Effect of Tree Nuts Consumption on Serum Lipid Profile in Hyperlipidemic Individuals: A Systematic Review

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ABSTRACT: Many epidemiological studies have regularly connected nuts intake with decreased risk for coronary heart disease. The primary mechanism by which nuts protect against cardiovascular disease is through the improvement of lipid and apolipoprotein profile. Therefore, numerous dietary intervention studies investigated the impact of nut consumption on blood lipid levels. Many studies have shown that nut intake can enhance the lipid profile in a dose-response way among individuals with increased serum lipids. This systematic review examines the effectiveness of nuts on the lipid profile among patients with dyslipidemia from different age groups. A total of 29 interventional studies from 5 databases met the inclusion criteria. In all, 20 studies were randomized controlled clinical trials, whereas 9 were crossover-controlled clinical trials. Participants included in the studies were different in terms of age, sex and, serum lipid profile. The studies were inconsistent in the type of tree nuts, duration, dose, and the nut forms. All studies indicated changes in the lipid profile after the intervention particularly on the total cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides, total cholesterol/high-density lipoprotein. Interventional periods ranged from 3 weeks up to 12 months with doses ranged from 15 to 126 gm. In conclusion, this review provides an evidence of favorable effect of nuts consumption of serum lipid profile.

KEYWORDS: Hypercholesterolemic, tree nuts, lipoproteins, LDL-c

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Introduction

Mediterranean diet is characterized with high consumption of seeds and nuts. Nuts consumption was associated with healthy cardiovascular system. Whether such association is existed among patients already with unhealthy lipid profile is still to be confirmed by researchers. Cardiovascular diseases (CVD) is one of the driving causes for mortality and morbidity all over the world. Hyperlipidemia, yielding from the anomalies of lipid homeostasis, is a major risk factor for CVD progression. Decreasing serum blood lipids can minimize the possibility of developing CVD as well as diabetes.[1] If the incidence of therapy for hyperlipidemia increased by 10%, this could prevent an evaluated 8000 deaths each year.[2] It has been also assessed that even modest steps, for instance, primary prevention guidelines suggested by the National Cholesterol Education Program Adult Treatment Panel III, could avoid roughly 10 000 deaths and 20 000 heart attacks due to cardiovascular disorders and conserve nearly US$3 billion in heart disorders–related medicinal expenses every year.[3]

Despite the fact that low-density lipoprotein (LDL-c) has been recognized as the first lipoprotein of interest, triglycerides, high-density lipoprotein (HDL-c), and total cholesterol (TC) further play a central roles in coronary heart disorders risk, with triglycerides, LDL-c, TC linked with risk and HDL probably play a preventive role.[4] Here, "lipid profile" point out to a collection of lipids including triglycerides, very-low-density lipoprotein cholesterol (VLDL-c), LDL-c, TC, and HDL-c.

Existing guidelines encourage lipid-lowering medications for individuals having a risk for CVDs (⩾7.5%), those with elevated LDL-c concentrations (⩾193 mg/dL), or a diabetic individual with elevated LDL-c concentration (⩾70 mg/dL).[4,5] Statins have displayed an efficient decrease in both cardiovascular incidents and LDL-c concentrations.[4,5] Yet, despite vigorous statin therapy to slow down atherosclerotic plaque progression and minimize the risk for cardiovascular complications,[6] a great proportion of patients taking statin medication do not attain the desirable values of LDL, and some patients cut off therapy due to adverse effects associated with the medication.[7-9]

Diet therapy to reduce cholesterol levels and to alter lipid profile plays a fundamental role in preventing hyperlipidemia as well as hypercholesterolemia.[10] Lately, consuming nuts has been cornerstone of intensive studies because of their possibility to minimize CVD risk and to reduce blood lipid concentrations depending on their unique nutritional characteristics.[11,12]

Nuts are considered one of the most nutrient-dense food, as they are an excellent source of fat (50%-75%), especially unsaturated fatty acids; furthermore, they contain considerable amounts of plant protein (10%-25%).[11-13] Moreover, they are an essential source of additional constituents such as minerals (potassium, magnesium, and copper), vitamins (Vitamin B6, Vitamin E, folic acid, and niacin), dietary fiber, and other bioactive compounds such as phytosterols and phenolic antioxidants.[2,11,12]

Former meta-analysis of controlled trials has concluded that tree nut consumption can improve blood lipid parameters in the general population.[14-17] However, the impact of nut intake on lipid parameter among hyperlipidemic population is not determined yet. In addition, prior analyses have not made an inference

Table 1. PICOS standards for exclusion and inclusion of articles.

