

The role of flaxseed (*Linum usitatissimum*) in improving plasma lipid profiles: a literature review

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ABSTRACT

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Several major risk factors contribute to cardiovascular diseases. One of these is dyslipidemia, an imbalance of plasma lipids such as total cholesterol (TC), low-density lipoprotein (LDL), triglycerides (TG), and high-density lipoprotein (HDL). While medications to lower lipids are widely used to improve lipid profiles, they have some limitations. Flaxseed is rich in α -linolenic acid, phytosterols, and lignans, which can improve lipid profiles. This study aimed to review the potential effects of flaxseed on lipid metabolism. Data was gathered from research databases such as Google Scholar, PubMed, Science Direct, and Springer for the past 5 yr. About 1,527 scientific articles were found, but after eliminating duplicates and screening of title and abstract, only 45 full-text articles were assessed, with 16 selected. The result showed that α -linolenic acid, phytosterols, lignans, and fibers in flaxseed improve TC, LDL, TG, and HDL through various mechanisms. In conclusion, flaxseed shows promise as a natural therapy for dyslipidemia, improving TC, LDL, VLDL, and TG levels, though HDL effects vary. Disparities are linked to demographics, form, dosage, and duration, highlighting the need for standardized research.

ABSTRAK

Beberapa faktor risiko mayor yang berkontribusi terhadap penyakit kardiovaskular. Salah satunya adalah dislipidemia, suatu ketidakseimbangan lipid plasma seperti kolesterol total (KT), *low-density lipoprotein* (LDL), *triglycerides* (TG), dan *high-density lipoprotein* (HDL). Meskipun obat-obatan penurun lipid telah digunakan secara luas untuk memperbaiki profil lipid, namun ternyata memiliki beberapa keterbatasan. Biji rami atau yang dikenal dengan *flaxseed* kaya akan asam linolenat (ALA), fitosterol, dan lignan, yang dapat memperbaiki profil lipid. Studi ini bertujuan untuk mengkaji potensi efek biji rami terhadap metabolisme lipid melalui tinjauan literatur. Data dikumpulkan dari beberapa *database* penelitian seperti Google Scholar, PubMed, Science Direct, dan Springer selama lima tahun terakhir. Sekitar 1.527 artikel ilmiah ditemukan, tetapi setelah dilakukan eliminasi duplikat dan penyaringan berdasarkan judul dan abstrak, hanya 45 artikel teks lengkap, dan 16 diantaranya yang dipilih. Hasilnya menunjukkan bahwa ALA, fitosterol, lignan, dan serat dalam biji rami memperbaiki TC, LDL, TG, dan HDL melalui berbagai mekanisme. Kesimpulannya, biji rami berpotensi sebagai terapi alami untuk dislipidemia, dengan memperbaiki kadar TC, LDL, VLDL, dan TG, meskipun efek pada HDL bervariasi. Perbedaan ini terkait dengan demografi, bentuk, dosis, dan durasi, sehingga menekankan perlunya penelitian yang terstandarisasi.

Keywords:
dyslipidemia;
flaxseed;
lipid profiles;
review

INTRODUCTION

Cardiovascular diseases, a major subset of non-communicable diseases, are a growing global health threat. The World Health Organization (WHO) reported that in 2019, cardiovascular diseases claimed an estimated 17.9 million lives, representing a third of all global deaths (32%). Notably, heart attacks and strokes accounted for 85% of cardiovascular deaths. Furthermore, around 17 million people under 70 died from non-communicable diseases, with 38% caused by cardiovascular diseases.¹ Indonesian Basic Health Research (*Riset Kesehatan Dasar/RISKESDAS*), a community-based study conducted every five years, also reported a concerning rise in non-communicable disease prevalence in Indonesia between 2013 and 2018, with cardiovascular disease prevalence increasing from 7 to 10.9%.^{2,3}

