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Doi

Studi Literatur Pengaruh Ekstrak Bawang Putih (*Allium Sativum L.*) terhadap Dislipidemia

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Abstract

*Dyslipidemia is a lipid metabolism disorder characterized by an increase in total cholesterol levels, low density lipoprotein (LDL), triglyceride levels, and low levels of high density lipoprotein (HDL) in the blood. Garlic compounds have lipid-lowering effects. The objective of this study is to reviewing several previous studies and literature studies evaluated this study to determine the effect of garlic extract (*Allium sativum L.*) on dyslipidemia. This research employed a literature review methodology, where relevant studies were collected by searching the internet using ProQuest, Pubmed, and Google Scholar search engines. The research results a total of 17 studies showed that garlic extract contains various compounds, the main ones being aliin and allicin. However, only 14 studies were able to reduce total cholesterol levels and other parameters such as triglyceride and LDL levels and increase HDL, while 3 studies were not able to reduce any of these parameters and increase HDL. This literature review study confirms the relationship between garlic extract *Allium sativum L.* has a role in dyslipidemia, but some researchers stated that garlic extract has not been able to reduce one of the parameters of dyslipidemia (total cholesterol, LDL, triglyceride levels and increase HDL levels.*

Keywords: *Garlic, Allium sativum L., Total cholesterol, HDL, LDL, Dyslipidemia*

Review Article

INTRODUCTION

Cardiovascular diseases, often known as CVD, are complex and multifactorial diseases that seriously jeopardize public health worldwide, with mortality and internal disease rates continuing to increase annually. According to the World Health Organization (WHO), every year, 17 million people die from cardiovascular disease, and by 2030, this number is expected to reach 24.8 million worldwide (Sukma, Berawi and Wahyudo, 2018). Risk factors for cardiovascular disease include hypertension, high cholesterol, alcohol consumption, and tobacco use (Yuniarifa, Djam'an and Purnasari, 2021).

Dyslipidemia is a disorder of lipid metabolism characterized by increased levels of total cholesterol, low density lipoprotein (LDL), triglyceride levels, and low levels of high-density lipoprotein (HDL) in the blood. This can lead to atherosclerosis and other cardiovascular problems (Alvin, Budianto and Widyastiti, 2018).

Data from the National Basic Health Research (*RISKESDAS*) in 2013 showed that 35.9% of the Indonesian population aged 15 years and over had abnormal cholesterol levels, or were not in accordance with NCEP ATP III (National Cholesterol Education Program, Adult Treatment Panel III), namely cholesterol levels with values ≥ 200 mg/dl. The female population is more likely to experience this than the male population. Figures show 15.9% of the population aged 15 years have a very high proportion of low-density lipoprotein (LDL) ≥ 190 mg/dl, and 22.9% with high density lipoprotein (HDL) levels less than 40 mg/dl, and 11.9% of triglyceride levels exceed 500 mg/dl and are categorized as very high (PERKENI, 2019).

In the treatment of dyslipidemia, there are several classes of drugs that are often used such as statins, nicotinic acid, fibrates, resins, ezetimibe and other derivatives. One of the most commonly used drugs is statins. As a first-line drug therapy, its side effects are an increased incidence of muscle pain, weakness and depression. In addition, statins do not reduce the risk of atherosclerotic cardiovascular events in patients aged 70 years or older. Drugs used as dyslipidemia therapy are generally still expensive, especially statins. On the other hand, herbal medicine has been used as an alternative medicine worldwide. Several rigorous clinical trials have illustrated that bioactive compounds from herbal medicines are effective and safe for improving lipid profiles (Ji et al., 2019).

Garlic is one of the most commonly used herbal medicines in Australia, the United Kingdom, Germany and the United States. Garlic with the Latin name *Allium sativum L.* has been used traditionally to treat various health conditions (Chan et al., 2020). Many traditional medicines are used in various provinces in Indonesia to treat health problems (Sukma, Berawi and Wahyudo, 2018). Due to its ability to relax vascular smooth muscle, garlic has been used as an herbal medicine for the treatment of hypertension and other heart diseases (Dharma and Maywidia Darma, 2016). There are various contents contained in garlic including, allylcysteine sulfoxide or alliin, allylalliin, propenyl alliin, and allicin including gamma glutamyl. Not only in the raw state of garlic when processed also has a very important content. When dry garlic bulbs are processed by adding yeast, a moisturizing process will occur and produce oil containing oligosulfides, diallyl-trithiaalkan-monosides or ajoene, vinyl dithiin fructose, allicin saponins and selenium (Sukma, Berawi and Wahyudo, 2018).

According to Vahidina et al., (2017) in Lee et al. research has shown compounds in garlic have lipid-lowering effects and antiplatelet activity that is simple and significant, in several other in vitro studies showing that garlic compounds can suppress LDL oxidation (Vahidinia et al., 2017). Research conducted by Limbu et al., (2019) as many as 112 patients consisting of 60 men and 52 women showed a short-term effect (90 days) of oral supplementation of garlic on the lipid profile of patients garlic (250mg) can reduce serum cholesterol levels, triglycerides, LDL cholesterol, and VLDL cholesterol and also increase HDL cholesterol significantly. (Limbu et al., 2019). Research by Pramitasari et al., (2018) proves that in the high cholesterol and cholic acid dyslipidemia group, given garlic extract 400 mg / 200 grams of body weight / day for 14 days shows that there is a relationship between the dose of

garlic extract to reduce total cholesterol levels, triglycerides, LDL / HDL ratios, and an increase in HDL levels (Prमितasari, Riana and Bahrudin, 2018).