PARAMETER	STANDARD
Population	Individuals with or at risk of elevated levels of any of these lipids "TC, LDL-c, HDL-c, TG," with no regard to age, sex, or ethnicity.
Intervention	Exclusively consuming nuts.
Comparators	Sufficient information to allow for comparison between pre- and postintervention in accordance with HDL-c, LDL-c, TC, TG levels.
Outcomes	Studies estimating the influence of consuming tree nuts as a major or minor outcome.
Study design	Observational study design or controlled trial.

Abbreviations: HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; PICOS, Participants, Intervention, Comparators, Outcomes, Study design; TC, total cholesterol; TG, triglycerides.

about the impact to a certain dose. So, this systematic review was performed to assess the relationship between the following tree nuts, "almond, nut, peanut, cashew, pistachio nut, pecan, pine nut, walnut, macadamia nut, Brazil nut, soy nut, and hazelnut," and blood lipid profile within hyperlipidemic population.

The aim of this systematic review was to investigate whether tree nuts, as part of the Mediterranean diet, can improve blood lipid parameters within hyperlipidemic individuals and as well as to find whether some kinds of tree nuts are better in enhancing blood lipid parameters, and the dose-response reports the effect on lipid parameters among hyperlipidemic individuals.

In this study, it was hypothesized that tree nut would reduce the levels of the main lipoprotein (TC, VLDL-c, LDL-c, TG) and increase the levels of HDL-c. Also, it was proposed that there will be potential variations in the influence of tree nuts among hyperlipidemic individuals.

Methods

Design of primary studies

To explore the role of tree nuts on lipid parameters within hyperlipidemic population, it was performed a systematic review of dose-response clinical trials[18-20] and controlled interventional trials.[20-46]

Data source and search strategy

This study has employed the PRISMA statement (2009)[47] procedure to systematically check the articles that have estimated the impact of eating nuts in hyperlipidemic individuals. An inclusive search in the databases of MEDLINE/PubMed (https://www.ncbi.nlm.nih.gov/pubmed/), Google Scholar (https://scholar.google.com/), Web of Science (https://clarivate.com/products/web-of-science/), Cochrane database (http://www.cochranelibrary.com/), and ElSEVIER-Embase (https://www.elsevier.com/) was made for articles from database inception to April 2019. The standard to explain a "clinical trial" was depending on trials with humans that were possibly designed to one or more interventions (that might contain control or other placebo groups), and with goal to estimate the impact of ingesting tree nuts on plasma lipids. Search key words included blood profile, hyperlipidemia, hypercholesterolemia, hyperlipemia, almond, nut, peanut, cashew, pistachio nut, pecan, pine nut, walnut, macadamia nut, Brazil nut, soy nut, and hazelnut. The Boolean operators "and not," "or," and "and" were applied to join the expressions used in the literature review. Sample search strategy is illustrated in Additional File 2. This review is not registered till this moment.

Inclusion and exclusion criteria

The primary stage of the search has consisted of screening abstracts and titles, and the next stage has consisted of checking full-text studies that met the following selection criteria: (1) individuals with hyperlipidemia which was identified as having an elevation in any of the lipid concentration "LDL-c, HDL-c, TC, TG"; (2) the presence of control group; (3) treatment or intervention group which is focusing on nut consumption. The following exclusion criteria have been used: (1) article not an original paper, (2) lack of comparison diet, (3) small sample size (<10), (4) animal studies, (5) trial duration of <3 weeks. In case the trial has more the one version, the most recent and informative one has been included. The PICOS (Participants, Intervention, Comparators, Outcomes, Study design) standards are shown in Table 1.

Data extraction

For every article, the following data were obtained: author publication year, sample size, age, volunteer's characteristics, search methodology, duration of consuming nuts, control diet, type of nut, the daily quantities, and their influence on plasma lipids. The study design and the overall estimated and chosen articles are shown in Figure 1. As a consequence of this search, 29 articles were chosen.