This increase in cardiovascular disease is linked to multiple risk factors, including diabetes, hypertension, physical inactivity, unhealthy diet, abnormal body mass index, smoking, and excessive alcohol consumption.⁴ Indonesian National Health Insurance Program (*Badan Penyelenggara Jaminan Sosial Kesehatan/BPJS Kesehatan*) highlights the significant economic burden of non-communicable diseases. In 2020, BPJS Kesehatan identified heart disease as the most expensive catastrophic disease, costing around Rp 8.6 trillion. It also represented the highest number of cases funded by BPJS Kesehatan (12,934,931 cases).⁵ Atherosclerosis, characterized by the build-up of cholesterol, fats, and/or calcium that hardens along the artery

walls, is a crucial factor in coronary heart disease. This build-up can lead to impaired heart function due to inadequate blood supply.⁶

Dyslipidemia is a condition characterized by abnormalities in lipid profiles, including abnormal levels of total cholesterol (TC), low-density lipoprotein (LDL), and triglyceride (TG), and decreased levels of high-density lipoprotein (HDL).⁷ Dyslipidemia is a major risk for several health conditions. These include cardiovascular disease, fatty liver disease (non-alcoholic), non-hemorrhagic stroke, and chronic pancreatitis. Several studies have shown that dyslipidemia and coronary heart disease are closely linked, with elevated cholesterol levels contributing to one-third of global ischemic heart disease cases.⁸ Improving plasma lipid profile is important for preventing cardiovascular disease and reducing mortality.⁹ While medications are available to treat dyslipidemia, long-term use can lead to side effects and increased economic burden. This highlights the need for alternative and adjuvant therapies for dyslipidemia, with herbal therapy being one viable option.¹⁰

The use of herbal therapy can be considered an option due to its relatively lower cost, good efficacy, and low side effects.¹¹ A diet high in saturated fat significantly increases LDL levels. Therefore, the recommended diet is to increase unsaturated fats such as monounsaturated fat (MUFA) and polyunsaturated fat (PUFA).⁶ Flaxseed, also known as linseed or by its scientific name *Linum usitatissimum*, is one of the oldest cultivated plants in the world and is recognized for its various benefits

as a food source, animal feed, and medicine.¹² Although flax is a summer crop that grows in temperate climates, it can also be cultivated in Indonesia, specifically in West Bandung Regency, West Java Province.^{13,14} Flaxseed can now be easily purchased in Indonesia through both online and offline stores. Flaxseed contains a high amount of PUFA. It is composed of 41% fat (73% PUFA and 8% MUFA), 21% protein, and 28-40% fiber. It also contains vitamins, minerals, phytosterols, and lignans. The main PUFA in flaxseed is alpha-linolenic acid (ALA) at 56.93%, followed by linoleic acid at 15.82%. Inside the body, ALA can be converted into docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Both DHA and EPA have several benefits for our health due to their anti-inflammation properties, role in neuron myelination, and ability to improve lipid metabolism. In addition to the benefit of omega-3 fatty acids, the fiber, phytosterols, and lignans in flaxseed also contribute to improving lipid levels and preventing atherogenic processes. Furthermore, high levels of phytosterols and lignans in flaxseed act as antioxidants.^{15,16}

Several studies have shown that flaxseed oil is effective in reducing small dense LDL (sd-LDL) levels, while also significantly reducing LDL and total cholesterol.^{17,18} Additionally, another study found that a combination of flaxseed oil with sesame oil can lower triglyceride levels and increase HDL levels.^{19,20} Flaxseed itself has also been linked to a reduction in the atherosclerotic process by reducing atheroma plaque formation and

improving its contractility.²¹ The effects of flaxseed on lipid profiles have been investigated in several studies, but the results are inconsistent. Some studies have shown potential benefits, while others have not. This review aimed to gather all current research on flaxseed to strengthen the evidence for its potential use as a therapeutic or adjuvant treatment for dyslipidemia. This would allow health professionals to provide specific recommendations for using flaxseed to prevent or treat dyslipidemia and cardiovascular diseases.