METHODS

This research was conducted through a literature study entitled The Effect of Garlic Extract (*Allium sativum* L.) on Dyslipidemia. This research method is to use SLR or Systemic Literature Review which is a method used to collect sources of information and data obtained from various journals both national and international. Broadly speaking, the method used in this research is to search and collect journals, skim, summarize, then draw conclusions by grouping the data and theories used to answer the research objectives.

After determining the research topic and problem formulation, data were searched from various sources available on the internet such as Google Scholar, ResearchGate, Pubmed, and Proquest and then using a searching strategy, namely searching various journals using the keywords "Garlic", "*Allium sativum* L.", "Total cholesterol levels", "HDL levels", "LDL levels", "Dyslipidemia" which are adjusted to the research criteria. After the journals were collected with a total of 17 journals consisting of national and international journals, data collection was carried out and summarized the appropriate research journals so that conclusions could be drawn by grouping the data used to answer the research objectives.

RESULTS

Table 1. Research Results Table

1	Title of Article	Effect of Garlic Extract (<i>Allium sativum</i>) on Reducing Total Cholesterol Levels of White Rats (<i>Rattus norvegicus</i>) with Hypercholesterolemia
	Methods	Rats were made dyslipidemic by giving egg yolk diet and propylthiouracil drug for 25 days. Garlic extraction method: maceration. Cholesterol level testing: day 1, 5 and 10 after administration of the test material. Parameters tested: Total cholesterol level. Variables: <ol style="list-style-type: none"> 1. Egg yolk diet and propylthiouracil drug (KN-) 2. Simvastatin 1.8mg/200grBW (KN+) 3. Garlic extract /200grBW: <ul style="list-style-type: none"> - P1: 0.108gr/200grBW - P2: 0.144gr/200grBW - P3: 0.18gr/200grBW
	Results and Conclusion	There is an effect of garlic extract (<i>Allium sativum</i>) on reducing total cholesterol levels in white rats (<i>Rattus norvegicus</i>) with hypercholesterolemia: <ol style="list-style-type: none"> 1. Dose of 0.108-gram at 1 day and 10 days 2. Dose of 0.18-gram at 1 day
2	Title of Article	Differences in the Effectiveness of Simvastatin, Garlic Extract (<i>Allium sativum</i>), Red Dragon Fruit Extract (<i>Hylocereus polyrhizus</i>) and Their Combinations on LDL and Total Cholesterol Levels

Methods	Mice were made dyslipidemic with a diet high in cholesterol and cholic acid for 14 days. Cholesterol level testing was done after 14. Extraction method: not described. Parameters tested: LDL levels and Total cholesterol levels Variables:
<ol style="list-style-type: none"> 1. Diet high in cholesterol and cholic acid (KN-) 2. Simvastatin 0.18 mg/200grBW / day (KN+) 3. Red dragon fruit extract 65mg/200grBW/day (P1) 4. Garlic extracts 400 mg/200grBW/day (P2) 5. Red dragon fruit extract 32.5 mg/200grBW/day and garlic extract 200mg/200grBW/day (P3) 	
Results and Conclusion	There was a significant decrease in posttest total cholesterol and LDL levels in K (+), P1, P2, P3 ($p < 0.05$) indicating: simvastatin, garlic extract, red dragon fruit extract both singly and in combination are effective for reducing total cholesterol and LDL levels in dyslipidemia rat models.
3 Title of Article	Comparison of the Effect of Garlic Extract (<i>Allium sativum L.</i>), Chitosan and Banana Horn Synbiotic Yogurt on the Lipid Profile of Hypercholesterolemic Sprague-Dawley Rats.
Methods	The population was male Sprague-Dawley rats. Rats were made dyslipidemic by feeding a high-fat diet for 14 days. Parameters tested: Total cholesterol, LDL, HDL and triglyceride levels. Cholesterol level testing was done after 28 days. Variables:
<ol style="list-style-type: none"> 1. High fat feed (KN-) 2. Garlic extract 400 mg/kgBW for 28 days. (P1) 3. Chitosan 400 mg/kgBW for 28 days (P2) 4. Plantain horn synbiotic yogurt for 28 days (P3) 	
Results and Conclusion	There are differences in serum total cholesterol, LDL cholesterol, triglycerides and HDL cholesterol levels between garlic extract (<i>Allium sativum L.</i>), chitosan and antler banana synbiotic yogurt, as evidenced by the p value: $p < 0.05$. Garlic extract (<i>Allium sativum L.</i>) has the best ability to improve lipid profile, followed by chitosan and antler banana synbiotic yogurt.
4 Title of Article	Preventive Effects and Mechanisms of Garlic on Dyslipidemia and Gut Microbiome Dysbiosis
Methods	The population is dyslipidemia rats with high fat feeding. Rats were made dyslipidemic by feeding a high-fat diet for 12 weeks. Extraction method: supplementation. Parameters tested: GOT, GPT, GGT levels, total cholesterol, LDL, HDL and triglyceride levels. Cholesterol level testing: 12 weeks Variables:
<ol style="list-style-type: none"> 1. Normal diet 2. Normal diet + garlic supplementation (5%) 3. Normal diet + dextrin (4%) 4. High fat diet 	

