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REVIEW

Effects of Polyphenol-Rich Foods on Lipids and Oxidative Stress Status in Patients with Hyperlipidemia: A Systematic Review of Randomized Controlled Trials

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Background: Hyperlipidemia has been demonstrated to be an autonomous predictor of numerous cardiovascular and cerebrovascular ailments, and research indicates that polyphenols have preventive and therapeutic effects on hyperlipidemia. Nevertheless, the impact of polyphenol-rich foods on blood lipids and oxidative stress status in patients with hyperlipidemia remains inconclusive.
Objective: To examine the impact of polyphenol-rich foods on lipid levels and oxidative stress in individuals with hyperlipidemia.
Methods: To retrieve papers published from the establishment of the database through October 9, 2023, eight databases were searched: the Chinese National Knowledge Infrastructure, the China Biomedical Literature Database, the Wanfang Database, the China Science and Technology Journal Database, PubMed, the Cochrane Library, Embase, and the Web of Science. The quality of include studies was assessed using the Cochrane Risk of Bias in Randomized Trials tool, v2.
Results: The study involved 13 surveys encompassing 640 patients diagnosed with hyperlipidemia. The scope of the food surveys included 12 commonly consumed food groups and medicinal and food homologous substances. All 13 studies reported the effects of polyphenol-rich foods on blood lipids, with significant improvements observed in blood lipid levels for 9 types of foods. Eight studies examined the impact on oxidative stress, and six foods demonstrated a significant reduction in oxidative stress levels. The observed effects were found to be influenced by factors such as dosage, duration of intervention, and gender.
Conclusion: Foods abundant in polyphenols play a crucial role in the prevention and treatment of hyperlipidemia by counteracting oxidative stress and regulating metabolic disorders. The confirmation of certain positive effects by several studies notwithstanding, discrepancies in results arise from various factors, necessitating further large-scale, prospective, well-designed randomized controlled studies to address this issue.
Keywords: polyphenols, hyperlipidemia, blood lipids, oxidative stress, systematic review

Introduction

Hyperlipidemia is a multifaceted disorder of lipid metabolism primarily characterized by dysregulation of cholesterol levels, including elevated total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) levels and reduced high-density lipoprotein cholesterol (HDL-C) levels.[1] In the United States, more than 100 million individuals (approximately 53% of adults) exhibit elevated LDL-C levels, with less than half of patients receiving treatment and fewer than 35% achieving optimal blood lipid control.[1] Moreover, the prevalence of hyperlipidemia has been progressively increasing in China, particularly among younger people, and this disease is a significant public health concern.[2] Various studies have consistently demonstrated that patients diagnosed with hyperlipidemia exhibit increased

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susceptibility to cardiovascular disease, furthermore, hyperlipidemia serves as a significant risk factor for stroke and thereby poses a substantial threat to human health.[3,4] The regulation of lipid metabolism is closely associated with oxidative stress and inflammation, which play significant roles in the development of dyslipidemia.[5]

The current standard of care for lipid-lowering therapy continues to be statin therapy,[6] However, drug therapy often falls short of achieving optimal outcomes for many patients, particularly those with familial hypercholesterolemia, and may also give rise to severe life-threatening adverse effects such as myalgia and rhabdomyolysis.[1] The development of hyperlipidemia is believed to be influenced by dietary and lifestyle factors, therefore, a healthy diet and lifestyle should serve as the cornerstone for dyslipidemia treatment.[7] Polyphenols are widely distributed in nature, are primarily found in plants and are particularly abundant in fruits and vegetables. These compounds serve as essential constituents that exert therapeutic effects within various medicinal and food homologous substances.[8,9] Polyphenols have been shown to demonstrate efficacy in improving blood lipids and preventing atherosclerosis and vascular diseases.[10–12] Dietary polyphenolic compounds possess favorable lipid-lowering, anti-inflammatory, and antioxidant effects and thus hold significant potential in human dietary management. Polyphenols have garnered considerable attention in recent years and are poised to become the “eighth major nutrient” for humans.[13,14] The impact of diet on the development of dyslipidemia, obesity, and other diseases has been well established,[15] there is an increasing preference among nutrition and food researchers for a polyphenol compound-based diet due to its inherent advantages in terms of safety, accessibility, and long-term intervention acceptability.

It is imperative to explore safe and cost-effective lipid control regimens in order to prevent complications such as cardiovascular disease and stroke resulting from hyperlipidemia. However, conflicting findings regarding the effects of polyphenolic compounds on lipids have emerged in several studies.[16–19] Therefore, this study conducted a systematic review of published randomized controlled trials to evaluate the efficacy of polyphenol-rich foods in managing lipid and oxidative stress levels among patients with hyperlipidemia, aiming to provide valuable insights for researchers.