MATERIAL AND METHODS

This study is a literature review, secondary information obtained from online sources, journal searches, journal reviews, and various publications. Various scientific articles were collected from several research databases such as Google Scholar, PubMed, Science Direct, and Springer. The subsequent keyphrases utilized in this review were “flaxseed”, “linseed”, “lipid profile”, “dyslipidemia”, and “hypercholesterolemia”. This study included articles that met the following criteria: 1) published in a journal; 2) English and Indonesian; 3) published in the past 5 yr (2020-2024); 4) discussing flaxseed effects on plasma lipid profiles 5) *in vivo* studies. Articles were excluded if they fell into any of these categories: 1) observational studies such as cohort studies, case-control studies, case series, or case reports; 2) inaccessible full text. Scientific articles that did not fulfill the specified criteria were excluded from this study. This study only reviewed *in vivo* studies because it is more reliable

due to differences in biokinetics and challenges in extrapolating results to humans. Absence of biokinetics in *in vitro* methods may lead to a misinterpretation of the data.²²

RESULTS

By performing searches in research databases, 1,527 scientific articles were initially identified using relevant

keywords and a publication timeframe of 5 yr. After removing duplicates and ineligible entries, 1,278 scientific articles were identified. Following the elimination screening of titles and abstracts, a total of 45 full-text scientific articles were evaluated for their eligibility. Only 16 scientific articles met the inclusion criteria and were integrated into the final review (TABLE 1).

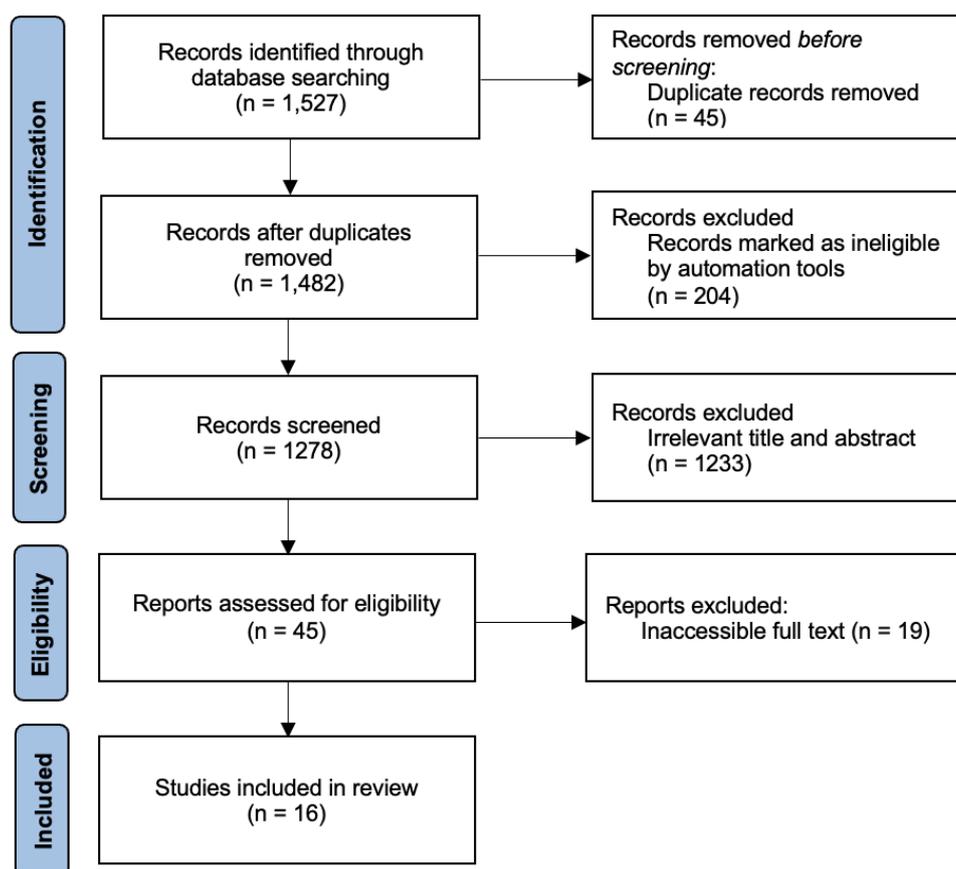


FIGURE 1. Literature review methodology using the PRISMA flow diagram

TABLE 1. Scientific articles that evaluate the role of flaxseed in improving plasma lipid profiles