	5. High fat diet + garlic supplementation (5%) 6. High-fat diet + dextrin (4%)
Results and Conclusion	The serum levels of T-Cho, TG, and LDL were significantly increased in the high-fat diet group ($p < 0.05$), and significantly reduced ($p < 0.05$) by garlic supplementation ($p < 0.05$).
5 Title of Article	Beneficial effects of <i>Allium sativum</i> L. stem extract on lipid metabolism and antioxidant status in obese mice fed a high-fat diet
Methods	The population was white mice. Rats were made dyslipidemic by feeding a high-fat diet for 8 weeks. Extraction methods: ethanol extract method, Kjeldahl method, Soxhlet method, and drying loss method. Cholesterol levels were tested after treatment for 4 weeks. Parameters tested: total cholesterol, HDL, LDL and triglyceride levels. Variables: <ol style="list-style-type: none"> 1. Normal diet (KN) 2. High fat diet + Orlistat (K+) 3. High fat diet (K-) 4. Garlic extract /kgBW for 4 weeks. <ul style="list-style-type: none"> - P1: 100 gr/kgBW - P2: 200 gr/kgBW - P3: 500 gr/kgBW
Results and Conclusion	The results found that there were significant differences in total cholesterol and triglycerides between rats fed a normal diet and rats fed a high-fat diet and garlic extract 100, 250, and 500 mg/kgBW. For HDL showed no significant difference.
6 Title of Article	Effect of Garlic and Lemon Juice Mixture on Lipid Profile and Some Cardiovascular Risk Factors in People 30-60 Years Old with Moderate Hyperlipidaemia: A Randomized Clinical Trial
Methods	The population was patients aged 30-60 suffering from hyperlipidemia. Extraction method: not described (raw garlic). The groups were divided into 4: control group, lemon juice treated group, garlic treated group and garlic and lemon juice mixture treated group. Parameters tested: Total cholesterol levels, LDL, HDL and triglyceride levels. Cholesterol level testing: day 0, 4 and 8. <ol style="list-style-type: none"> 1. High fat diet (K-) 2. Garlic extracts 20 g (P1) 3. Combination of 20 g garlic extract and 1 tbsp lemon juice. (P2) 4. Lemon juice 1 tablespoon (P3)
Results and Conclusion	The results showed significant differences between the levels of total cholesterol ($p < 0.05$), HDL ($p < 0.05$), LDL ($p < 0.05$) and triglycerides ($p < 0.05$) before treatment with garlic and a mixture of garlic and lemon.

7	Title of Article	Effects of Garlic Supplement on Cholesterol and Triglyceride Levels in Wistar Rats Fed a Diet High in Palm Oil
	Methods	The population was white rats (<i>Rattus norvegicus</i>) with hypercholesterolemia. Rats were made dyslipidemic by feeding a diet high in palm oil. Parameters tested: Total cholesterol levels and triglyceride levels. Cholesterol level testing: day 1 and 26 after administration of the test material. Variables <ol style="list-style-type: none"> 1. Normal diet (KN) 2. High palm oil diet (K-) 3. Diet high in palm oil and garlic supplement (P)
	Results and Conclusion	The results showed a significant difference with a value of $P < 0.05$. This shows that the effect of garlic supplements can reduce cholesterol levels significantly in a high palm oil diet.
8	Title of Article	Effect of Garlic Ethanol Extract on Total Cholesterol, LDL and HDL Levels in Hypercholesterolemic White Rats
	Methods	The population was White Rats (<i>Rattus norvegicus</i>) with hypercholesterolemia. Extract method: using ethanol. Rats were made dyslipidemic by being given a high-cholesterol diet. Parameters tested: Total cholesterol, HDL and LDL levels. Cholesterol level testing: day 1 and 14 after administration of the test material. Variables: <ol style="list-style-type: none"> 1. Normal diet (KN) 2. High cholesterol diet (K-) 3. Simvastatin 0.72 mg /200gram BW (P+) 4. Garlic Extract /200gramBW <ul style="list-style-type: none"> - P1: 3.6 mg - P2: 7.2 mg - P3: 10.8 mg - P4: 14.4 mg - P5: 18 mg
	Results and Conclusion	The results showed that the average decrease in total cholesterol levels after treatment was significant with a value of $p < 0.05$, indicating that there was a significant difference in the decrease in total cholesterol levels after treatment. Further statistical testing to determine differences between control and treatment groups found that each group had a significant difference with a value of $p < 0.05$.
9	Title of Article	The Effect of Garlic on Reducing Cholesterol Levels in the Elderly of the Delitua Health Center Working Area
	Methods	The population is the elderly in the Deli Tua Health Center Working Area. Cholesterol assessment was carried out before and after the intervention with the provision of garlic
	Results and Conclusion	Average initial cholesterol levels: 206,33. Cholesterol levels after giving garlic extract: 181.83. T test results $p = 0.031$.
10	Title of Article	Effect of Single Garlic Ethanol Extract (<i>Allium sativum L.</i>) on Cholesterol Levels of White Mice (<i>Mus musculus</i>)

