REVIEW ARTICLE

Efficacy of Bay Leaf (*Syzygium polyanthum*) in Regulating Lipid Profile in Dyslipidemia Model Rats: A Systematic Review

Trisilya Mita Anggrek[1], Indri Safitri Mukono[2*], Maftuchah Rochmanti[3], Citrawati Dyah Kencono Wungu[2]

[1]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[2]Department of Physiology and Medical Biochemistry, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[3]Department of Anatomy, Histology, and Pharmacology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

ABSTRACT

Introduction: Cardiovascular disease is the leading cause of death in the world, more than any other disease. The leading cause of cardiovascular disease is dyslipidemia. Long-term use of simvastatin can cause other diseases. One of the medicinal plants known to have anti-cholesterol effects is a bay leaf (*Syzygium polyanthum*). This study aimed to determine how the administration of bay leaf extract regulates lipid profiles.
Methods: This study used a systematic review based on PRISMA guidelines. Sampling in this study was done by collecting studies available in e-databases: PubMed and Google Scholar, with the inclusion criteria being experimental studies about the effect of bay leaf extract administration in regulating lipid profile in rats.
Results: This study consisted of 10 experimental studies on rats. Eight studies showed an improved lipid profile, while two other studies did not show an improving lipid profile after the administration of bay leaf extract.
Conclusion: Most studies revealed that bay leaf extract positively improves lipid profiles by lowering total cholesterol, LDL, and triglycerides, increasing HDL levels, and having antioxidant and anti-inflammatory effects.

Keywords: *Syzygium polyanthum*, bay leaf, lipid profile; cardiovascular disease

Correspondence: Indri Safitri Mukono
E-mail: indrisafitri@yahoo.com

Article history: •Received 4 October 2023 •Revised 15 November 2023 •Accepted 2 December 2023 •Published 31 January 2024

INTRODUCTION

Dyslipidemia is a condition in which there is an imbalance of lipids such as cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and high-density lipoprotein (HDL). Cholesterol is typically produced by the body. However, constantly eating foods with high-fat content leads to dyslipidemia. This condition will increase the risk of atherosclerotic plaque formation in micro-blood vessels. If there is a blood vessel injury, the LDL component can pass through the blood vessel channel and enter the subendothelium, causing the lipids to be oxidized and foam cells to form (Singh et al., 2014).

Cardiovascular disease ranks as the leading cause of death in the world, surpassing all other diseases. According to the World Health Organization (WHO), more than 17 million people die from coronary heart disease, which ranks first among the top ten death-causing diseases (Setyaningrum and Rejecky, 2020). Coronary heart disease is a condition when the heart's blood vessels (coronary arteries) are blocked by fatty deposits, accompanied by plaque buildup that disrupts the flow of blood to the heart muscle, resulting in disruption of heart function (Wihastuti et al., 2016).

Dyslipidemia treatment can be done in various ways, such as changing lifestyle, maintaining ideal body weight, avoiding foods that contain high fat, doing physical activity, avoiding alcohol and cigarettes, or taking drugs to lower blood fat levels. One drug that is often used to lower blood fat levels is simvastatin (PERKI, 2017), which works by preventing cholesterol formation by inhibiting the enzyme HMG CoA reductase (3-hydroxy-3-methylglutary-CoA reductase). However, long-term use of simvastatin can cause side effects such as hepatotoxicity, malaise, rhabdomyolysis, and myopathy. The high side effects of long-term drug use have caused people to start looking for medicinal plants for dyslipidemia. One of the medicinal plants known to have anti-cholesterol effects is bay leaf (*Syzygium polyanthum*). Besides being a seasoning for cooking, bay leaves are also used as medicinal plants for generations (Mahmood et al., 2015). Previous research states that bay leaves contain gallic tannins, galocatechins, flavonoids, saponins, and volatile oils (sesquiterpenes). In addition, bay leaves also contain several vitamins, including vitamin A, vitamin C, vitamin E, Thiamin, Riboflavin, Niacin, vitamin B6, vitamin B12, and folate. These ingredients can inhibit the formation of LDL, HDL, VLDL, and HMG CoA reductase and reduce serum cholesterol levels by various mechanisms. However, in a study conducted by Shinta and Kartasurya (2014), the administration of bay leaf decoction or extract could not reduce LDL cholesterol levels in Sprague Dawley rats fed a high-fat diet compared to simvastatin.