Authors	Design	Subjects	Duration	Intervention	Results
Kanikowska <i>et al.</i> ¹⁵	Pilot study, prospective	6 people, assuming 70 kg BW	30 weeks	GF 0.4 g/kg BW (in biscuit)	<ul style="list-style-type: none"> • TC and LDL significantly reduced, but there were no changes in HDL and TG. • ALA reduces TC and LDL. While exhibiting antiatherogenic, anti-inflammatory, and anti-proliferative properties, its limited effect on (LpA) and CRP suggests its primary action targets cholesterol metabolism pathways.
Shahidi <i>et al.</i> , ¹⁶	Experimental study with pre and post-test only control group design	40 male rats, 200 20 g BW	21 d	FO 9.3 g/kg BW	<ul style="list-style-type: none"> • TC, LDL, VLDL, and TG were significantly reduced, while HDL was significantly increased. • ALA and DHA reduce lipid levels by inhibiting lipid synthesis in the liver, enhancing lipoprotein breakdown, and increasing HDL levels.
Afzal <i>et al.</i> ²³	Experimental study with posttest only control group design	60 male rats, 130 4 g BW	8 wk	FE 6 g/kg BW & FP 12 g/kg BW	<ul style="list-style-type: none"> • TC, LDL, and TG were significantly reduced, while HDL was not significantly increased. • Soluble dietary fiber, PUFA, lignan, and phytosterols work synergistically to improve lipid profile, while tocopherol and β- carotene prevent lipid oxidation.
Bhasin <i>et al.</i> ²⁴	Experimental study with pre and posttest only control group design	24 male rats, 200-220 g BW	2 wk	FP 3 g/kg BW	<ul style="list-style-type: none"> • TC, LDL, VLDL, and TG were significantly reduced, while HDL was significantly increased. • ALA reduce TGs, inhibit thromboxane A2 synthesis, lower procoagulant activity. Additionally, SDG lignans also contribute to improving lipid profile.

TABLE 1. Cont.

Authors	Design	Subjects	Duration	Intervention	Results
Hadi <i>et al.</i> ²⁵	Metaanalysis	62 randomized control trial with 3772 participants	-	-	<ul style="list-style-type: none"> • TC, LDL, and TG were significantly reduced, while there were no changes in HDL. • ALA promotes cholesterol efflux from macrophages by inhibiting stearyl-CoA desaturase-1. Omega-3 fatty acids also reduce TG and improve lipoprotein profiles by shifting sd-LDL particles to larger. Flax lignans, metabolized to enterolignans (enterodiol and enterolactone) by gut microbiota, lower cholesterol by influencing lipid synthesis pathways and reducing the expression of enzymes involved in cholesterol production.
Hussien <i>et al.</i> ²⁶	Experimental study with post-test only control group design	15 male rats, 170-180 g BW	30 d	FE 3 g/kg BW & 6 g/kg BW	<ul style="list-style-type: none"> • TC, LDL, and VLDL were significantly reduced, while HDL was significantly increased. • ALA, lignans, and dietary fiber reduce inflammation and lipid levels due to their antioxidant effects.
Khalil <i>et al.</i> , ²⁷	Experimental study with pre and post-test only control group design	25 male rats	28 d	FE 3 g/kg/BW	<ul style="list-style-type: none"> • TC, LDL, and TG were significantly reduced, while HDL was significantly increased. • SDG lignans enhance bile acid excretion, exhibit antioxidant effects, and influence cholesterol metabolism in the liver.
Qaiser <i>et al.</i> ²⁸	Experimental study with randomized post-test only control group design	32 female rats, 200 g BW	15 d	FP 7.5 g/kg/BW	<ul style="list-style-type: none"> • TG showed a greater reduction compared to TC. There was no significant reduction of LDL or increase of HDL. • Combination of omega-3 fatty acids, lignans, phenolic compounds, and fibers reduce oxidative stress, inflammation, and lipid accumulation in the blood.

TABLE 1. Cont.