Methods	<p>The population was white mice (<i>Mus musculus</i>). Mice were made dyslipidemic with quail egg yolk diet for 24 days. Parameters tested: total cholesterol levels. Cholesterol level testing: day 24 after garlic administration.</p> <p>Variables:</p> <ol style="list-style-type: none"> 1. Standard feed (KN) 2. White egg yolk feed (K-) for 24 days. 3. Single garlic extract/day for 24 days. <ul style="list-style-type: none"> - P1: 0.007 g/head - P2: 0.014 g/head
Results and Conclusion	<p>The results after treatment for 24 days concluded quantitatively, (K-) had the highest average cholesterol levels, while P1 and P2 had slightly lower average cholesterol levels than K-. At a dose of 0.007 g/day and a dose of 0.014 g/day, single garlic ethanol extract can help reduce cholesterol levels in mice given quail egg yolk (but not significant).</p>
11 Title of Article	<p>Effect of Single Garlic Ethanol Extract (<i>Allium sativum</i> L.) on Cholesterol Levels of White Mice (<i>Mus musculus</i>)</p>
Methods	<p>The population is male mice (Wistar). Mice made dyslipidemia were given alloxan at a dose of 160 mg / kg BW intra peritoneal single dose to achieve the effect of Diabetes Mellitus (for 3 days). Parameters tested: Total cholesterol levels. Testing of cholesterol levels: day 4 and 15 after administration of the test material.</p> <p>Variables:</p> <ol style="list-style-type: none"> 1. Normal diet (KN) 2. Diet with alloxan (K-) 3. Garlic bulb skin extract at a dose of mg / kg BW orally for 14 days <ul style="list-style-type: none"> - P1: 1000 mg/kgBW - P2: 2000 mg/kgBW - P3: 4000 mg/kgBW
Results and Conclusion	<p>The results showed that there were significant differences between groups P1, P2 and P3. In reducing cholesterol levels. The p-value is not included. Garlic bulb skin extract at doses of 1000 mg / kg BW, 2000 mg / kg BW and 4000 mg / kg BW can reduce total blood cholesterol levels in male Wistar rats with diabetes mellitus</p>
12 Title of Article	<p>A Mechanism Based Pharmacological Evaluation Of Efficacy Of <i>Allium Sativum</i> In Regulation Of Dyslipidemia And Oxidative Stress In Hyperlipidemic Rats</p>
Methods	<p>The population was mice (Charles Foster strain) with hypercholesterolemia. Rats were made dyslipidemia high fat diet for 30 days. Cholesterol level testing: 31st and 60th day after administration of test materials. Parameters tested: total cholesterol, HDL, LDL and triglyceride levels.</p> <p>Variables</p> <ol style="list-style-type: none"> 1. Normal diet (KN)

		<ol style="list-style-type: none"> 2. Gemfibrozil (50 mg/kgBW) (K+) 3. High fat diet (K-) 4. Garlic extract 200 mg/kgBW (KI)
	Results and Conclusion	The results showed that there were significant differences in total cholesterol, HDL, LDL and triglycerides between K- and P1 groups. p-value is not quantified. There is an effect of garlic extract (<i>Allium sativum</i>) on reducing total cholesterol levels in hypercholesterolemic rats.
13	Title of Article	Effects of dietary garlic supplements on serum lipid profiles, LDL oxidation and weight gain in Western diet-fed rats.
	Methods	<p>The population was male rats (Wistar). Rats were made dyslipidemic by feeding a high protein and fat diet for 14 weeks. Cholesterol level testing: at week 14 after treatment. Parameters tested: total cholesterol, HDL, LDL and triglyceride levels</p> <p>Variables:</p> <ol style="list-style-type: none"> 1. Normal diet (KN) 2. High fat diet (K-) 3. 5% garlic supplement (P1) 4. Shredded garlic 10% (P2)
	Results and Conclusion	The results showed that there was a decrease in the difference in cholesterol levels of P1 and P2 compared to the K- group, but not significant. Garlic 5% and garlic 10% supplements were not able to reduce total blood cholesterol levels in male Wistar rats with diabetes mellitus.
14	Title of Article	Effect of <i>Nigella Sativa</i> and <i>Allium Sativum</i> Coadministered with Simvastatin in Dyslipidemia Patients: A Prospective, Randomized, Double-Blind Trial.
	Methods	<p>The population was patients aged 24-57 with hyperlipidemia. Cholesterol assessment after therapy. Parameters tested: total cholesterol, HDL, LDL and triglyceride levels.</p> <p>Variables:</p> <ol style="list-style-type: none"> 1. Simvastatin 10 mg 1x/day after dinner (P1) 2. Simvastatin 10 mg + Blackseed 500 mg and garlic oil capsules 250 mg 1x/day after dinner (P2)
	Results and Conclusion	Combination therapy of blackseed 500 mg and garlic 250 mg was able to reduce cholesterol levels lower (170.1-181.9) than dyslipidemia patients who were given simvastatin therapy (192.39-204.81) There were highly significant differences ($p \leq 0.01$) for Non-HDL, cholesterol, triglycerides and ldl and there were significant differences ($p=0.03$) for HDL between the two treatment groups. (simvastatin and combination of blackseed with garlic).
15	Title of Article	Short-term Effect of Garlic Extract on Patients with Dyslipidemia
	Methods	The population was Patients over 30 years of age and suffering from cholesterol. Cholesterol assessment was