Results

Twenty-nine interventional studies met the inclusion criteria, with 1003 participants identified with elevated lipid profile. The design of most of the studies was a randomized controlled

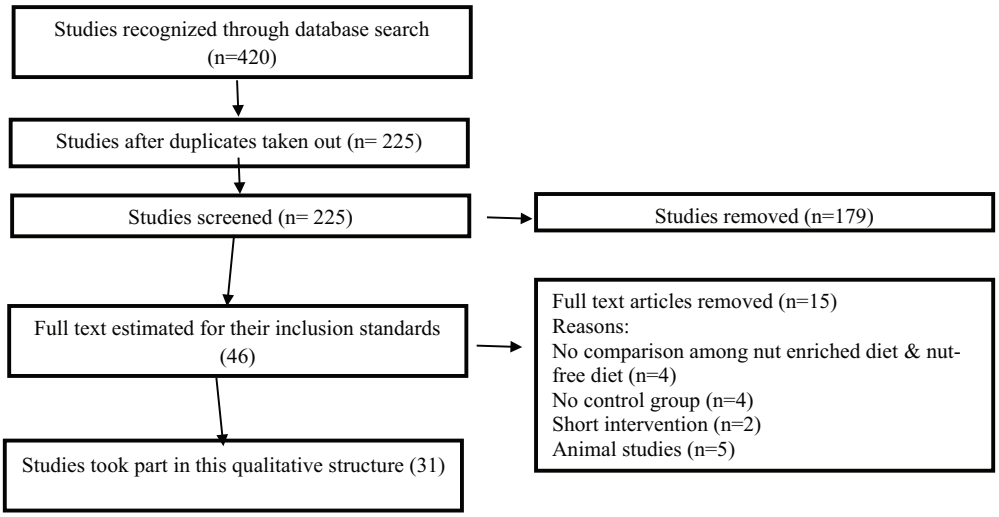

Figure 1. Flow chart of literature search procedure.

clinical trial, followed by controlled clinical trial and randomized case control with or without crossover. The sample size ranged from 10 to 90 patients, with age ranged from 21 to 65 years and only 1 study has included adolescents. The outcome measures reported were mainly TC, LDL-c, HDL-c, TG, TC/HDL-c, and VLDL-c.

Various types and forms of nuts were used in the interventions; the majority was whole nuts with or without skin. Few studies (3/29) have used nuts oil in form of capsules and only 1 study used a blend of whole nuts and oil.

Discussion

As this review focused on evaluation, the effectiveness of types of nuts, dose and duration of the intervention on lipid profile, each type of nut and intervention is discussed briefly and separately in this session.

Walnuts

Supplementation trials

The influence of consuming walnuts on serum plasma lipid has been discussed thoroughly. In a research performed by Chisholm et al,[23] a 2-period crossover trial was used to see whether a daily capsule of walnut around 78 g would have additional benefits on lowering lipid parameters, besides a low-fat diet (30% of total fat). Following a walnut diet has produced a significant decrease in TC (24%), LDL-c (28%) levels, and significant elevation in HDL-c (14%).[23]

Trials incorporating walnut as oil

The effectiveness of consuming walnut oil on lipid parameters has been studied extensively. In a recent randomized controlled trial performed by Zibaeenezhad et al,[44] it has been discovered that the regular consumption of 12 walnut oil capsules, which consists of 1.25 cc Persian walnut, over a period of 3 months, has effectively decreased TC, LDL-c, TG, and total/HDL ratio. The inclusion of walnut oil has also lead to a significant elevation in HDL-c levels in hyperlipidemic patients, whereas there was no alteration in the placebo group.[44] In a former trial done by Zhao et al,[43] it was noticed that the daily incorporation of 37 g walnut plus 15 g walnut oil into a regular diet has significantly reduced TG, TC, and LDL-c concentrations, whereas there were no significant changes in the placebo group. In another trial performed by Zibaeenezhad et al,[46] it was concluded that the daily consumption of walnut oil can be used as an effective antihypertriglyceridemic therapy among hyperlipidemic patients.

