhibit oxidative stress by inhibiting Cholesteryl Ester Transfer Protein (CETP). CETP is a plasma protein that mediates the exchange of cholesteryl esters from HDL with triglyceride molecules from LDL, VLDL, and chylomicrons, leading to increased cholesterol in VLDL and increased triglycerides in HDL. Increased CETP activity causes the release of Apo A1 from HDL so that Apo A1 can circulate freely and be removed from plasma. This reduces the capability of HDL and leads to HDL's failure to return cholesterol, thus raising the amount of cholesterol-rich LDL in the blood. Inhibiting CETP activity will lower LDL levels in the blood [8]. This result is consistent with a recent clinical trial by Vezza et al. (2024), where the administration of black garlic extract at a 14 mg dose to subjects with hypercholesterolemia (LDL level of 100-190 mg/dl) significantly reduced LDL levels ($P<0.004$) compared to pre-treatment LDL levels [22]. This demonstrates that black garlic indeed has good potential in humans. However, larger clinical studies are still needed to confirm these findings.



S-allyl-L-cysteine (SAC)

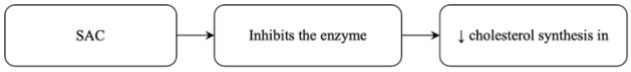
S-allyl-L-cysteine (SAC) is the most abundant organosulfur compound derived from garlic (*Allium sativum*) and is biosynthesized through the hydrolysis of γ-glutamyl-S-allyl-cysteine (GSAC) by the enzyme γ-glutamyl transpeptidase (γGTP). SAC is a compound produced during the aging process of black garlic [7]. SAC is known as a water-soluble bioactive compound with very high antioxidant capacity and has long been used both as a common dietary supplement and in traditional medicine. SAC has been reported to possess various significant biological effects, including antidiabetic, cholesterol-lowering, anticancer, and antihepatotoxic properties. In addition, the SAC content in black garlic is known to repair oxidative damage as well as help address cardiovascular disorders, Alzheimer's disease, stroke, and age-related diseases [23].

S-allyl-L-cysteine (SAC) has a positive influence on lipid profile, helping to reduce the risk of cardiovascular disease. SAC has been shown to lower total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, while increasing high-density lipoprotein (HDL) cholesterol, commonly known as good cholesterol. This is related to its ability to affect transcription factors such as PPARγ, which play a role in the regulation of fat metabolism and lipogenesis. SAC also helps reduce inflammation and oxidative stress, two main factors impacting metabolic lipid disorders [24]. Furthermore, SAC also has hepatoprotective effects. A study demonstrated that SAC can reduce elevated levels of ALT and AST, which are markers of liver damage, and suppress hepatocyte necrosis and inflammation in rats induced with CC14 .

Research by Valls et al. (2022) showed that consumption of black garlic extract at a dose of 250 mg containing 1.25 mg SAC per day for six weeks significantly reduced diastolic blood pressure in human subjects with hypercholesterolemia [25]. However, further studies are needed to test the effectiveness of this extract on blood lipid levels in subjects. S-allyl-cysteine (SAC) has a similar effect to statins by inhibiting the enzyme HMG-CoA reductase, which is involved in cholesterol synthesis in the liver. Inhibition of this enzyme's activity can reduce cholesterol production in the liver by allyl and allicin compounds found in black garlic [26]. Research by Siddiqui et al. (2020) also showed that simvastatin combined with SAC produced better outcomes in lowering total cholesterol, triglycerides, and LDL, as well as increasing HDL levels, with a p value of 0.005 [27].

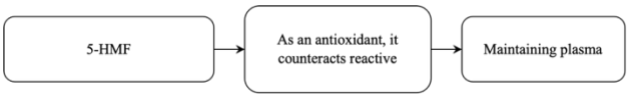
This demonstrates that administration of black garlic extract can be beneficial in improving hyperlipidemic conditions, making black garlic considered effective as an antihyperlipidemic due to its high S-allyl-L-cysteine (SAC) content [7]. According to Amor et al. (2019), SAC and alliin (SAC sulfoxide) contributed the most to metabo-

lic and vascular changes in their study on rats induced with a high-fat and sucrose diet. The study found significant reductions in blood triglyceride and total cholesterol levels, as well as increased HDL cholesterol and improvements in blood vessel structures damaged by a high-fat diet.



5-HMF

5-Hydroxy Methylfurfural is a compound found in black garlic that is formed during the fermentation process at temperatures of 60-77 degrees Celsius for 30-90 days. 5-Hydroxy Methylfurfural serves as an antioxidant that helps protect body cells from damage caused by free radicals [28]. There is a term called the Maillard reaction, which is a complex chemical process that occurs between amino acids and reducing sugars at high temperatures during the fermentation of garlic, resulting in the formation of 5-HMF. The reaction involves the condensation of amino acids with reducing sugars, leading to the formation of Amadori compounds and reactive aldehydes, after which 5-HMF is formed and the color of the garlic changes to dark brown [29]. The mechanism of the 5-HMF compound in black garlic to address dyslipidemia is as an antioxidant. The 5-HMF compound in black garlic can help prevent an increase in malondialdehyde (MDA) levels in the blood, where 5-HMF acts as an antioxidant by counteracting reactive oxygen species (ROS), thereby protecting the lipid membrane [30].