		done on day 0 and after 90 days of treatment. Parameters tested: total cholesterol, HDL, LDL and triglyceride levels. Variables: 1. Placebo-treated group (KN) 2. Group given Lasuna capsules containing 250 mg garlic (P1)
	Results and Conclusion	On day 0, there was no significant difference between KN and P1 (p: 0.53 > 0.05). On day 90 after therapy, there was a significant difference between the KN group and the P1 group (p: 0.001 < 0.05).
16	Title of Article	The Study of antihyperlipidemic effect of allium sativum in rats induced with hyperlipidemia using fat rich diet.
	Methods	The population was rats. Rats were made dyslipidemia by feeding a high fat diet for 15 days. Parameters tested: total cholesterol, HDL and triglyceride levels. Cholesterol level testing: on day 15 after treatment.
	Results and Conclusion	The results showed that the administration of garlic for 14 days in groups P1 and P2 was able to reduce total cholesterol levels, triglycerides and increase HDL, the P-value was not listed.
17	Title of Article	Effect of Garlic Ethanol Extract (<i>Allium Sativum</i> , Linn) on Reducing Cholesterol Levels in Mice (<i>Mus Musculus</i>)
	Methodes	The population is white mice (<i>Mus musculus</i>) with hypercholesterolemia. Mice were made dyslipidemic by being given a high-fat diet for 2 weeks. Parameters tested: total cholesterol levels. Cholesterol level testing: done after 7 days of garlic administration. Variables: 1. Normal diet (KN) 2. Simvastatin 0,052 ml (K+) 3. High-fat diet (K-) 4. Garlic extract for 7 days P1: 0,2 ml - P2: 0,3 ml - P3: 0,5 ml
	Results and Conclusion	The results showed that after testing, the significance result was 0.00 < 0.05 between group K- with P1, P2 and P3. While the effectiveness test and the highest decrease in cholesterol levels is P3.

DISCUSSION

The constituents and benefits of garlic

Of the 17 studies, researchers used more macerated extracts, including: (Hewen, Nurina and Liana, 2019), (Kim et al., 2013), (Brajawikalpa & Kautama 2016), (Dewi et al., 2021), (Wijayanti, Rosyid and Izza 2017), (Shrivastava et al., 2012), (Narkhede et al., 2020), (Isfanda &Andri 2021). In addition, in the study (Vahidinia et al., 2017) garlic was made into supplements and fried onions, Chen et al. (2019) in their research made garlic into supplements. And the rest do not explain the extraction method. The content contained in garlic is the alkaloid compound alliin and allicin. Other ingredients

most commonly found in garlic are vitamin c and also nicotinic acid (niacin), saponins, terpenoids, flavonoids and amino acids.

1st study, (Hewen, Nurina and Liana, 2019) maceration extraction method on garlic, found that garlic contains alkaloid compounds, namely allicin. 2nd study, (Yuniarifa, Djam'an and Purnasari, 2021) did not show the method of making the extract, but according to his research, garlic extract contains kaempferol glycoside which is a strong scavenger and can form hydroxyl radicals and can prevent oxidation of LDL. Garlic extract contains S-ethyl-cysteine (SEC), S-allyl cysteine (SAC), S-propyl cysteine (SPC) which has a concentration of 2-4 mmol/liter. Other compounds include allyl methyl sulfide, diallyl disulfide (DADS), dipropyl sulfide, diallyl trisulfide (DATS), diallyl sulfide (DAS), and dipropyl disulfide which have the function of inhibiting the speed of cholesterol synthesis in the Hydroxymethylglutaryl-CoA reductase enzyme reaction. 3rd study, (Alvin, Budianto and Widyastiti, 2018) did not show the method of making the extract, but according to his research, garlic extract contains alliin and allicin. The compound γ -glutamyl-cysteine is an intermediate compound for the formation of other organosulfur compounds, including alliin and S-allyl cysteine (SAC). The enzyme alliinase will then convert alliin into allicin. Allisin is a precursor to the formation of allyl sulfide compounds, such as diallyl trisulfide (DATS), diallyl disulfide (DADS), diallyl sulfide (DAS) and dipropyl disulfide.