Trials incorporating walnut in the diet

In a feeding study about walnuts, Muñoz and his partners[31] saw an effective reduction in TC and LDL-c after moderate intake of walnuts (41-56 g/d), whereas there was no alteration in lipid profile in the control group. Zambón et al[42] observed a significant decrease in TC, LDL-c concentrations, and LDL/HDL-c ratio (9%, 11.2%, and 8%, respectively) (11.2%) after replacing walnuts for a portion of the monounsaturated fatty acids in a cholesterol-lowering Mediterranean diet. In identical research, it was also observed that daily consumption of walnut (40-65 g) ameliorates endothelial role in hypercholesterolemic volunteers beyond the effective improvements in lipid profile.[37] In another trial, the inclusion of walnut (42.5 g, 6 d/wk) has produced a considerable increase in HDL and decrease in TG levels, whereas the control diet did not result in any changes in lipid profile.[36] In another trial performed by Tufail et al,[41] it was observed that the daily intake of 30 g walnut has effectively elevated HDL-c levels by 6.3%.

Studies have also shown that walnut inclusion even in tiny amounts (≈20 g/d) can ameliorate blood lipid.[33,45] Olmedilla-Alonso et al[33] confirmed significant reductions in TC and TG after the daily consumption of meat supplemented with walnuts over a period of 5 weeks. In another trial, it was noticed a

great decrease in TG by 17% and increase in HDL by 9% after the regular inclusion of walnut (20 g) for 8 weeks.[45]

Furthermore, the consumption of walnuts over a long period of time (ie, 1 year) can exert advantageous properties on lipid profile. In a randomized crossover trial, the advantageous influence on plasma lipid profile was more apparent among hypercholesterolemic volunteers who consumed a diet enriched with walnut (28-64 g/d) for 1 year.[40] Trials on the influence of tree nuts consumption on lipid profile are epitomized in Table 2.

Almonds

Trials incorporating almond in the diet

Outcomes of clinical studies performed in individuals with elevated LDL or TC concentration have elucidated the cholesterol-lowering properties in controlled or free-living conditions which indicate that almond consumption can enhance plasma lipid profile whether it is consumed in little quantities (20 g/d)[21] or considerable quantities (100 g/d).[39] Spiller et al[39] noticed that the daily consumption of 100 g almond over a period of 4 weeks has triggered a significant decrease in TC (16%) and LDL-c (19%) in comparison with dairy or olive oil diets; however, HDL-c levels remain stable. On the contrary, Bento et al[21] have observed that the daily consumption of almond (20 g) effectively reduced TC, LDL, and non-HDL cholesterol levels, whereas the control diet did not make any alteration on blood lipids.

Clinical trials also showed that even moderate intakes of almond have positive impacts on lipid profile. Berryman et al[22] noticed that replacing a carbohydrate-rich snack (eg, muffin) with 43 g/d of almond over 6 weeks could be an effective dietary strategy to block the beginning of cardio-metabolic disorders. As the daily consumption of 43 g almond has ameliorated LDL-c, VLDL-c, and LDL-c/HDL-c ratio in normal weight subjects with high LDL-c.[22] In another trial, daily consumption of almond diet, which represents 20% of the overall calories, during a period of 4 weeks produced a significant decrease in LDL-c, TC, and LDL/HDL-c ratio.[28] In a crossover study, exchanging 40% of the fat in the Mediterranean diet with almond, virgin olive oil, or walnut over a period of 4 weeks was linked with a great decrease in LDL-c, TC, and LDL-c/HDL-c, but no alteration was noticed in HDL-c levels.[24]

Trials incorporating almond as oil

The effectiveness of consuming almond oil on lipid parameters has also been studied widely. In 2017, Zibaeenezhad and his colleagues have found that consuming *Amygdalus scoparia* kernel oil for 2 months have significantly reduced serum triglyceride levels (24.80 ± 51.70) but did not effectively alter serum TC, LDL, and HDL cholesterol levels.[48] Two years later, a randomized controlled trial performed by Zibaeenezhad et al[49] demonstrated that enriching the diet enriched with 10 mL of almond oil, 2 times per day for 1 month, significantly reduced the lipid profiles (TC and LDL), but it did not significantly influence the TG and HDL levels among hyperlipidemic individuals.