Various studies have proven that the administration of bay leaves can regulate lipid profiles. However, there are also contradictory results of these studies, so the authors

Available at https://e-journal.unair.ac.id/CIMRJ ; DOI: 10.20473/cimrj.v5i1.51386

are interested in conducting a systematic review to further discuss the effect of bay leaf (*Syzygium polyanthum*) in regulating lipid profiles in dyslipidemia model rats.

METHODS

The PICO (Population, Intervention, Comparability, Outcome) approach was used in this systematic review. The population of the study was dyslipidemia model rats. The intervention was the administration of bay leaf, and the comparability of the study was met by comparing with rats that were not treated with bay leaves. The outcome of the research was the lipid profiles (total cholesterol, LDL, HDL, and TG).

Once the PICO was determined, specific article inclusion and exclusion criteria were also chosen to focus the search. The inclusion criteria for this study were literature containing the keywords ("Bay Leaf") AND ("Lipid profile" OR "LDL" OR "HDL" OR "Cholesterol") available on e-databases: PubMed and Google Scholar, the articles were full-text, the treatment in rats was explained, using English or Indonesian, using analytical descriptive methods in determining research samples, and had a central topic of discussion regarding the effect of bay leaves (*Syzygium polyanthum*) in regulating lipid profiles in dyslipidemia model rats, published since 2014. The exclusion criteria were that the literature was not available in full-text, did not discuss the efficacy of bay leaves in regulating lipid profiles in dyslipidemia model rats, duplication of literature, and incomplete data.

Software like Mendeley was used to avoid duplication and the PRISMA method was applied to obtain research studies that fit the inclusion criteria. The tool to assess the research studies obtained was the Systematic Review Center for Laboratory Animal Experimentation (SYRCLE) risk of bias tool because the literature study design used in this systematic review was animal studies.

Research journals that met the inclusion and exclusion criteria were collected and extracted, including the name of the researcher, year of study, location of study, sample characteristics, sample size, the intervention provided, lipid profile measured, and results of the investigation. The summary of the research journal was entered into a table sorted alphabetically and the year of publication of the journal.

RESULTS

Based on the keywords, 1,287 pieces of literature were found. Through the duplication-checking process, 36 duplicate literatures were found. These results were then screened using the criteria of year and article type, resulting in 1,251 pieces of literature. Researchers excluded 321 kinds of literature that did not match the title and abstract, and 311 types of literature could not be accessed in full-text, so 619 full-text literature were obtained according to the topic. After 619 types of literature were reviewed, there were 156 kinds of literature with irrelevant populations, 16 literature with irrelevant outcomes, and 437 literature with unrelated study designs. Finally, ten literatures were analyzed in this systematic review (Figure 1).

The quality of the literature was assessed using SYRCLE's risk of bias tool adapted from the Cochrane Risk of Bias (RoB). A "yes" rating indicates a low risk of bias; a "no" rating indicates a high risk of bias; the rating was "unclear" if insufficient details were reported to assess the risk of bias properly (Hooijmans et al., 2014). Details of the scoring on each component are listed in Table 1.

The literature characteristics used in this systematic review included author name, year of study, study location, sample characteristics, sample size, intervention, lipid profile measured, and study results, which can be seen in Table 2.