4th researcher, namely (Chen et al., 2019) used a method by making garlic into a supplement, it was found that garlic contains fructans (548 mg/g), alliin (7 mg/g), and other organosulfur derivatives, including allicin (5 mg/g), G-SAC (4 mg/g), and S-allyl cysteines (SAC, 2 mg/g). Alliin and Allicin play a role in reducing cholesterol levels in the blood of hypercholesterolemic rats. 5th researcher, (Kim et al., 2013) used ethanol extract method, kjeldahl method, soxhlet method, and drying loss method. Finding allicin content that is useful in lowering cholesterol in the blood.

The 6th study conducted by (Aslani et al., 2016) did not show the method of making extracts, but according to his research garlic contains allicin and several other compound components that play a role in the process of lowering cholesterol in the blood. The 7th study conducted by (Asnel, Kadri and Arisanty, 2015) did not show the method of making the extract, but according to his research, garlic bulb extract contains 10 mg alliin and/or 4000 μ g allicin.

The 8th study by (Brajawikalpa & Kautama, 2016) extract method using ethanol, found that garlic ethanol extract contains allicin, vitamin C and niacin which play a role in lowering cholesterol levels. The 9th study by (Marlina & Ginting, 2021) did not show the method of making extracts, but the phytochemicals contained in garlic, namely allyl sulfide, which functions as an anticancer, antimicrobial, anti-oxidation, anti-thrombotic, anti-inflammatory, stimulates the immune system, can regulate blood pressure, and can reduce blood cholesterol content, the compound is allicin. The 10th study was conducted by (Dewi et al., 2021) using the maceration extraction method 3 times. According to his research, garlic ethanol extract contains allicin which plays a role in lowering cholesterol. The 11th study by (Wijayanti, Rosyid and Izza, 2017) using the maceration method found that Garlic Bulb Peel Extract (EKUBP) contains alkaloid compounds, polyphenols, flavonoids, saponins, and tannins.

The 12th study conducted by (Shrivastava et al., 2012) maceration extraction method on garlic, found that garlic contains compounds that play a role in lowering cholesterol content in the blood. The 13th study by (Vahidinia et al., 2017) with the extraction method, garlic made supplements and crude extracts showed that garlic contains allicin which plays a role in lowering cholesterol levels. The 14th study by (Alobaidi, 2014) did not show the method of making extracts and phytochemical results from garlic. The 15th study by (Limbu et al., 2019) did not show the method of making extracts, but according to his research garlic has hydrogen sulfide production content and allicin content liberated from alliin and alliinase enzymes which are thought to have angiotensin II inhibitors and vasodilating effects. The 16th study by (Narkhede et al., 2020) using maceration extraction method found that garlic contains saponin compounds, terpenoids, flavonoids, amino acids, volatile oils and cardiac glycosides that play a role in lowering cholesterol levels. The 17th study by (Isfanda & Andri, 2021) using maceration extraction method found that garlic contains allicin compounds.

It is known from these data that the most content of garlic and useful in lowering cholesterol levels are allicin, niacin, vitamin C and saponins. Allicin binds to the sulfhydryl (SH) group which is a functional part of coenzyme A in the body's cholesterol formation process. Vitamin C lowers cholesterol in people who have high cholesterol levels, but not in people who have normal cholesterol levels. This proves that vitamin C plays a homeostatic role in lowering cholesterol. Niacin suppresses the activity of the enzyme lipoprotein lipase by inhibiting the flow of free fatty acids from adipose tissue, thereby reducing VLDL production in the liver and can inhibit fat mobilization so that total cholesterol and LDL cholesterol production can decrease. Niacin can also increase HDL concentration (Brajawikalpa & Kautama, 2016).

Saponins can form insoluble complex bonds with cholesterol so that cholesterol cannot be absorbed by the intestine, and flavonoids can neutralize free radicals that protect the pancreas. Saponins can inhibit the absorption of cholesterol and bile acids in the intestine, thus spurring cholesterol synthesis in the liver which is converted into bile acids which are then secreted into the intestine. This causes secretion by the feces to be greater than absorption by the intestines, Saponins are not absorbed in the intestines, but are metabolized in the colon into saponin aglycones and sugars by microflora. Alkaloid compounds in garlic bulb skin also have a role in lowering cholesterol levels through the mechanism of inhibiting the activity of pancreatic lipase enzymes so as to increase fat secretion through feces, as a result the absorption of fat by the liver is inhibited so that it is not converted into cholesterol. (Wijayanti, Rosyid and Izza, 2017).