Pyruvate

Pyruvate, or pyruvic acid, is the end product of the final glycolysis pathway and plays an important role as an intermediate molecule in the metabolism of proteins, fats, and carbohydrates. Pyruvate is a three-carbon molecule that becomes a key component in cellular metabolism, both under aerobic and anaerobic conditions [31]. Pyruvate is divided into two types: endogenous pyruvate and exogenous pyruvate. Endogenous pyruvate is produced through the glycolysis process from glucose, while exogenous pyruvate is obtained from external sources and transported into cells via monocarboxylate transporters (MCT). Exogenous pyruvic acid can function as an antioxidant and help reduce oxidative stress [32].

Thiosulfate

Thiosulfate is a compound produced during the fermentation process of black garlic through specific chemical reactions. Thiosulfate is an antioxidant that helps protect the cells in the body from damage caused by free radicals. Several studies have stated that thiosulfate content is found in greater amounts in black garlic, as the thiosulfate compound emerges during the fermentation process. Side effects of thiosulfate compounds include allergic reactions, nausea, and vomiting [6].

Alkaloids

Alkaloids are secondary metabolite compounds in plants that have been proven to have various benefits. Alkaloids can cause damage to fungal cell membranes, destroy cancer cells, inhibit the growth of viruses and bacteria by inhibiting DNA, RNA polymerase, as well as cellular respiration [33]. In black garlic, alkaloids are compounds that have strong antioxidant effects [29]. According to research by Ha & Kim (2017), the antioxidant content in black garlic can activate the Nrf2 pathway, which can provide protection against oxidative stress [7]. Reduced oxidative stress will inhibit the oxidation of LDL and lead to a decrease in atherogenic effects. Moreover, Nrf2 can also act as an anti-hyperglycemic agent by increasing insulin sensitivity.

Development Potential

Garlic (*Allium sativum* L.) is one of the plants that has many benefits, both in food and health. With technological advances, garlic is not only used as a kitchen ingredient, but can also undergo a heating process to produce a new product known as black garlic. Black garlic is the result of processing garlic by heating it at high temperatures over a certain period. This process not only changes the color of the garlic to black, but also alters the bioactive compounds within the garlic itself, one of which is S-Allyl-cysteine (SAC). S-Allyl-cysteine (SAC) is a compound that acts as an antioxidant, which can prevent cell damage caused by free radicals [34]. Other compounds that can be found in black garlic include flavonoids, thiosulfate, pyruvate, alkaloids, and hydroxymethylfurfural. Black garlic extract is known to provide many health benefits, such as antioxidant, anti-inflammatory, anticancer, and antibacterial effects [5,19]. Black garlic extract has been proven effective in lowering triglyceride and cholesterol levels in the body due to its high antioxidant content, thus helping to address hyperlipidemia [35].

Conclusion

Dyslipidemia is a disorder of lipid metabolism in the blood characterized by an increase in total cholesterol, LDL cholesterol, triglycerides, and a decrease in HDL cholesterol. Dyslipidemia is divided into two categories: primary dyslipidemia and secondary dyslipidemia. Primary dyslipidemia is caused by genetic factors, whereas secondary dyslipidemia is caused by a high-fat diet, the use of certain medications, and the influence of pre-existing comorbid diseases. Dyslipidemia does not present with specific symptoms or clinical complaints. Complications caused by dislipidemia include coronary heart disease, str-

oke, acute pancreatitis, hepatosplenomegaly, paresthesia, difficulty breathing, and even impaired consciousness.

Supplementary Material

None

Author Contributions

SJ : Conceptualization, Methodology, Writing-Original Draft. **AR**: Data Curation, Formal Analysis, Visualization. **TYL** : Supervision, Funding Acquisition, Writing- Review & Editing. **RSI** : Supervision, Writing- Review & Editing. **IKAS** : Supervision, Writing- Review & Editing. **AKZ** : Supervision, Writing- Review & Editing. **MWA** : Supervision, Writing- Review & Editing. **AKZ** : Supervision, Writing- Review & Editing. **LAIFW** : Supervision, Writing- Review & Editing **W** : Conceptualization, Supervision, Writing- Review & Editing. **RYP** : Supervision, Writing- Review & Editing All authors should have approved the final version of the manuscript and agree to be accountable for their contributions.

Conflict of Interest

The authors have no financial conflicts of interest to declare.

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