Methods

The present study was prospectively registered with PROSPERO (registration number: CRD42023486762) and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement in composing this article.[20]

Inclusion Criteria

Participants: Patients aged 18 years and older who have been diagnosed with hyperlipidemia based on lipid screening and management criteria,[21] as well as patients exhibiting elevated lipids;

Intervention: The participants were administered foods rich in polyphenol compounds (Phenol Explorer Datebase[22] on polyphenol content in foods greater than 10mg/100g fresh weight);

Control: The control group was administered either a standard diet or a placebo;

Outcome: Main outcome: Blood lipids: serum TC, TG, HDL-C, and LDL-C levels. Secondary outcome: The oxidative stress index serves as an indicator of antioxidant capacity;[23]

Study type: randomized controlled trial.

Exclusion Criteria

(1) Participants had other diseases; (2) Interventions combined with other pharmaceutical agents or active substances; (3) Interventions involving polyphenol extracts or nutritional supplements; (4) Studies for which the complete text was not accessible; (5) Excluded duplicate studies; (6) Excluded research proposals, conference papers, and abstracts.

Search Strategy

The search was independently conducted by two researchers (Jia and Zhang) and systematically covered eight databases, namely, Chinese National Knowledge Infrastructure (CNKI), the Wanfang Database, the China Biomedical Literature Database (CBM), China Science and Technology Journal Database, PubMed, the Cochrane Library, Embase, and the Web of Science. Subject terms were utilized in combination with free words for the search. The search period ranged from the inception of the databases to October 9, 2023. The search terms utilized in the database encompass both Chinese and English languages. The specific search strategies can be found in additional file 1.

Literature Screening and Data Extraction

The literature was independently retrieved by two researchers (Jia and Zhang). The retrieved literature was subsequently imported into EndNote20 literature management software for deduplication. The title and abstract were subsequently carefully reviewed to exclude irrelevant literature. Finally, a thorough examination of the full text was conducted to select the final literature based on predefined inclusion and exclusion criteria. Information from the selected literature, including first author, year of publication, study population, sample size, intervention details (such as type and duration), and outcome indicators, was independently extracted by both researchers. In case of any disagreements during this process, they were resolved through discussion with a third researcher.

Literature Quality Assessment

The Cochrane Risk of Bias Assessment Tool for Randomized Trials, Version 2 (RoB 2)[24] was utilized by two investigators (Jia and Zhang) to assess the included literature. The assessment encompassed a randomization process, deviation from expected interventions, missing outcome data, outcome measures and selection of reported outcomes. Based on the RoB 2 results, each article was categorized as "high risk", "some problems", or "low risk". In case of disagreement during the aforementioned process, a third researcher acted as an arbitrator to reach a consensus.

Methods of Data Analysis

In this review, we will perform descriptive analyses of eligible outcomes based on the intervention population, intervention food, and impact of the intervention on lipids and various markers of oxidative stress.

Results

Literature Search results

After conducting the initial database search, we identified a total of 3502 relevant documents. After removing 806 duplicates, we further excluded 2638 documents that clearly did not meet the inclusion criteria based on title and abstract screening. Subsequently, we carefully reviewed the full texts of 58 remaining articles that potentially met the inclusion criteria. Upon closer examination, we excluded an additional 45 and ultimately included a final set of 13.[16–19,25–33] The detailed process and outcomes of literature screening are visually presented in Figure 1.

Basic Characteristics of the Included Literature

A total of 13 studies[16–19,25–33] were included in this study; 640 patients were included from 8 countries: China, Iran, India, United States, Italy, United Kingdom, France, and Thailand. Among these studies, there were 7 randomized controlled trials[25–31] and 6 randomized crossover trials.[16–19,32,33] This study included twelve types of polyphenol-rich foods, namely, sesame seeds, soybeans, fenugreek seeds, flaxseeds, roses, passion fruits, olives, sea buckthorn berries, strawberries, apples, oranges and black tea. Notably, among them are sesame seeds, soybeans, fenugreek seeds, sea buckthorn berries, roses and olives, which possess both medicinal and food homologous substances. (Table 1)

Methodological Quality of Studies

All included studies were randomized controlled trials, but bias emerged during the randomization process. Only three studies[29,31,32] provided detailed descriptions of randomization methodology and allocation concealment. Additionally, in two studies,[19,25] there may have been biased blinding of participants and investigators. Finally, three studies[29,31,32] were deemed to have a "low risk of bias", while ten studies[16–19,25–28,30,33] were categorized as having "some concern". The results of the methodological quality assessment for the included literature are presented in Figure 2.