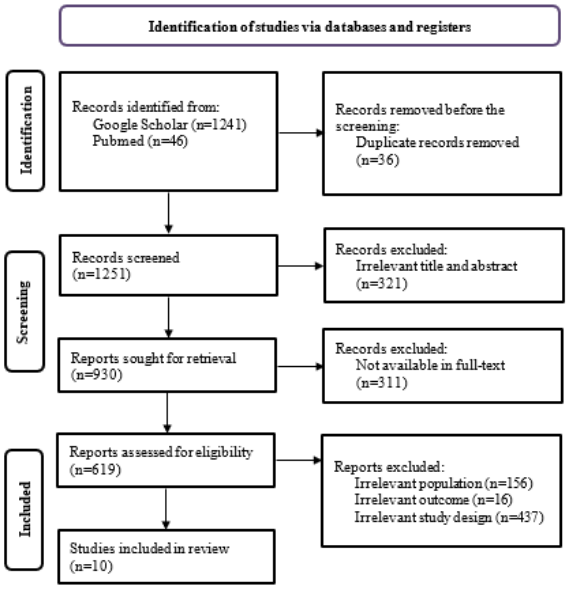

Figure 1. PRISMA Flow Chart 2020

DISCUSSION

The lipid profile is one of the most critical components of health. Lipid profile includes total cholesterol, TG, LDL, and HDL levels. Lipid profile imbalance is a risk factor for metabolic diseases, especially cardiovascular diseases, that have increased morbidity and mortality worldwide over the past few years (PERKI, 2017). The link between lipid profile and cardiovascular disease lies in atherogenesis. Atherogenesis is the formation of atheroma plaques on the blood vessel wall preceded by the migration of oxidized LDL-C in the tunica intima of arteries, which then triggers the inflammatory process and the arrival of macrophages. The collection of macrophages that phagocytize oxidized LDL-C forms foam cells. The inflammation produces cytokines that trigger the proliferation and migration of arterial smooth muscle cells from the tunica media to the tunica intima. The process eventually forms a plaque that disrupts blood flow (Bergheanu et al., 2017).

Bay leaf is a natural ingredient studied for its benefits on lipid profiles, both in humans and animals. Bay leaves have the effect of increasing the levels of antioxidant enzymes and HDL, reducing TG, total cholesterol, and serum LDL levels (Sakaganta and Sukohar, 2021). This herbal plant contains 0.17% essential oil, citral, eugenol, tannin, flavonoids, and metal chavicol, which have antioxidant, astringent, and lipid profile-lowering effects (Susyani et al., 2020). However, the research results on the efficacy of bay leaves provide different results. The following is a discussion of the effect of bay leaves on each lipid profile from a review of studies conducted.

The polyphenol content in bay leaves also influences the lipid profile. Hyperlipidemia, caused by insulin deficiency, triggers fat metabolism through lipoprotein lipase and hormone-sensitive lipase enzymes that hydrolyze triglycerides. It leads to an increase in blood fat levels followed by a decrease in adipose tissue fat levels. Thus triggering a reduction in blood lipid

Table 1. Literature quality assessment results

Study	Presence of bias									
	Was the allocation sequence adequately generated & applied?	Were the groups similar at baseline or were they adjusted for confounders in the analysis?	Was the allocation adequately concealed?	Were the animals randomly housed during the experiment?	Were the caregivers and/or investigators blinded from knowledge which intervention each animal received during the experiment?	Were animals selected at random for outcome assessment?	Was the outcome assessor blinded?	Were incomplete outcome data adequately addressed?	Are reports of the study free of selective outcome reporting?	Was the study apparently free of other problems that could result in high risk of bias?
Tondy et al. (2021)	Yes	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	No	Unclear	Unclear
Shinta & Kartasurya (2014)	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Unclear
Fitriarini & Rahayuningsih (2014)	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Unclear
Rosyada & Rahayuningsih (2014)	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Unclear
Florean (2016)	Unclear	Yes	Unclear	Yes	Unclear	Unclear	Unclear	No	Unclear	Unclear
Irmadoly et al. (2014)	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	No	Unclear	Unclear
Hidayat & Wulandari (2021)	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	No	No	Unclear
Iriani et al. (2021)	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	No	Unclear	Unclear
Hidayat & Hayati (2020)	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	No	Unclear	Unclear
Afrilliani et al. (2014)	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	No	Yes	Unclear

levels, leading to an improved lipid profile (Daher et al., 2021).

In the study of Mayasari and Setyaningrum (2022), the optimal antihypercholesterolemia effect was found in male Wistar rats by administering ethanol extract of bay leaves at 1g/kg BW for six weeks. Different things were shown in the research of Septianingrum and Widaryati (2014), which showed a significant decrease in total cholesterol levels (p=0.001) in the group with the intervention of bay leaf boiled water compared to the control group. A substantial reduction in total cholesterol in dyslipidemia patients who received bay leaf extract therapy 2x200 mg/day and 2x300 mg/day was also seen in the research of Prianwari and Syafril (2020). This difference in the results could be due to the duration of intervention in the Septianingrum and Widaryati (2014) and Prianwari and Syafril (2020) studies being longer than that in Susyani et al. (2020) studies, so that the effect of bay leaf administration was more visible. The impact of lowering total cholesterol was also supported by animal research conducted by Al-Samarrai et al. (2017) on rabbits. From the results of this study, a significant decrease in total cholesterol and triglyceride levels was found in the consumption of bay leaves compared to the control, both in raw form and flavonoid extracts.