Mengetahui data cara membuat dislipidemia

Based on this literature study, researchers have mostly used high-fat diets in creating dyslipidemia models. (Chen et al., 2019) created hypercholesterolemic mice by feeding a high-fat diet consisting of 21% protein, 40% fat, 10% carbohydrate, 4% cellulose, and about 570 kcal/100 g total calories. (Kim et al., 2013) created hypercholesterolemia in mice by feeding a high-fat diet with 45% energy from fat. The AIN-93G pure diet contains 15.8% energy from fat (70gkg-1 soybean oil), 20.3% energy from protein and 63.9% energy from carbohydrates. (Shrivastava et al., 2012) to make rats dyslipidemia by giving fat - 45%, fructose - 17% and cholesterol - 12.5g / 4057 Kcal for 30 days. (Isfanda & Andri, 2021) the high fat diet given consisted of standard feed (provit 511), egg yolk, coconut oil, chicken fat. Feeding was given for 2 weeks. (Asnel, Kadri and Arisanty, 2015) to make rats dyslipidemia by giving a diet high in palm oil. (Dewi et al., 2021) rats are made dyslipidemia by giving quail egg yolk as much as 2% of their body weight, as well as standard food and sufficient water. (Narkhede et al., 2020). Hyperlipidemia was induced in rats by feeding a high-fat diet for 15 days. Apart from using a high-fat diet, the researchers used a high-cholesterol diet. In his research (Yuniarifa et al., 2021) a diet high in cholesterol and cholic acid comes from food that has been made according to standards with a composition of 1% cholesterol and 0.25-0.5% cholic acid. Brajawikalpa and Kautama (2016) did not show how to make rats dyslipidemia. Their study only said that the rats were given high-cholesterol feed.

Researchers in making dyslipidemia models use other dietary ingredients. (Hewen, Nurina and Liana, 2019) made hypercholesterolemia by inducing rats to feed hypercholesterolemia in the form of a mixture of egg yolk and propylthiouracil drugs given for 25 days. (Vahidinia et al., 2017) giving the diet is done by giving 21% crude protein, 5.5% crude fiber, 4.5-5.1% crude fat, 0.5% NaCl, 0.7% mineral mixture (manganese, zinc, iron, copper, cobalt and selenium) and vitamins (B2, B1, K, E, D3, A), with a total energy of 2547 kcal/kg diet. (Wijayanti, Rosyid and Izza, 2017) to make rats become diabetes mellitus by giving alloxan at a dose of 160 mg / kg BW intra peritoneal single dose to achieve the effect of Diabetes Mellitus. But the administration of alloxan needs to be aware, because alloxan can cause damage to pancreatic beta cells. Alloxan can be injected intraperitoneally, subcutaneously and intravenously. The dose used is different, intravenous 65 mg/kg BW, while subcutaneous and intraperitoneal 2-3 times the intravenous dose. (Riduan, 2015). Some studies did not intervene to provide a high-fat diet because the research was conducted in humans.

Analyzing the effect of garlic extract (*Allium sativum* L.) in reducing LDL-cholesterol levels and increasing HDL-cholesterol.

Garlic extract has a role in lowering total cholesterol levels. From a total of 17 studies, there are 14 studies that state that garlic extract is able to reduce total cholesterol levels, LDL, triglycerides and increase HDL levels in different research subjects, doses and times significantly.

1st Researcher, namely (Hewen, Nurina and Liana, 2019) stated that there was an effect of garlic extract (*Allium sativum*) on reducing total cholesterol levels in white rats (*Rattus norvegicus*) with hypercholesterolemia at a dose of 0.108 grams / 200 grams of BW on 1 day and 10 days, a dose of 0.18 grams / 200 grams of BW on 1 day administration. 2nd study, (Yuniarifa et al., 2021) there are differences in the effectiveness of simvastatin 0.18 mg / 200g BW / day, garlic extract (*Allium sativum*) 400 mg / 200g BW / day, red dragon fruit extract (*Hylocereus polyrhizus*) 65 mg / 200g BW / day and their combination (red dragon fruit extract 32.5 mg / 200g BW / day and garlic extract 200 mg / 200g BW / day) on LDL and total cholesterol levels in dyslipidemia male rats during 14 days of treatment. 3rd study, (Alvin, Budianto and Widyastiti, 2018) garlic extract (*Allium sativum* L) 400 mg /kgBW for 28 days, chitosan 400 mg/kgBW for 28 days and banana horn synbiotic yogurt for 28 days can reduce serum total cholesterol, LDL cholesterol, triglycerides and HDL cholesterol levels. 4th study, (Chen et al., 2019) garlic supplementation can reduce total cholesterol, TG, and LDL levels in rats fed a high-fat diet for 12 weeks. 6th study, (Aslani et al., 2022) showed that giving garlic and a mixture of garlic + lemon can reduce total cholesterol, LDL and triglyceride levels in obese people, and increase HDL levels in the blood of patients experiencing hyperlipidemia.

The 8th study by (Brajawikalpa & Kautama 2016) found that Garlic Extract at doses of 3.6; 7.2; 10.8; 14.4; and 18 mg/200gramBW was able to reduce total cholesterol levels, LDL and increase HDL in rats fed a high-fat diet. In this study it was also mentioned that the dose that had almost the same as the positive control (Simvastatin 0.72mg/200gram BW) was the highest dose of ethanol extract, namely 18mg/200gramBW. The 9th study by (Marlina and Ginting, 2021) showed that there was an effect of giving garlic to reduce cholesterol levels in the elderly at the Delitua Health Center in 2020. The 10th study by (Dewi et al., 2021) found that at a dose of 0.007 g / day and a dose of 0.014 g / day a single garlic ethanol extract can help reduce cholesterol levels in mice given quail egg yolk for 24 days. The 11th study by (Wijayanti, Rosyid and Izza, 2017) showed that garlic bulb skin extract at doses of 1000 mg / kg BW, 2000 mg / kg BW and 4000 mg / kg BW was able to reduce total blood cholesterol levels in male Wistar rats with diabetes mellitus.