Authors	Design	Subjects	Duration	Intervention	Results
Dutra <i>et al.</i> ²⁹	Experimental study with randomized posttest only control group design	21 female goats, 41.06 kg BW	80 d	GF 4.5 g/kg BW, 9 g/kg BW, & 13.5 g/kg BW	<ul style="list-style-type: none"> LDL, VLDL, and TG were significantly increased, while TC and HDL were not significantly changed. Flaxseed supplementation may worsen the lipid profile by providing an excess of fatty acids, which can be metabolized and transported in the bloodstream.
Masjedi <i>et al.</i> ³⁰	Meta-analysis	14 randomized control trial with 1107 participants	-	-	<ul style="list-style-type: none"> TC, LDL, and TG were significantly reduced, while there were no changes in HDL. ALA reduce fat deposition in adipose tissues, suppressing lipogenic enzymes, enhancing for oxidation, and shifting sd-LDL particles to larger. Lignans reduce cholesterol by acting on cholesterol-synthesis pathways, including the inhibition of certain enzymes like stearyl-CoA desaturase.
Pattanayak <i>et al.</i> ³¹	Experimental study with randomized posttest only control group design	36 male rats, 150-200 g BW	2 mo	FE 0.1 g/kg BW, 0.2 g/kg BW, & 0.4 g/kg BW	<ul style="list-style-type: none"> TC, LDL, and VLDL significantly decreased in all groups, while TG significantly decreased in 400 mg/kg group. There were no changes in HDL. ALA mediates cholesterol metabolism, lignans modulate enzymes, fiber induces satiety, and antioxidant activity contributes to the overall effects.
Sharma <i>et al.</i> ³²	Experimental study with pre and posttest only control group design	100 people	-	-	<ul style="list-style-type: none"> TC, LDL, VLDL, and TG were significantly reduced, while there were no changes in HDL. ALA and lignans prevent diseases including dyslipidemia through some mechanisms.

TABLE 1. Cont.

Authors	Design	Subjects	Duration	Intervention	Results
Toulabi <i>et al.</i> ³³	Randomized control trial	112 people	-	-	<ul style="list-style-type: none"> • TC was significantly reduced at 12th week. • Omega 3 fatty acids, lignans, and fiber works synergistically to improve lipid profiles. Lignans reduce cholesterol absorption and improving lipid metabolism, while the fiber helps lower cholesterol by binding bile acids in the gut.
Yang <i>et al.</i> ³⁴	Metaanalysis	31 randomized control trial with 1698 participants	-	-	<ul style="list-style-type: none"> • TC, LDL, and TG significantly reduced, while there were no changes in HDL. • ALA promotes cholesterol efflux from macrophages and inhibiting lipid peroxidation. Lignans also improve lipid profile and reduce cholesterol-related marker (Apo-B) and also reduce LDL oxidation. Soluble fiber binds to bile acids in the intestines, promotes their excretion and prevents their reabsorption. Flaxseed also reduces inflammatory markers (IL-6 and hs-CRP).
Seliema <i>et al.</i> ³⁵	Experimental study with posttest only control group design	30 male rats, 17010g BW	8 wk	FO 3.2 g/kg BW	<ul style="list-style-type: none"> • TC, LDL, VLDL, and TG were significantly reduced, while HDL was significantly increased. • ALA improved lipid metabolism, insulin sensitivity, adiponectin secretion, and reduced of adipose tissue inflammation.
Iqbal <i>et al.</i> ³⁶	Experimental study with pre and posttest control group design	75 people, 70 kg BW	2 mo	GF 0.14 g/kgBW	<ul style="list-style-type: none"> • LDL was significantly reduced, and HDL was not. • ALA and lignans exert lipid-lowering effects by inhibiting cholesterol synthesis and enhancing the hepatic bile acid synthesis. They also possess antiinflammatory properties.
Massoud <i>et al.</i> ³⁷	Parallelgroup, randomize, dplacebo-controlled trial	229 people, 70 kg BW	12 wk	FO 0.6 g/kgBW	<ul style="list-style-type: none"> • TC, LDL, and TG was significantly reduced. • ALA and lignans reduce bile acids reabsorption, prompting the liver to use cholesterol for bile acid production.