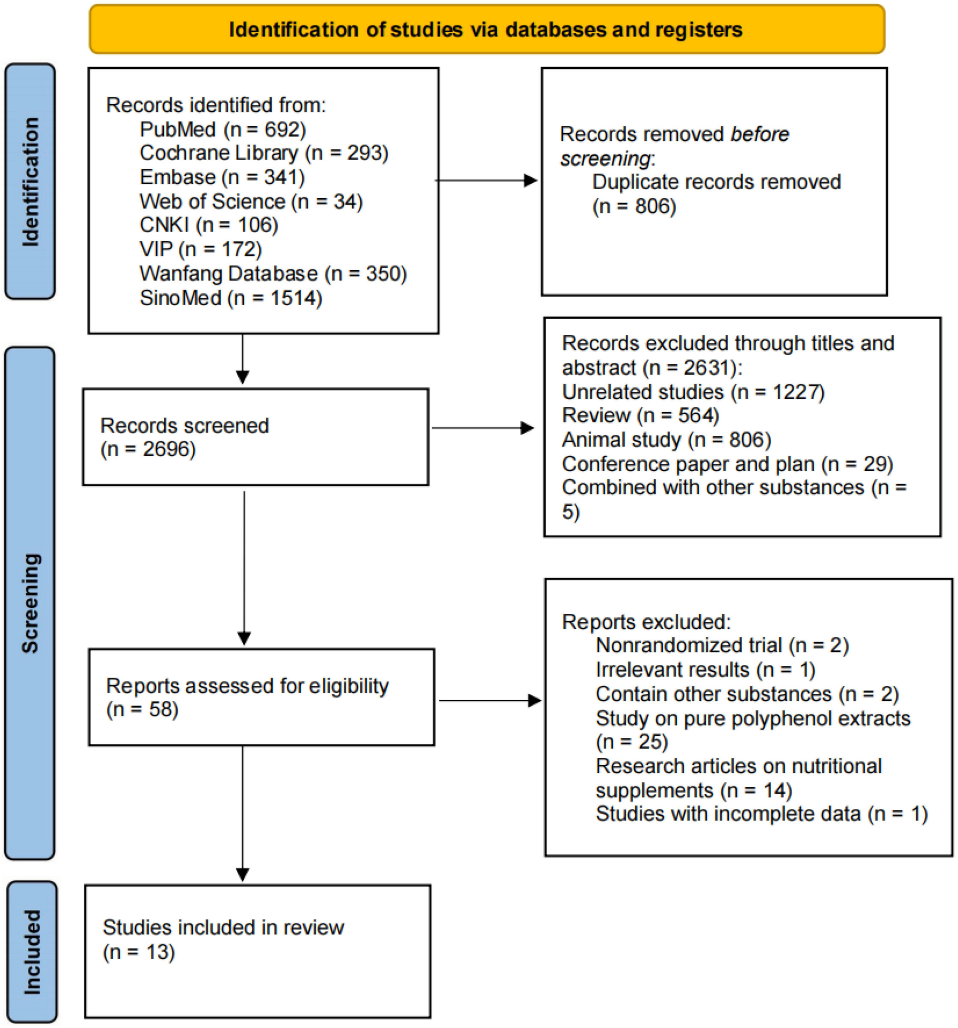

Figure 1 Literature screening process.
Note: Adapted from Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. J Clin Epidemiol. 2021;134:178–189.[20]

Effect of Polyphenol-Rich Foods on Blood Lipids in Patients with Hyperlipidemia

Thirteen studies[16–19,25–33] have reported the impact of polyphenol-rich foods on blood lipid levels in hyperlipidemic patients. Among these, eight studies[17,19,25–28,30,31] have demonstrated that the consumption of polyphenol-rich foods can effectively improve lipid profiles in individuals with hyperlipidemia. These foods include sesame seeds, flaxseeds, sea buckthorn, fenugreek seeds, soybeans, roses, passion fruits, strawberries and apples. However, the effect of flaxseed[26] on blood lipids was found to be significant only during a specific time period and did not persist after 10 weeks. Additionally, the effects may vary between sexes; however, flaxseed intervention was observed to reduce HDL-C levels in men but had no effect on women's lipid profiles. On the other hand, strawberry beverages[17] exhibited more pronounced effects on improving blood lipids among female patients with hyperlipidemia. Similarly, the impact of sea buckthorn[31] varies depending on the duration of intervention: HDL-C levels decrease within the first 6 weeks but increase thereafter. Five other studies,[16,18,29,32,33] including those involving orange juice, olives, black tea, strawberries and apples, did not find any significant effects of polyphenol-rich foods on blood lipids among individuals with hyperlipidemia. The varying conclusions regarding strawberry and apple plants could be attributed to differences in polyphenol dosage or intervention duration. In Leailin Huang's study,[18] although strawberry beverages did not exhibit