Dose-response trial

A dose-response rapport was recognized with the blending of almonds into a step II diet by Jenkins et al.[19] They have noticed that the inclusion of a full portion of almond (73 ± 3 g) over a period of 4 weeks has elicited an effective reduction in LDL and elevation in HDL-c levels. They also reported an effective decrease in TC after consuming almond in full and half portions.[19] In another randomized crossover trial, the combination of roughly 68 g of almond, which represents 20 of the overall energy, into 2000-calorie step I diet triggered remarkable modification in lipid parameters among volunteers with mild hyperlipidemia. The dose-response way was seen for TC, LDL-c, and LDL/HDL ratio.[20]

Hazelnut

Some findings indicated that hazelnuts exert a favorable impact on blood lipid concentrations. Deon et al[25] have noticed a significant reduction in LDL-c and elevation in HDL/LDL-c ratio after consuming hazelnuts either with skin or without skin (15-30 g/d) during a period of 8 weeks. Mercanligil et al[30] found that hazelnut has a lipid-lowering capacity, as they have observed that the daily inclusion of hazelnut (40 g) have a positive alteration in blood lipids among hypercholesterolemic men and thereby favorably influencing the coronary heart disease risk. In another randomized controlled trial, it has been also noticed that hazelnut intake by 49-86 g/d over a period of 12 weeks can effectively ameliorate TG, TC, LDL, and HDL among hypercholesterolemic volunteers, whereas there was no variation in lipid concentration in the hazelnut-free diet.[34]

Pistachio Nuts

To date, 2 studies have been performed to confirm the cholesterol-lowering properties of consuming pistachio nuts among hypercholesterolemic individuals. In a crossover study conducted by Sheridan et al,[38] it was confirmed that regular inclusion of pistachios (2-3 oz) during a period of 4 weeks has stimulated a great decrease in TC/HDL and LDL/HDL ratios, as well as a significant increase in HDL concentrations. In a former trial, Edwards et al[26] found that regular ingestion of pistachios (100 g) has stimulated a notable reduction in LDL/HDL, TC/HDL, and TC concentrations, effective elevations in HDL concentrations, as well as effective elevations in HDL-c concentrations.

Dose-response trial

A dose-response connection was noticed with the combination of pistachios into a low-fat diet. Volunteers ingested a low-fat diet with either (1) 32 to 63 g or (2) 63 to 120 g in a randomized crossover-controlled study. The findings showed a significant

Table 2. Effects of tree nuts consumption on lipid parameters in hyperlipidemic individuals.

	FIRST AUTHOR	NO. OF VOLUNTEERS (M/F)	AGE, Y	VOLUNTEERS CHARACTERISTICS	STUDY DESIGN	LENGTH OF STUDY	CONTROL GROUP	DAILY QUANTITY AND KIND OF NUTS	OUTCOME
1	Chisholm et al[23]	21 men	<65	Polygenic hyperlipidemia	CO	4 wk	Low-fat diet without walnut	78 g walnut	↓TC (0.25 mmol/L), LDL-c (0.36 mmol/L); ↑HDL (0.15 mmol/L)
2	Damasceno et al[24]	18 (9/9)	56 ± 13	Hypercholesterolemic	CO	4 wk/ period)	Mediterranean diet	40-65 g walnut	↓LDL-c in all treatment groups, specifically, 7.3%, 10.8%, and 13.4% after the VOO, walnut, and almond diets, respectively
3	Muñoz et al[31]	10 males	48-71	Polygenic hypercholesterolemia	CO	6 wk	Mediterranean—type, cholesterol-lowering diet	41-56 g walnut	↓TC (4.2%), LDL-c (6.0%); ↔HDL-c, TG
4	Olmedilla-Alonso et al[33]	25 (15/10)	54.4 ± 8.1	Elevated cholesterol concentrations	RCT (CO)	5 wk	Meat products without walnut	19.4 g walnut	↓TC (4.5%), LDL-c (5.1%)
5	Rajaram et al[36]	25 (14/11)	23-65	Normal to mild hyperlipidemia	RCT	4 wk	Usual diet without fish or nuts (30% total fat and $<10\%$ SFAs)	42.5 g walnut	↓TG (1.11 ± 0.11 mmol/L), total/HDL-c, LDL/HDL-c ratios, ↑HDL-c (1.18 ± 0.05 mmol/L)
6	Ros et al[37]	18 (8/12)	55	Hypercholesterolemic	CO	8 wk	Cholesterol-lowering Mediterranean diet	40-65 g walnut	↓TC ($-4.4 \pm 7.4\%$), LDL-C ($-6.4 \pm 10.0\%$); ↔LDL:HDL-c ratio
7	Torabian et al[40]	87 (38/49)	54 ± 10.2	Normal to mild elevation in total cholesterol	CO	12 mo	Regular diet without walnut	28-64 g walnut	↓ TC, TG, LDL-c; ↔HDL-c, LDL/HDL-c ratio
8	Tufail et al[41]	40 (NR/NR)	NR	Hyperlipidemic	CT	2 mo	Regular diet without dried fruits and nuts	30 g walnut	↑HDL-c (6.3%)
9	Zambón et al[42]	49 (NR/NR)	56	Polygenic hypercholesterolemia	CO	6 wk	Cholesterol-lowering Mediterranean diet	46 g walnut	↓TC (9%), LDL-c (11.2%), LDL/HDL-c ratio (8%)
10	Zhao et al[43]	23 (20/3)	49.8 ± 1.6	Moderate hypercholesterolemia	RCT (CO)	6 wk	American diet	37 g walnut plus 15 g walnut oil	↓TC, LDL-c, and TG