Note. FE: flaxseed extract; FP:flaxseed powder; FO: flaxseed oil; GF: ground flaxseed; HGD: hyperglycaemic diet; HFD: high fat diet; TC: total cholesterol; LDL: low-density lipoprotein; sd-LDL: small-dense low-density lipoprotein; VLDL: very low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; TG: triacylglycerol

DISCUSSION

In these studies, 16 scientific articles were reviewed, which included 7 human studies and 9 animal studies. Both human and animal studies were included because there are discrepancies between animal models and human reality, with poor quality in animal studies due to methodological flaws, and limitations of human studies. There are also different research questions, as animal studies often prioritize understanding the underlying mechanism of a disease, while humans primarily focus on the effectiveness of interventions.³⁸ Afzal *et al.*,²³ reported that 5% flaxseed extract significantly decreases TC, LDL, and TG levels, but does not significantly increase HDL levels compared to 10% flaxseed powder. Flaxseed contains soluble dietary fiber and secoisolariciresinol diglycoside (SDG), which contribute to lipid metabolism. However, previous studies conducted by Coudray *et al.*,³⁹ and Khalesi *et al.*,⁴⁰ found that rats preferred a control diet over a diet containing a higher percentage of flaxseed. Another study by Bhasin *et al.*²⁴ found that flaxseed powder does not affect normal lipid levels, but it significantly reduces TC, LDL, VLDL, and TG while increasing HDL in groups with abnormal lipid levels. These findings suggest that flaxseed can be used as a preventive agent against dyslipidemia and atherosclerosis. Flaxseed is rich in phytoestrogens and lignans, known for their lipid-lowering and antioxidant properties. More importantly, it is also a high source of ALA, an omega-3 that can be converted into EPA, thereby replacing arachidonic acid in membrane phospholipids and influencing inflammatory pathways.²⁴

α -Linolenic acid (ALA) can be converted into two essential fatty acids: docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Both DHA and EPA contribute to improving lipid metabolism through some mechanisms.

These mechanisms are increased catabolism of Apo-B-containing lipoproteins, decreased Apo-B production in the liver, increased triglyceride clearance through lipoprotein lipase (LPL), promotion of very low-density lipoprotein (VLDL) conversion to low-density protein (LDL), reduced LDL synthesis, decreased post-prandial lipemia, enhanced HDL remodeling through cholesteryl ester transfer protein (CETP) and lecithin cholesterol acyltransferase (LCAT), and increased cholesterol and bile acid excretion through the reversed cholesterol transport. Furthermore, omega-3 fatty acids may also prevent atherosclerosis by reducing the formation of foam cells, the initiators of atherosclerosis. This may occur through several mechanisms, including inhibiting cholesterol absorption and biosynthesis by lowering the expression of CD36 and ACAT1 enzymes through the PPAR- pathway, and by increasing cholesterol efflux from macrophages through the degradation of ABCA1 through the PPAR/LXR/ABCA1 pathway.⁴¹⁻⁴³ Chera *et al.*,⁴⁴ found that flaxseed polyphenols reduced NF- κ B signaling molecule levels and decreased reactive nitrogen species (RNS) and ROS levels, exhibiting anti-inflammatory, antioxidant, and antitumor properties. Reduction of NF- κ B activity is important because NF- κ B induces pro-inflammatory gene expression, such as those encoding chemokines and cytokines.⁴⁵ Flavonoids prevent atherosclerosis by inhibiting the expression of oxidized LDL, Apo-B100, NF- κ B, PI3K-AKT signaling pathway, and platelet formation, as well as increasing the expression of the Nrf2/HO-1 and SOD pathways.⁴⁶ Phenolic compounds, such as lignan and flavonoid in flaxseed, act as an antioxidant that neutralize reactive oxygen species (ROS), which are the primary cause of endothelial dysfunction. Additionally, phenolic compounds exhibit vasoprotective properties by increasing the production

of nitric oxide, which aids in the relaxation of blood vessels. Phenol also regulates prostaglandin 2, a potent inhibitor of platelet aggregation and a vasodilator when NO is reduced. Lignan reduces oxidized LDL by decreasing the activity of platelet-activating factor acetyl-hydrolase, thereby reducing foam cell formation, endothelial cell cytotoxicity, adhesion molecules secretion, and monocyte migration.⁴⁷