Table 1 Basic Characteristics of the Included Studies

First Author, Publication Year	Country	Related Polyphenol Types	Study Design	Patients	Sample Size (T/C)	Sex (Male/ Female) (T/C)	Intervention, Time	Control Condition	Outcomes	Time Points of Measurements	Outcome Details
Beitollah Alipoor,[25] 2012	Iran	Lignans	RCT	Patients with HLP	38 (19/19)	Unreported	Follow a daily diet and exercise plan, consuming 40 grams of white sesame seeds every day, 60 days	Follow a daily diet and exercise plan, 60 days	①: a, b, c, d; ②: f, g, h	After 60 days	The levels of TC, LDL-C, and TBARS were reduced, while the activities of GPX and SOD were increased
LeAnne T. Bloedon,[26] 2013	America	Lignans	RCT	Hypercholesterolemic men and postmenopausal women	62 (30/32)	T: 16/14C: 15/17	A low-fat, low-cholesterol diet supplemented with 20 grams of flaxseed in the morning and evening, 10 weeks	A low fat, low-cholesterol diet and consuming a bran product similar to flax baking product twice daily, 10 weeks	①: a, b, c, d, e; ②: i	After 5, 10 weeks	After 5 weeks of intervention, TC and LDL-C were significantly reduced, but the effect was not sustained after 10 weeks. There was no significant effect on TG and VLDL-C. HDL-C decreased in men but remained unchanged in women, and there was no significant impact on markers of oxidative stress
Jan Fedacko,[27] 2016	India	Flavonoids	RCT	Patients with HLP	60 (29/31)	T: 24/5 C: 25/6	American Heart Association Step 1 Diet + 20.0g of fenugreek seed powder dissolved in 300mL of water, taken before meals three times daily, 12 weeks	American Heart Association Diet + 1.0 g sachet of powdered microcrystalline cellulose dissolved in 300 mL of water, taken three times daily before meals, 12 weeks	①: a, b, c, d	After 4, 8, 12, 24 weeks	The intervention group exhibited significantly reduced concentrations of TC, LDL-C, and TG, while HDL-C levels were significantly elevated
Farzad Shidfar,[28] 2009	Iran	Flavonoids	RCT	Postmenopausal women with hypercholesterolemia	42 (21/21)	Female	Consumption of 50 grams of soy protein (roasted soybeans) containing 164 mg of isoflavones per day, 10 weeks	Consumption of 50 grams of whey protein per day, similar in appearance to roasted soybeans, 10 weeks	①: a, b, c, d; ②: j	After 10 weeks	The intervention group significantly decreased LDL-C, TC, LDL-C/ HDL-C, and TG/HDL-C, and significantly increased HDL-C and PON1 activity

(*Continued*)

Table 1 (Continued).

First Author, Publication Year	Country	Related Polyphenol Types	Study Design	Patients	Sample Size (T/C)	Sex (Male/ Female) (T/C)	Intervention, Time	Control Condition	Outcomes	Time Points of Measurements	Outcome Details
Lorenza Conterno,[29] 2019	Italy	Polyphenol	RCT	Patients with hypercholesterolemia	62 (34/28)	Unreported	90g single dose of olive puree cookies once a day, 8 weeks	Wheat flour crackers similar in appearance, flavor, and texture, once a day, 8 weeks	①: a, b, c, d; ②: i	After 8 weeks	There were no significant changes in TC, HDL, LDL, and TG, and a trend toward lower Ox LDL in the intervention group, but the effect was not significant
Jurairat Khongrum,[30] 2022	Thailand	Polyphenol	RCT	Patients with dyslipidemia	40 (20/20)	Unreported	Polyphenol-rich juice drink (300 mL) once a day, 8 weeks	Placebo drink (300 mL) once a day, 8 weeks	①: a, b, c, d; ②: k, l	After 4, 8 weeks	Significant reduction in LDL-C and TG levels, no significant improvement in TC, HDL-C, reduction in MDA, and enhancement of GSH, and improvement in oxidative stress in the intervention group
Fangfei Zhou,[31] 2022	China	Flavonoids	RCT	Hypercholesterolemic men and postmenopausal women	111 (56/ 55)	T: 8/48 C: 12/43	Consumption of 30 g of sea buckthorn puree after meals, 3 times daily, 12 weeks	Consumption of 30 g placebo after meals 3 times daily, 12 weeks	①: a, b, c, d	After 6, 12 weeks	Sand buckthorn fruit puree had no effect on serum TC, LDL-C and TG levels. However, HDL-C levels were reduced in the first 6 weeks and increased in the second 6 weeks
Rasa Troup,[32] 2015	America	Flavonoids	Cross RCT	Patients with hypercholesterolemia	57 (30/27)	32/25	Low-flavonoid diet + 5 cups of black tea daily, 4 weeks	Low-flavonoid diet + 5 cups of black tea-based placebo per day, 4 weeks	①: a, b, c, d	After 7,14,21,28 days	Drinking 5 cups of black tea per day for 4 weeks did not significantly change TC, LDL-C, HDL-C, or TG concentrations
Joel Constans,[33] 2014	France	Flavonoid	Cross RCT	Hypercholesterolemic men	25	Male	Break-in period 4 weeks after classic French diet + 200 mL of orange juice 3 times/day (212 mg of hesperidin), 4 weeks	Break-in period 4 weeks classic French diet after + 200mL of control drink 3 times/day, 4 weeks	①: a, b, c, d; ②: f, g	After 8 weeks	Daily intake of orange juice significantly increased antioxidant effects, but had no significant effect on blood lipids