The cholesterol-lowering effect is due to the content of tannin compounds in bay leaves. Tannin in the gastrointestinal system will bind to its receptors on the surface of epithelial cells to inhibit fat absorption. In addition, tannin can bind to HMG-CoA reductase so that the formation of blood cholesterol is inhibited. Another content that plays a role in lowering blood cholesterol is the saponin compound. Saponins function to bind cholesterol to bile acids, which are then immediately excreted through feces. In addition to tannins and saponins, bay leaves also have flavonoid compounds in the form of quercetin, which has the effect of inhibiting HMG-CoA reductase activity (Susyani et al., 2020). The inhibitory effect is supported by the results of research by Hidayat and Wulandari (2021), which showed that the lowest HMG-CoA reductase activity was seen in the group with 100 mg/kgBW and 200 mg/kgBW bay leaf extract diets compared to the group with simvastatin and control.

On the other hand, acetyl-coA levels in the blood also play a role in the process of cholesterol formation (Hidayat and Hayati, 2020). Acetyl-CoA is a precursor in the metabolism of glucose, protein, and fat (Hidayat and Hayati, 2020). An increase in glucose levels or other energy sources, such as protein and fat, can increase the production of acetyl-cacao through beta-oxidation (Hidayat and Hayati, 2020). Bay leaf extract can improve metabolism and glucose uptake into cells, thus preventing acetyl-coal accumulation by reducing the beta-oxidation process, leading to a decrease in blood cholesterol levels (Hidayat and Hayati, 2020).

Bay leaves contain vitamin B3 (niacin), which affects blood HDL levels. Niacin inhibits changes and disposal of apolipoprotein-A1 (Apo-A1) by the liver so that HDL precursors increase. Apo-A1 is an HDL precursor in the form of pre-beta HDL, which will be converted to HDL alpha through the process of esterification of free cholesterol into cholesterol esters by the enzyme lecithin-cholesterol acyltransferase (Susyani et al., 2020).

In a study using hyperlipidemic white rat samples, the average HDL post-intervention of the bay leaf decoction diet in the group given therapy was more significant than the control group (Hidayat and Wulandari, 2021). This effect was also seen in the research of El-Shahat et al. (2022) with the supplementation of bay leaf extract 200 ml/kgBW/day. A study conducted by Zahra et al. (2019) also showed similar results. Bay leaves were able to increase the blood HDL cholesterol levels of rats for seven days even though they were still below the group of rats with gemfibrozil administration of 21.6 mg/200 g BW rats (Zahra et al., 2019).

In studies using animal samples, different results were found regarding the impact of bay leaf consumption on LDL. The results of Iriani et al. (2021) showed the effect of bay leaf intervention on significantly lowering LDL. Meanwhile, the results of Hidayat and Wulandari's (2021) study showed an increase in LDL levels in the group with bay leaf extract intervention, although it is lower than in the group without intervention. It showed an inhibited rise in LDL by the administration of bay leaf extract.

Lipoprotein-a is a particle consisting of apolipoprotein-a and glycoprotein encoded by the LPA gene and binds to apolipoprotein-b on LDL. These particles increase LDL-C deposits in the tunica intima, making it an independent