Seliema *et al.*,³⁵ and Shahidi *et al.*,¹⁶ found a similar result to Bhasin *et al.*,²⁴ that flaxseed oil significantly decreases TC, LDL, VLDL, and TG while increasing HDL. Fat storage in the liver is reduced by alpha-linolenic acid because it promotes the beta-oxidation of fatty acids and decreases their synthesis. Flaxseed oil was as effective as omega-3 supplements in improving lipid profiles, suggesting its potential as a cost-effective alternative for omega-3 supplementation. Additionally, flaxseed oil controls hepatic fatty acid metabolism by regulating triglyceride levels through the sterol regulatory element-binding protein-1 (SREBP-1) and peroxisome proliferative-activated receptor (PPAR) pathway. Beyond its lipid-lowering effects, flaxseed also has anti-coagulant and anti-allergic properties. This is partly due to its ability to decrease thromboxane A2 synthesis and reduce membrane-dependent responses. Hussien *et al.*,²⁶ further highlight the role of high fiber content in flaxseed's hypocholesterolemic effect. Fiber can reduce lipid oxidation, interrupt enterohepatic circulation of cholesterol, and potentially bind to fat molecules for excretion.^{26,27,48} A reduction in cholesterol levels attenuates the development of atherosclerosis, which is attributed to the inhibition of foam cell formation, a key process in the initiation and progression of atherosclerosis. Foam cells are formed when macrophages engulf cholesterol but fail to eliminate excess cholesterol within their cells.^{42,43} Khalil *et al.*,²⁷ identified SDG as the

main lignan found in defatted flaxseed. Lignan contributes to the hypolipidemic effect by increasing the levels of the 7- α -hydroxylase enzyme, which converts cholesterol into bile acids. Increased bile acid excretion promotes the elimination of LDL cholesterol by hepatocytes and enhances the expression of LDL receptors. Additionally, SDG reduces lipid peroxidation by chelating iron.^{27,49}

Conversely, Dutra *et al.*,²⁹ reported that flaxseed supplementation in their study led to an increase in TC, VLDL, TG, and HDL. Elevation of TG could be due to a higher dietary intake of fatty acids exceeding the body's energy needs. However, the elevation of TC, VLDL, and HDL is likely due to the inclusion of flaxseed oil in the diet. Flaxseed ingestion increases circulating lipoproteins, explaining its effects on lipid concentrations in the plasma. Flaxseed oil is a rich natural source of omega-3 fatty acids.²⁹ Similarly, Yang *et al.*,³⁴ confirmed that excessive dietary flaxseed intake of more than 30 g/d may not provide a health benefit. Apo-A1 is the primary protein component of HDL and plays an important role in HDL metabolism. The low Apo-A1 levels observed in this study may explain why HDL levels were not significantly increased.³⁴ Kanikowska *et al.*,¹⁵ also observed significant reductions in TC and LDL following flaxseed supplementation, but no significant changes in TG or increases in HDL. These findings suggest that flaxseed may primarily influence the cholesterol pathway. Furthermore, the minimal effect on triglycerides may be associated with a wide range of concentrations observed in this small group of patients.¹⁵

In contrast, Mirfattahi *et al.*,⁵⁰ showed that flaxseed consumption lowered triglyceride levels but did not significantly change total cholesterol. Edel *et al.*,¹⁷ found that flaxseed consumption for one month resulted in no significant changes in TC, LDL,

and HDL. Qaiser *et al.*,²⁸ reported that flaxseed decreased TG more effectively than TC. This finding is attributed to the increased HDL level caused by flaxseed, which facilitates the mobilization of TG and TC from plasma to hepatocytes for bile acid production.²⁸

Disparities in the findings among these studies may be attributed to several factors, including differences in demographic characteristics, variations in the form, dosage, and duration of flaxseed supplementation employed in each study.^{28,37} Demographic factors, such as sex and age, can also affect lipid profiles due to differences in metabolism and hormone levels.⁵¹ Hadi *et al.*,²⁵ stated that flaxseed supplementation for less than 12 wk improved TC, but not the LDL, which required more than 12 wk for a significant reduction.²⁵ The form

of flaxseed supplementation also affects the result, as Nowak *et al.*,⁵² stated that flaxseed extract is superior to oil or ground seed as it can inhibit oxidation of fatty acids in flaxseed, prolong shelf life, and maintain its biological activity.⁵² The 16 studies above showed that flaxseed oil (FO) and flaxseed powder (FP) show better efficacy in improving HDL compared to flaxseed extract (FE) or ground flaxseed (GF). A dose of approximately 3-12 g/kg BW in animals and 0.14-0.6 g/kg BW in humans yields better results in improving lipid profiles. In animals, results were observed as early as 2 wk, but more consistent reductions were seen after 8 wk. In humans, studies lasting 8-12 wk showed significant reductions in lipid parameters, especially TC, LDL, and TG.