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Britt Burton-Freeman,[17] 2014	America	Polyphenol	Cross RCT	Overweight HLP patients	24	10/14	Drinking an active strawberry drink (containing 10 grams of freeze-dried fruit), 6 weeks	Drinking placebo (pbo) drinks, 6 weeks	①: a, b, c, d; ②: i	After 12 weeks	Strawberry drinks resulted in significant reductions in postprandial TC, LDL, and TG concentrations, as well as a reduction in OxLDL, with the effect being more pronounced in women
Lealin Huang[18] 2021	America	Polyphenol	Cross RCT	Patients with moderate HLP	46	21/25	Two drinks (25 g, equivalent to 250 g of fresh strawberries, spaced at least 6 hours apart) per day, 4 weeks	Drinking energy-matched control powder daily, 4 weeks	①: a, b, c, d	After 4 weeks	Strawberry drink did not affect human measurements of fasting lipids, but had an overall therapeutic effect on vascular function (flow-mediated dilation was significantly increased)
Athanasios Koutsos,[19] 2020	England	Anthocyanin	Cross RCT	Mild hypercholesterolemia	43	18/25	Consumption of 2 fresh apples (340 g coreless) per day, 8 weeks	Consumption of 500 mL of control apple juice drink (100 mL concentrate + 400 mL water) per day, 8 weeks	①: a, b, c, d	After 1, 8, 12, 20 weeks	Fresh apples reduced serum TC, LDL cholesterol and TG, but there was no significant difference in HDL compared to the control group.
S Auclair,[16] 2010	France	Polyphenol	Cross RCT	Hypercholesterolemic men	30	Male	Consume two bags of freeze-dried apples rich in polyphenols daily, which is equivalent to about two 135g fresh apples, while maintaining a normal diet, 4 weeks	Consume two bags of freeze-dried apples with low polyphenol content daily while maintaining a regular diet, 4 weeks	①: a, b, c, d; ②: m, n	After 4, 8 weeks	The regular consumption of apples rich in polyphenols did not show any significant impact on lipid levels or plasma antioxidant capacity

Notes: ① Blood lipid: a. LDL-C; b. TC; c. HDL-C; d. TG; e. very low density lipoprotein cholesterol, ② oxidative stress index: f. glutathione peroxidase(GPX); g. superoxide dismutase(SOD); h. thiobarbituric acid reactive substances(TBARS); i. oxidized LDL(Ox LDL); j. paraoxonase 1 (PON1); k. malondialdehyde(MDA); l. glutathione(GSH); m. ferric-reducing ability of plasma(FRAP); n. oxygen radical absorbance capacity(ORAC).