Table 2. Study characteristics

Authors (Year)	Location	Sample characteristic	Total sample	Intervention	Measured lipid profile	Results
Tondy et al. (2021)	Meand, Indonesia	Healthy rats weighing 150-200 g	44 rats (11 groups)	Control group: CMC diet Group -1: 100 mg/kg BW intraperitoneal benzene every six days Group -2: 100 mg/kg BW benzene every three days Group +1: 100 mg/kg BW vitamin C + benzene every six days Group +2: 100 mg/kg BW vitamin C + benzene every three days For the 21-day experimental period, Group 1-6 rats received extracts at 400, 600, and 800 mg/kgBW plus 100 mg/kgBW benzene.	Total cholesterol, TG, HDL, LDL	The administration of bay leaf extract at doses of 400, 600, and 800 mg/kg BW plus benzene 100 mg/kg BW can reduce triglyceride levels ($p<0.05$) and LDL ($p<0.05$) and increase HDL levels ($p<0.05$).
Shinta & Kartasurya (2014)	Diponegoro, Indonesia	Male Sprague Dawley rats aged 7-8 weeks with a weight of 180-200 grams	24 rats (4 Group)	All four groups were fed a standard diet and a high-fat diet. Group 1: control Group 2: 0.18 g/kg BW simvastatin Group 3: 0.034 g/kg BW bay leaf extracts Group 4: 0.72 g/kg BW bay leaf decoction	LDL	The administration of bay leaf extract or decoction cannot reduce LDL cholesterol levels. However, the increase in LDL cholesterol levels in the decoction group is lower (38.3 mg/dL) compared to the positive control group (79.7 mg/dL) and higher than the increase in the bay leaf extract group (26.2 mg/dL) and simvastatin (2.9 mg/dL).
Fitriarini & Rahayuningsih (2014)	Diponegoro, Indonesia	Male Sprague Dawley rats aged 7-8 weeks with a weight of 180-200 grams	24 rats (4 Group)	All four groups were fed a standard diet and a high-fat diet. Group 1: control Group 2: 0.018 g/kg BW simvastatin Group 3: 0.034 g/kg BW bay leaf extract made from 0.72 g of bay leaves Group 4: 2.7 ml bay leaf decoction made from 0.72 g of bay leaves	HDL	In Groups 1, 3, and 4, there was a significant decrease in HDL levels ($p=0.000$), while Group 2 (simvastatin) showed stable HDL levels. However, the group that was given bay leaf extract was better able to inhibit the rate of decline in HDL levels when compared to bay leaf decoction.
Rosyada & Rahayuningsih (2014)	Diponegoro, Indonesia	Male Sprague Dawley rats aged 7-8 weeks with a weight of 180-200 grams	24 rats (4 Group)	All four groups were fed a standard diet and a high-fat diet. Group 1: control Group 2: 0.018 g/kg BW simvastatin Group 3: 0.034 g/kg BW bay leaf extract Group 4: 0.72 g/kg BW bay leaf decoction	Total cholesterol	The treatment that has the effect of restraining the rate of increase in total cholesterol levels is 0.018 grams of simvastatin, 0.034 grams of bay leaf extract, and 0.72 grams of bay leaf decoction.
Florean (2016)	Banda Aceh, Indonesia	Male Wistar rats	25 rats (5 Group)	Group 1: negative control Group 2: simvastatin Group 3: 1.25 g/KgBW bay leaf extract Group 4: 2.5 g/KgBW bay leaf extract Group 5: 5 g/KgBW bay leaf extract	Total cholesterol	Treatment doses of 2.5 g/KgBW and 5 g/KgBW were effective in reducing total cholesterol levels ($\Delta 35.40 \pm 12.60$; $\Delta 34.60 \pm 11.17$) although not comparable to the control group given simvastatin ($\Delta 50.40 \pm 9.86$).
Irmadoly et al. (2014)	Palembang, Indonesia	Male Wistar rats	30 rats (5 Group perlakuan)	Group A: negative control Group B: simvastatin Group C: Water methanol fraction Group D: N-hexane fraction Group E: Ethyl acetate fraction C, D, and E intervened by giving the same dose of bay leaf extract fraction, namely 20 mg/200 g BW, for 21 days with once-daily administration.	Total cholesterol, TG, HDL, LDL	Ethyl acetate fraction of bay leaf extract significantly reduced serum triglyceride levels ($p=0.033$), and n-hexane fraction significantly increased serum HDL levels ($p=0.03$).
Hidayat & Wulandari (2021)	Palembang, Indonesia	Male Wistar rats weighing 200 -250 grams	30 rats (5 Group)	Group 1: Group normal Group 2: hypercholesterolemic rats without treatment Group 3: hypercholesterolemic rats with simvastatin treatment Group 4: hypercholesterolemic rats with extract Sp 100 mg/kg BW Group 5: hypercholesterolemic rats with extract Sp 200mg/kg BW	Total cholesterol, LDL	Bay leaf extract and simvastatin treatment increase HDL levels and normalize elevated cholesterol and LDL levels.
Iriani et al. (2021)	Bali, Indonesia	Male Wistar rats aged 8-12 weeks with a weight of weighing 160-250 grams	32 rats (8 Group)	Group 1: aqua dest (negative control) Group 2: simvastatin 0.36 mg/kg BW (positive control) Group 3: ethanol extract of bay leaf 252 mg/kg BW Group 4: ethanol extract of bay leaf 504mg/kg BW Group 5: ethanol extract of bay leaf 756mg/kg BW, Group 6: bay leaf decoction 25%/kg BW Group 7: bay leaf decoction 50% mg/kg BW Group 8: bay leaf decoction 75% mg/kg BW	LDL	The decrease in LDL levels was better in all treatment groups compared to the negative control ($p<0.05$). The treatment of 756mg/kgBW ethanol extract of bay leaves showed better results ($p<0.05$) than the positive control.
Hidayat & Hayati (2020)	Palembang, Indonesia	Male Wistar rats weighing 200 -250 grams	30 rats (5 Group)	Group 1: normal rats Group 2: hypercholesterolemia rats (negative control) Group 3: hypercholesterolemia rats + bay leaf extracts (50 mg/kg) Group 4: hypercholesterolemia rats + bay leaf extracts (100 mg/kg) Group 5: hypercholesterolemia rats + bay leaf extracts (200mg/kg)	Total cholesterol	Bay leaf extract effectively reduces total cholesterol levels by regulating Acetyl CoA production ($p=0.00$).
Afrilliani et al. (2014)	Yogyakarta, Indonesia	Male Wistar rats aged eight weeks with a weight of weighing 150-200 grams	25 rats (5 Group)	Group 1: positive control Group 2: bay leaf decoction 0.18 gr/200 gr BW Group 3: bay leaf decoction 0.27 gr/200 gr BW Group 4: bay leaf decoction 0.36 gr/200 gr BW Group 5: simvastatin 0.18 mg/200 gr BW	LDL	The administration of bay leaf decoction at doses of 0.18, 0.27, and 0.36 gr/200 gr BW reduced serum LDL cholesterol levels ($p=0.000$).