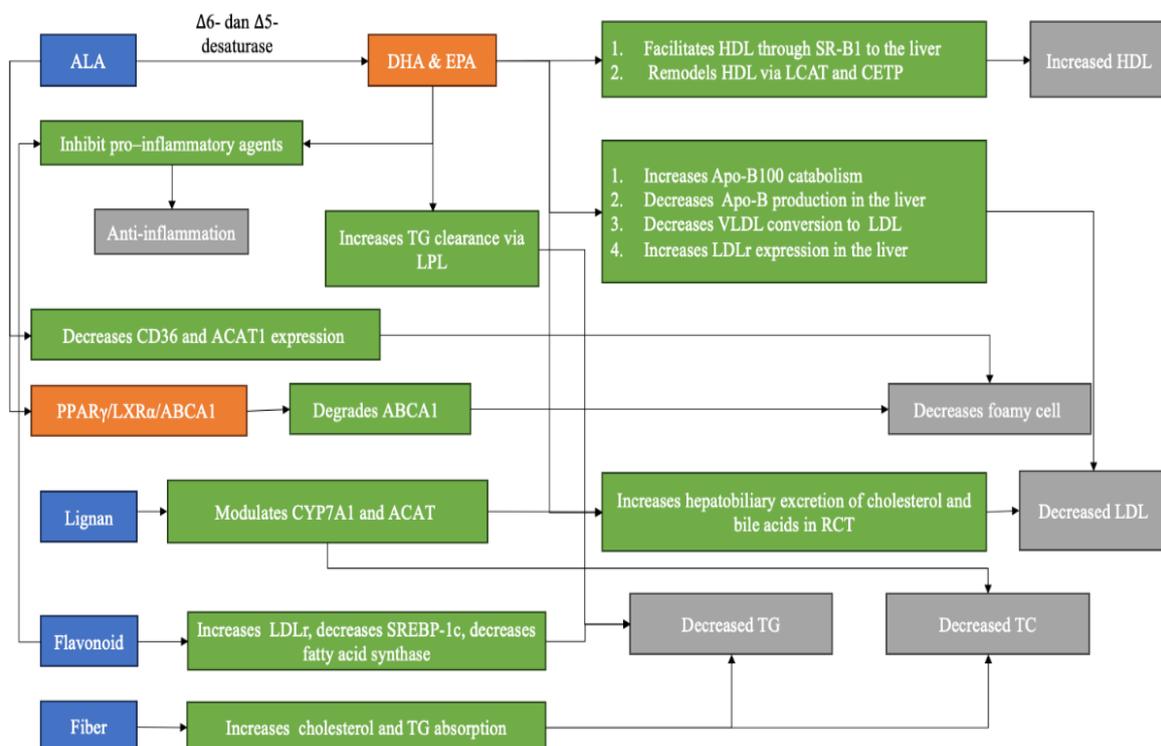


FIGURE 2. Mechanism of flaxseed's bioactive compounds in improving lipid profiles

TABLE 2. The function of flaxseed's bioactive compounds in lipid parameters

Flaxseed's bioactive compound	Effects on lipid parameter
ALA	<ul style="list-style-type: none"> • Decreases TC, LDL, and TG • Increases HDL
Lignan	Decreases TC and LDL
Phytosterol	Decreases LDL
Flavonoid	Decreases TC and LDL
Fiber	Decreases TC and TG

CONCLUSION

In conclusion, flaxseed has promising potential as a natural therapy for dyslipidemia. Flaxseed's bioactive compounds, such as ALA, lignan, flavonoid, and fiber, each play a distinct role in improving lipid profiles. There is a consistent reduction in total cholesterol TC, LDL, VLDL, and TG across most studies. However, the impact on HDL varies, with some studies reporting significant increases while others show no notable changes. Notably, TG reduction was particularly prominent in certain cases. Despite some variability in HDL response, the overall lipid-lowering effects of flaxseed highlight its potential as a therapeutic agent for improving lipid profiles. However, some studies have shown disparate results, which may arise from differences in demographics, as well as variations in the form, dosage, and duration of flaxseed used.

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