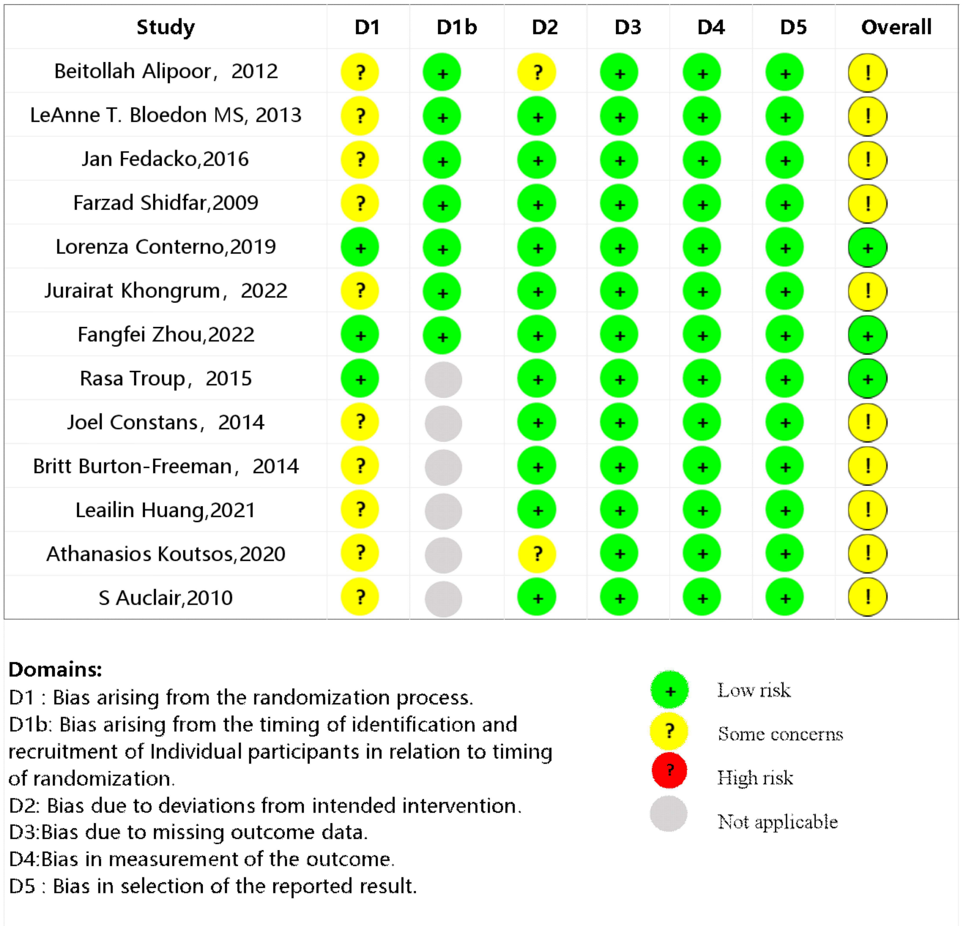

Figure 2 Results of methodological quality evaluating.
Note: Adapted from Cumpston M, Li T, Page MJ, et al. Upduidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev. 2019; 10: ED000142.[24]

a significant effect on blood lipids, they overall improved vascular function, as evidenced by significantly enhanced flow-mediated dilation.

Effect of Polyphenol-Rich Foods on the State of Oxidative Stress in Patients with Hyperlipidemia

Eight studies[16,17,25,26,28–30,33] reported the antioxidant effects of polyphenolic-rich foods in hyperlipidemic patients. The consumption of polyphenol-rich foods, such as sesame seeds, soybeans, roses, passion fruit, orange juice and strawberries, has been demonstrated in five studies[17,25,28,30,33] to effectively improve oxidative stress levels in hyperlipidemic patients. The impact of polyphenol-rich foods, which included olives, flaxseed, and apples, on oxidative stress status in hyperlipidemic patients was not found to be significant in three studies.[16,26,29] However, a study of olives[29] indicated a tendency toward reducing oxidized LDL in the intervention group, although these findings did not reach statistical significance.

Discussion

The present study included a total of 13 randomized controlled trials encompassing 640 hyperlipidemic patients to evaluate the effects of polyphenol-rich foods on individuals with hyperlipidemia. Despite demonstrating some positive effects, the findings exhibit certain inconsistencies due to various contributing factors.

Effect of Polyphenol-Rich Foods on Blood Lipids and Oxidative Stress Status in Hyperlipidemic Patients

This study revealed that a diverse range of polyphenol-rich foods exhibited favorable effects on lipid profiles and oxidative stress in individuals with hyperlipidemia. Notably, sesame, flaxseed, soybean, fenugreek seed, apple, and strawberry significantly reduced total cholesterol levels. Additionally, fenugreek seeds, soybeans, roses, passion fruit, apples, and strawberries effectively reduced triglyceride levels. Sesame seeds, flaxseed, apple, strawberry rose passion fruit soybean and fenugreek seeds were identified as effective at improving LDL-C levels. Sea buckthorn berries, soybeans, fenugreek seeds, and strawberries were associated with increased HDL-C levels. Furthermore, the same seeds, soybeans, roses, passion fruit orange juice, and strawberries exhibited antioxidant properties.

Among these foods, sesame, soybean, sea buckthorn, fenugreek seeds, rose and olive are considered homologous medicinal and food substances according to Chinese medicine theory. The concept of "food as medicine" has a positive impact on the prevention and management of chronic diseases, aligning with the Chinese medicine principle of preventing illnesses before they occur.[34,35] Many medicinal and food homologous substances are abundant in flavonoids and other polyphenolic compounds, which serve as effective components in the reduction of blood lipids.[36] In a study conducted by Wang Ling et al[37] it was discovered that hawthorn, a medicinal and food homologous substance rich in bioactive compounds such as flavonoids, triterpenoids, and phytosterols, can regulate blood lipids by inhibiting the activities of 3-hydroxy-3-methylglutarate monoacyl-CoA reductase and cholesterol acyltransferase, increasing the level of low-density lipoprotein receptors, and regulating various lipid metabolic enzymes. Another study investigating the composition and mechanism of action of sea buckthorn in treating hyperlipidemia[38] revealed that its main active components were flavonoids. The lipid-lowering mechanism may involve promoting the conversion of cholesterol to bile acids and cholesterol efflux while inhibiting de novo synthesis of cholesterol. Additionally, an intervention study conducted by Jana Kopčeková et al[39] revealed that daily consumption of 50 mL of sea buckthorn juice for 8 weeks among 19 hypercholesterolemic women resulted in reduced risks associated with cardiovascular diseases, including body fat accumulation, visceral fat deposition, LDL-C levels, and C-reactive protein levels. Furthermore, several basic studies on polyphenol extracts have demonstrated their ameliorative effects on hyperlipidemia as well as their positive impact on inhibiting atherosclerosis,[40–42] aligning with the findings from the present investigation.