risk factor for cardiovascular disease. Low levels of lipoprotein-a benefit the patient. The increase in the effect of bay leaf in lowering LDL was positively correlated with the dose of administration (Iriani et al., 2021).

In addition to playing a direct role in regulating blood lipid profile levels, bay leaves have an antioxidant effect that benefits the body's metabolism. In the research results of Hidayat and Wulandari (2021), the group with bay leaf extract diet had the lowest catalase and superoxide dismutase activity compared to the group without bay leaf intervention. It is supported by a significant increase in catalase and superoxide dismutase levels in the research of El-Shahat et al. (2022). Both enzymes are the body's cellular antioxidants. Superoxide dismutase is a metalloenzyme that catalyzes the conversion of superoxide anion to hydrogen peroxide and molecular oxygen (Younus, 2018). Catalase is a heme enzyme that converts toxic hydrogen peroxide into water and molecular oxygen compounds (Krych-Madej and Gebicka, 2017).

These data proved the potential of antioxidants in neutralizing reactive oxygen species (ROS), so that the activity of antioxidant enzymes is minimal. Research shows a correlation between ROS and the pathophysiology of atherosclerosis. ROS induces cell wall lipid peroxidation that results in cell injury, including vascular endothelial damage. The injury elicits an immunologic response in the form of activated macrophages to migrate to the area of injury and form thrombosis. This process can be accompanied by the attachment of oxidized LDL, the formation of foam cells, and the development of atherosclerotic plaques (Ngestiningsih et al., 2019).

A limitation of this systematic review was the possibility of bias, as studies with positive or significant results showing the effect of bay leaf on lipid profile regulation are more likely to be published. To overcome this, we searched different reputable scientific databases to retrieve as many relevant publications as possible. Thus, we could have a chance to get publications with negative results. The following limitation is the completeness of the data in each literature. The findings from one of the literature may be incomplete. Heterogeneity in study design, population, interventions, and outcomes may also make it difficult to combine study results and draw conclusions. Other limitations may occur due to researcher limitations, such as language, time, and expertise.

CONCLUSION

The administration of bay leaves can improve lipid profiles by lowering total cholesterol, LDL, and TG and increasing HDL levels in dyslipidemia model rats. For further research, it is hoped that research on bay leaves can be conducted in the human population so that evidence of the impact of bay leaf consumption can be more substantial and can be implemented in the therapy of metabolic syndrome patients, especially in Indonesia.

ACKNOWLEDGEMENT

None.