(Continued)

Table 2. (Continued)

	FIRST AUTHOR	NO. OF VOLUNTEERS (M/F)	AGE, Y	VOLUNTEERS CHARACTERISTICS	STUDY DESIGN	LENGTH OF STUDY	CONTROL GROUP	DAILY QUANTITY AND KIND OF NUTS	OUTCOME
11	Zibaeenezhad et al[44]	90 (NR/NR)	35-75	Hyperlipidemic and type 2 diabetic	RCT	90 d	Regular diet without walnut	12 walnut oil capsule	↓TC, TG, LDL, total/ HDL; ↑HDL
12	Zibaeenezhad et al[45]	43 (NR/NR)	NR	Hyperlipidemic	Randomized case-control trial	8 wk	Regular diet without nuts	20 g walnut	↓TG (17.1%) ↑HDL (9%)
13	Zibaeenezhad et al[46]	60 (NR/NR)	NR	Hyperlipidemic	Randomized case-control trial	45 d	Regular diet without walnut	6 walnut capsules	↓TG
14	Bento et al[21]	20 (NR/NR)	21-57	Hypercholesterolemic	RCT (CO)	6 wk/ period and 4 wk of washout	1 corn starch tablet/d	20 g almond	↓TC (8.1 ± 2.4%), LDL-c (9.4 2.4%), non-HDL-c (8.1 ± 3.0%)
15	Berryman et al[22]	48 (22/26)	30-65	High LDL-c concentrations	RCT (CO)	6 wk/ period and 2 wk of washout	Diet with an isocaloric muffin without almond. "26% total fat, 15% PRO, 58% CHO)	43 g almond	↓TC (−5.3 mg/dL), non-HDL-c (−6.9 mg/dL), LDL-c (5.3 mg/ dL), VLDL-c (2.31 mg/dL), LDL-c/HDL-c ratio (0.20)
16	Li et al[28]	20 (9/11)	58 ± 2	Type 2 diabetes mellitus with mild hyperlipidemia	CO	4 wk/ period and 2 wk of wash out	NCEP-ATPIII: step II diet	56 g almond	↓TC (6.0%), LDL-c (11.6%), LDL/HDL-c ratio (9.7%)
17	Spiller et al[39]	45 (12/33)	53 ± 10	Hyperlipidemic	RCT (PL)	4 wk	Dairy diet or olive oil diet without almond	100 g almond	↓TC, LDL-c, total/HDL-c ratio; ↔ HDL-c
18	Jenkins et al[19]	27 (15/12)	64 ± 9	Hyperlipidemic	CO	4 wk/ period and >2 wk of washout	Full dose of low saturated fat (<5% energy) whole-wheat muffins	73 g almond at full portion. 37 g almond at half portion	↓LDL-c and ↑HDL-c in full-dose; ↓TC in full and half portion
19	Sabaté et al[20]	25(14/11)	41 ± 13	Healthy and mild hypercholesterolemia	RCT (CO)	4 wk/ period and 2 wk of wash out	Step I without almond	34 g almond at low dose; 68 g almond at high dose	↓TC (0.24 mmol/L), LDL-c (0.26 mmol/L), LDL: HDL-c (8.8%) after high-almond diet; ↑HDL-c (0.02 mmol/L) after high-almond diet