The 12th study by (Shrivastava et al., 2012) showed that there were significant differences in total cholesterol, HDL, LDL and triglycerides between rats fed a high-fat diet and rats fed a high-fat diet and 200 mg/kgBW garlic extract. The 14th study by (Alobaidi, 2014). Combination therapy of blackseed 500 mg and garlic 250 mg can reduce cholesterol levels lower (170.1-181.9) than dyslipidemia patients given simvastatin therapy (192.39-204.81). The 15th study by (Limbu et al., 2019) giving Lasuna capsule therapy containing 250 mg of garlic for 90 days was able to reduce cholesterol levels in patients with cholesterol. The 16th study by (Narkhede et al., 2020) found that 100 and 200mg/kgBW garlic extract for 14 days was able to reduce total cholesterol and triglyceride levels in rats fed a high-fat diet, and was able to increase HDL levels in rats. The 17th study by Isfanda and Andri (2021) showed that at doses of 0.2 ml, 0.3 ml and 0.5 ml of garlic ethanol extract can help reduce cholesterol levels in mice given a high-fat diet. The highest cholesterol reduction occurred in the group given a dose of 0.5 ml garlic extract.

Of all the studies, there are 3 that state that garlic extract has not been able to reduce one of the parameters, namely: total cholesterol levels, LDL, Triglycerides and raise HDL levels significantly. 5th researcher, namely Kim et al. (2013) showed that the administration of garlic extracts at doses of 100, 250, and 500 mg/kgBW was able to reduce total cholesterol and triglyceride levels in rats fed a high-fat diet after treatment for 4 weeks. But it cannot significantly increase HDL levels. The 7th study, (Asnel, Kadri and Arisanty, 2015) states that garlic supplements have an effect on lowering cholesterol

in rats fed a diet high in palm oil but not significantly. But able to reduce triglyceride levels significantly. The 13th study by (Vahidinia et al., 2017) found that 5% garlic supplements and 10% shallots were not able to reduce total blood cholesterol levels in male Wistar rats with diabetes mellitus.

From the description of the data above, garlic extract is able to reduce total cholesterol levels, LDL triglycerides and increase HDL, but this lipid profile improvement does not cover all lipid profiles. Giving a combination of garlic extract with other ingredients can improve almost all lipid profiles. (Alvin, Budianto and Widyastiti, 2018) in his research combined garlic extract (*Allium sativum* L) 400 mg/kgBW, chitosan 400 mg/kgBW and banana horn synbiotic yogurt for 28 days was able to improve total cholesterol, LDL cholesterol, triglycerides and serum HDL cholesterol. Research by Aslani et al. (2022) showed that giving garlic and a mixture of garlic + lemon juice was also able to reduce total cholesterol, LDL and triglyceride levels in obese people, and increase HDL levels in the blood. In giving garlic extract, it is also necessary to pay attention to how to make the research subject dyslipidemia. This is in line with the opinion (Vahidinia et al., 2017) which states that it is likely that the absence of the effect of garlic extract on lowering cholesterol levels is due to the dietary patterns used.

If categorized from the research subject, there are 13 studies that use rat or mice animal subjects and 4 studies using humans. Garlic extracts both singly and in combination when given to experimental animals or humans are significantly able to reduce total cholesterol, LDL, and triglyceride levels, and increase HDL levels. There are studies that prove that giving garlic to humans is able to properly improve the human lipid profile, including: Researcher 6, namely Aslani et al. (2022) regarding the administration of garlic plus lemon juice. The 14th study by (Alobaidi, 2014) regarding the combination of 500 mg blackseed and 250 mg garlic. The 15th study by (Limbu et al., 2019) gave Lasuna capsule therapy containing 250 mg of garlic for 90 days. The 9th study by (Marlina and Ginting, 2021) also showed that giving garlic to reduce cholesterol levels in the elderly with a population of 12 people.

Comparison between positive control (drug) and garlic has a difference in effectiveness. From 17 studies, the effective dose of garlic in reducing total cholesterol, LDL, triglyceride and raising HDL levels ranged from 3.6 mg-180 mg/200grBW, 100-500 mg/KgBW. The 8th study by Brajawikalpa and Kautama (2016) mentioned that the dose that has almost the same as giving positive control (Simvastatin 0.72mg/200gram BW) is a dose of ethanol extract 18mg/200gram BW. The 17th study by Isfanda and Andri (2021) showed that the highest cholesterol reduction occurred in the group given a dose of 0.5 ml of garlic extract, where this dose was equivalent to the positive control, namely Simvastatin 0, 052 ml.

CONCLUSION

Based on the data from the analysis of the literature review that has been carried out, it is concluded that with this literature review study, it is generally found that there is a relationship between garlic extract (*Allium sativum* L.) to improve the condition of patients with dyslipidemia, but some researchers state that garlic extract has not been effective in improving one of several dyslipidemia parameters (total cholesterol, LDL, triglyceride levels and raising HDL levels).

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