CONFLICT OF INTEREST

No conflict of interest is present in this study

FUNDING DISCLOSURE

This research received no external funding

AUTHOR CONTRIBUTION

All author have contributed to all process in this research.

REFERENCES

Afrilliani DA, Supriyanta B, Rahayu M. 2014. Pengaruh pemberian rebusan daun salam (Eugenia polyantha wight.) terhadap kadar kolesterol low density lipoprotein (ldl) serum tikus putih (Rattus norvegicus) hiperkolesterolemia. Jurnal Teknologi Laboratorium 3(2):69–76.

Al-Samarrai OR, Naji NA, Hameed RR. 2017. Effect of Bay leaf (Laurus nobilis L.) and its isolated (flavonoids and glycosides) on the lipids profile in the local Iraqi female rabbits. Tikrit Journal of Pure Science 22(6):72–75. https://doi.org/10.25130/tjps.v22i6.793.

Bergheanu SC, Bodde MC, Jukema JW. 2017. Pathophysiology and treatment of atherosclerosis: Current view and future perspective on lipoprotein modification treatment. Netherlands Heart Journal 25(4):231–242. https://doi.org/10.1007/s12471-017-0959-2.

Daher CF, Taleb RI, Mroueh MA, et al. 2021. Laurus nobilis leaves extract protects against high fat diet-induced type 2 Diabetes in rats. Journal of Pharmacognosy and Phytotherapy 13(3):82–90. https://doi.org/10.5897/JPP2021.0609.

El-Shahat AN, Azeem AMA, el Megid MHMA. 2022. Protective Effect of Laurus nobilis Extract against Hypercholesterolemia Damage in Male Rats. Pakistan Journal of Zoology 55(4):1613–1619.

Fitriarini S and Rahayuningsih HM. 2014. Perbedaan pengaruh antara ekstrak dan rebusan daun salam (Eugenia polyantha) dalam pencegahan penurunan kadar kolesterol hdl pada tikus Sprague dawley. Journal of Nutrition College 3(1):184–191.

Florean MR. 2016. Uji efektivitas ekstrak daun salam (Eugenia polyantha) terhadap penurunan kadar kolesterol total darah tikus jantan (Rattus norvegicus) galur wistar. Skripsi. Banda Aceh: Universitas Syiah Kuala.

Hidayat R and Hayati L. 2020. The Effect of Bay Leaf Extract (Syzygium polianthum) Against Cholesterol Regulation in Hypercholesterolemic Rats. Eureka Herba Indonesia 1(2):23–26. https://doi.org/10.37275/ehi.v1i2.6.

Hidayat R and Wulandari P. 2021. The Effect of Syzygium-polyanthum Extract in Lipid Profile of Hypercholesterolemic Animal Model. Journal of Hunan University Natural Sciences 48(5):239–244.

Hooijmans CR, Rovers MM, de Vries RBM, et al. 2014. SYRCLE's risk of bias tool for animal studies. BMC medical research methodology 14:43. https://doi.org/10.1186/1471-2288-14-43.

Iriani Y, Ramona Y, Astiti NPA. 2021. Potential of ethanol and decoction extracts of bay leaves to improve lipid profile (Ldl-Cholesterol) of Wistar rats. Metamorfosa: Journal of Biological Sciences 8(1):89–98. https://doi.org/10.24843/metamorfosa.2021.v08.i01.p09.

Irmadoly N, Wirajaya F, Chalista S, et al. 2014. Uji aktivitas antidislipidemia in vivo fraksi ekstrak daun salam (Eugenia polyantha) pada tikus galur wistar yang diinduksi diet tinggi lemak. Jurnal Kedokteran dan Kesehatan 1(1):21–23.

Krych-Madej J and Gebicka L. 2017. Interactions of nitrite with catalase: Enzyme activity and reaction kinetics studies. Journal of Inorganic Biochemistry 171:10–17. https://doi.org/10.1016/j.jinorgbio.2017.02.023.

Mahmood H, Abid AR, Riaz R, et al. 2015. Relation of cholesterol level to dietary fat intake in patients of ischemic heart disease. Cardiovascular Pharmacology 4(2):1000141. https://doi.org/10.4172/2329-6607.1000141.

Mayasari S and Setyaningrum L. 2022. Effectiveness Of Antihypercholesterolemia Ethanol Extract Of Bay Leaf (Syzygyum Polyanthum) In Male Rats With Diabetes Mellitus Strain Wistar. Jurnal Kesehatan dr. Soebandi 10(1):33–38.