By summarizing the shared characteristics of healthy dietary patterns, such as the Mediterranean diet, Japanese diet, DASH diet, and Jiangnan diet, Han Shifan et al[8] discovered that non-essential nutrients (non-nutrients) play a beneficial role in disease prevention and health maintenance. They also posited that various chronic diseases, including cardiovascular diseases, share a common feature: low-grade, chronic, and systemic inflammation. The metabolic cascade involved is known as "inflammatory transfer", which encompasses cellular oxidative stress, the progression of atherosclerosis, and insulin resistance. Polyphenols and other non-nutrients primarily exert their preventive effects against cardiovascular diseases through their ability to counteract or reduce oxidative stress while inhibiting inflammation. Simultaneously, the "family nurse dietary therapy theoretical model" is proposed for the prevention and treatment of chronic diseases using non-nutrients. By prioritizing non-nutrients, this model employs anti-inflammatory, antioxidant stress, and metabolic disorder interventions to support the management of chronic conditions. A previous study revealed that medicinal and food homologous substances can harness the polyphenols present in these plants to effectively ameliorate clinical symptoms of patients with chronic diseases through three pathways: anti-inflammatory action, antioxidative stress response, and improvement of metabolic disorders.[43] Additionally, there is evidence indicating that bergamot, which is rich in polyphenols, can effectively reduce blood lipids in rats fed a high-fat diet. This effect is primarily achieved through the regulation of an enzyme involved in cholesterol transesterification between lipoproteins, thereby improving metabolic disorders. Simultaneously, the beneficial impact of regulating paraoxonase 1 may be exerted by inhibiting the activation of NF-kB, specific protein 1 (SP1), and sterol regulatory element binding protein 2 (SREBP2) to suppress oxidized LDL and attenuate the progression of atherosclerosis.[44] The flavonoid polyphenol anthocyanins can enhance Nrf2 activation and antioxidant gene expression in cells, thereby safeguarding macrophages and endothelial cells against oxidative stress through the inhibition of NOX and iNOS while activating eNOS.[45] Dietary polyphenols have also been found to possess antioxidant and anti-inflammatory properties in numerous studies, and their consumption has been inversely associated with the development of metabolic syndrome.[46,47] Furthermore, foods abundant in polyphenols exert a positive impact on blood vessels, potentially enhancing vasodilation capacity by downregulating NOx2-mediated oxidative stress and ultimately augmenting nitric oxide (NO) production.[48]

Natural polyphenol-rich foods are considered safe for human consumption. Among the studies included, safety was evaluated in 5 studies.[19,26,27,31,33] No adverse reactions were reported in the studies involving apple or orange juice. However, mild gastrointestinal reactions, dizziness, and other symptoms were observed in studies on fenugreek seeds and flaxseed. Allergic reactions were reported by one participant in the sea buckthorn study, but no serious adverse events occurred. According to the European Commission Regulation (EC) No. 258/1997, it is recommended that individuals consume up to 1000 mg of polyphenol extract per day.[48] Therefore, in daily life, when consuming foods rich in polyphenols and nutritional products made from polyphenol extracts, it is important to pay attention to the dosage of polyphenol intake to prevent adverse reactions caused by excessive consumption.