Ngestiningsih D, Rahayu RA, Batubara L. 2019. Effect of Superoxide Dismutase (SOD) Supplementation Towards Plasma Levels of Malondialdehyde (MDA), Total Cholesterol and LDL Cholesterol in the Elderly. Journal of Biomedicine and Translational Research 5(2):29–33. https://doi.org/10.14710/jbtr.v5i2.4679.

PERKI. 2017. Panduan Tata Laksana Dislipidemia. Jakarta: Perhimpunan Dokter Spesialis Kardiovaskular Indonesia.

Prianwari C and Syafril S. 2020. The Relationship Between Lipoprotein (A) And Lipid Profile In Patients Treated With Bay Leaf Extract [Syzygium Polyanthum (Wight) Walp] In Patients Dyslipidemia. Jetromi 2(4):183–188. https://doi.org/10.32734/jetromi.v2i4.4780.

Rahayu S and Hosizah. 2021. Implementasi Sistem Rujukan Layanan Kesehatan: Systematic Literature Review. Indonesian of Health Information Management Journal (INOHIM) 9(2):138-152.

Rosyada SM and Rahayuningsih HM. 2014. Perbedaan pengaruh antara ekstrak dan rebusan daun salam (Eugenia polyantha) dalam pencegahan peningkatan kadar kolesterol total pada tikus Sprague dawley. Journal of Nutrition College 3(1):142–149. https://doi.org/10.14710/jnc.v3i1.4542.

Sakaganta ARI and Sukohar A. 2021. Daun Salam (Syzygium Polyanthum) Sebagai Penurun Kadar Kolesterol Dalam Darah. Medula 10(4):618–622.

Septianingrum W and Widaryati. 2014. Pengaruh Pemberian Air Rebusan Daun Salam terhadap Kadar Kolesterol pada Lansia Hiperkolesterol di Trimulyo Sleman. Skripsi. Sleman: Stikes 'Aisyiyah Yogyakarta.

Setyaningrum N and Rejecky A. 2020. Pengaruh Pelatihan Bantuan Hidup Dasar Terhadap Motivasi Untuk Memberikan Pertolongan Pada Korban Henti Jantung Oleh Mahasiswa Pramugari. Surya Medika: Jurnal Ilmiah Ilmu Keperawatan dan Ilmu Kesehatan Masyarakat 15(2):64–68. https://doi.org/10.32504/sm.v15i2.198.

Shinta AP and Kartasurya MI. 2014. Perbedaan perubahan kadar kolesterol ldl setelah pemberian ekstrak dan rebusan daun salam (Eugenia polyantha) pada tikus Sprague dawley yang diberi pakan tinggi lemak. Journal of Nutrition College 3(1):90–97. https://doi.org/10.14710/jnc.v3i1.4536.

Singh R, Kishore L, Kaur N. 2014. Diabetic Peripheral Neuropathy: Current Perspective And Future Directions. Pharmacological Research 80:21–35. https://doi.org/10.1016/j.phrs.2013.12.005.

Susyani, Zurio A, Terati. 2020. The Bay Leaves Tea Can Decrease Cholesterol Levels Of Patients With Cardiovascular Disease. World Journal of Advance Healthcare Research 4(3):173–177.

Tondy, Nasution AN, Lister INE, et al. 2021. Antihyperlipidemia activity of sygyzium polyanthum ethanol extract on benzene induced rats. Inhence.

Wihastuti TA, Andarini S, Heriansyah T. 2016. Patofisiologi Dasar Keperawatan Penyakit Jantung Koroner: Inflamasi Vaskular. Malang: Universitas Brawijaya Press.

Younus H. 2018. Therapeutic potentials of superoxide dismutase. International Journal of Health Sciences 12(3):88–93.

Zahra HA, Julianti E, Yusraini E. 2019. Pengujian Efek Hipokolesterolemia Minuman Rebusan Daun Salam yang Mengandung Ekstrak Kayu Manis Secara In-Vivo pada Tikus Percobaan (Testing The Hypocholesterol Effects of Drink of Boiled Bay Leaf Stew Containing Cinnamon Extract In-Vivo in Experimentals Rats). Jurnal Rekayasa Pangan dan Pertanian 7(1).