The lack of positive effects on patients observed in some of the included studies[16,18,29,32] could be attributed to variations in intervention duration, polyphenol dosage, and food preparation technique. In two studies examining the impact of polyphenol-rich apples on individuals with hyperlipidemia,[16,19] Athanasios Koutsos' research[16] utilized fresh apples containing high levels of polyphenols for a duration of 8 weeks, with an average apple weight of 340 g. This intervention resulted in a significant amelioration of blood lipid profiles in patients diagnosed with hyperlipidemia. Conversely, in the study conducted by S Auclair,[19] no significant impact on blood lipids or oxidative stress was observed in patients with hyperlipaemia after a 4-week intervention involving freeze-dried apples rich in polyphenols, which equated to approximately 270 grams of fresh apples. A comparative study[49] on the polyphenol and antioxidant capacity of eight fruits revealed that the peel exhibited the highest polyphenol content, followed by the pulp, while also demonstrating the highest antioxidant capacity. The observed variations in effects could be attributed to factors such as apple processing technique, duration of processing, temperature conditions, and fruit variety. Further investigations[50,51] indicated that both storage conditions and apple variety influenced the levels of polyphenols and antioxidant capacity. Additionally, different drying treatments involving varying processing methods, durations, and temperatures were found to impact the polyphenol content. Similarly, a study focusing on cereals[52] reported that diverse processing methods employed for cereals could influence their polyphenol content as well as their antioxidant effects. The impact of a polyphenol-rich diet on patients with hyperlipidemia may be influenced by sex. In these two studies, the effect of polyphenol-rich food varied between the sexes.[17,26] Therefore, during dietary management for hyperlipidemic patients, the amount of polyphenol-rich foods and the preparation process should be taken into consideration, fresh unprocessed foods should be selected for long-term consumption as much as possible, and appropriate polyphenol-rich foods should also be selected for patients according to their sex to make better use of their effects.

Practical Implications

Previous studies[53,54] have demonstrated that diet is as effective at promoting health as medical treatment is, particularly for lifestyle-related diseases, which can be prevented by 47% through dietary adjustments. One of the global objectives set by the World Health Organization is to achieve a 25% reduction in cardiovascular diseases, a goal that can be accomplished solely through dietary interventions. With the advancement of society, the focus on human health has shifted toward prevention and maintenance, leading to an accelerated pace in managing a healthy diet. Polyphenolic compounds are abundant in plant-based herbs and foods and serve as efficacious bioactive substances within numerous medicinal and food homologous substances. In the Tang Dynasty, Yang Shangshan wrote in "Huangdi's Inner Jing Tai Su": "With its hunger is called food, with its disease is called medicine"; medicine and food homology is a characteristic theory of traditional Chinese medicine disease prevention and treatment. Moreover, a predominantly plant-based diet is a healthy dietary pattern that can effectively prevent chronic diseases related to diet and is widely recommended in various dietary guidelines.[8,55]

Dietary interventions are emerging as a promising "upstream" approach for improving chronic diseases, but the integration of food and medicine is becoming a significant trend.[56] The consumption of dietary polyphenols can directly or indirectly enhance the management of oxidative stress and regulate inflammation, thereby mitigating the onset and progression of chronic diseases; incorporating polyphenol-rich foods into one's diet effectively alleviates symptoms associated with cardiovascular disease.[57] Natural medicinal substances that share similarities with food have gained attention due to their diverse sources, economic safety, abundance in non-nutrients, and potential use as food additives. This novel dietary regulation trend holds great promise for preventing the occurrence of hyperlipidemia and offers broad prospects for its prevention and treatment, as well as associated complications. Moreover, exploring the potential of agricultural products rich in non-nutrients, particularly polyphenols, is crucial for maximizing the medicinal value of such crops while simultaneously stimulating agricultural economic development.

Strengths and Limitations

The strengths of this study lie in the inclusion of high-quality randomized controlled trials from eight countries, ensuring reliable and robust results. The limitations of the present study include the restriction of the search to Chinese and English language articles, which may lead to potential oversight of important studies and impact the overall analysis. Additionally, variations in dosage and intervention duration among different types of polyphenol-rich foods hindered the possibility of conducting a meta-analysis.

Conclusion

The study findings demonstrated that a majority of foods abundant in polyphenols exhibited significant improvements in the lipid profile of patients diagnosed with hyperlipidemia, encompassing levels of total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol. Simultaneously, specific polyphenol-rich food choices exhibited potential to mitigate oxidative stress among those affected by hyperlipidemia. Although its positive effects have been confirmed by numerous experiments, inconsistencies in the results have emerged, potentially due to variations in factors such as polyphenol content, intervention duration, and gender. Therefore, future research should focus on conducting large-scale prospective studies with well-designed randomized controlled trials. The theoretical model of "family nurse dietary therapy" suggests that polyphenols play a crucial role in the prevention and treatment of chronic diseases, primarily by regulating metabolic disorders and reducing oxidative stress. It is essential to optimize intervention programs involving polyphenol-rich foods, with particular emphasis on harnessing the potential of non-nutrient components for effectively preventing and treating chronic diseases.

Abbreviations

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; HLP, hyperlipidemia.

Data Sharing Statement

The original data involved in the manuscript can be obtained from the references.

Author Contributions

Yt J proposed the subject of this study. A comprehensive literature search and data extraction were conducted by Yt J, Yh Z, and QZ to assess the risk of bias in included studies. The data analysis was performed by Yt J and QZ, while the paper writing was solely undertaken by Yt J. Subsequently, the paper underwent a thorough review and revision process involving QZ, Yh Z, HW, JL, RF Z, WF, Qm N and Yx Z. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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