(Continued)

Table 2. (Continued)

	FIRST AUTHOR	NO. OF VOLUNTEERS (M/F)	AGE, Y	VOLUNTEERS CHARACTERISTICS	STUDY DESIGN	LENGTH OF STUDY	CONTROL GROUP	DAILY QUANTITY AND KIND OF NUTS	OUTCOME
20	Deon et al[25]	60 (34/26)	11.6 ± 2.6	Primary hyperlipidemia	RCT (PL)	8 wk	Diet consultation (30% total fat, 15% PRO, 55% CHO) without HZNs	15-30 g hazelnut with or without skin (HZN-S, HZN + S)	↓LDL-c at both HZN-S and HZN + S; ↑HDL-c/LDL-c at both HZN-S and HZN + S; ↓non-HDL-c at HZN-S
21	Mercanligil et al[30]	51 males	48 ± 8	Hypercholesterolemic	CT	8 wk	Diet high CHO, low fat and low cholesterol	40 g hazelnut	↓VLDL-c (29.5%), TG (31.8%), Total/HDL-c, LDL/HDL-c ratios; ↑HDL-c (12.6%); ↔TC, TG
22	Orem et al[34]	21 (18/3)	44.6 ± 10.4	Hypercholesterolemic	RCT (CO)	12 wk	NCEP-ATPIII; (<7% of energy from SFA, <200 mg/d dietary cholesterol) without hazelnut	49-86 g hazelnut	↓TC (–7.8%), TG (–7.3%), LDL-c (–6.17%); ↑HDL-c (6.07%)
23	Edwards et al[26]	10 (4/6)	46	Moderate hypercholesterolemia	RCT (CO)	3 wk	Regular diet	60 g pistachio	↓TC, total/HDL-c, LDL/HDL-c ratios; ↑HDL
24	Gebauer et al[18]	28 (10/18)	48 ± 1.5	Elevated LDL levels	RCT (CO)	4 wk	Low-fat diet without pistachios	32-63 g pistachios at low dose; 63-126 g pistachios at high dose	↓ TC, LDL, and non-HDL at low and high dose; ↓TG, TC/HDL and LDL/HDL at high dose
25	Sheridan et al[38]	15 (11/4)	60 ± 3	Moderate hypercholesterolemia	CO	4 wk	Regular diet without pistachios	56-84 g pistachio	↓TC/HDL-c (–0.38), LDL-c/HDL-c (–0.40); ↑HDL-c (2.3); ↔TC, TG, LDL-c, VLDL-c
26	Griel et al[27]	25 (10/15)	54	Mildly hypercholesterolemic	RCT (CO)	5 wk	AAD (33% total fat containing 13% SFA, 11% MUFA, 5% PUFA)	42.5 g macadamia	↓TC (4.94 ± 0.17 mmol/L), LDL-c (3.14 ± 0.14 mmol/L), non-HDL-c (3.83 ± 0.17), total: HDL-c (4.60 ± 0.24), LDL: HDL-c (2.91 ± 0.17); ↔TG

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Table 2. (Continued)

	FIRST AUTHOR	NO. OF VOLUNTEERS (M/F)	AGE, Y	VOLUNTEERS CHARACTERISTICS	STUDY DESIGN	LENGTH OF STUDY	CONTROL GROUP	DAILY QUANTITY AND KIND OF NUTS	OUTCOME
27	Mah et al[29]	51 (20/31)	55.7 ± 1.42	Elevated LDL-c or at risk of elevated LDL-c	RCT (CO)	28 d/ period and 2 wk of washout	Potato chips (29% total fat, 18% PRO, 54% CHO) without cashews	48-64 g cashew	↓ LDL-c (2.3%), TC (3.9%), non HDL-c, TC/HDL-c; ↔ TG, HDL-c
28	O'Byrne et al[32]	25 women	50-65	Hypercholesterolemic	CT	6 mo	Low-fat diet "LF" without nuts. (Total fat < 30%, PRO 15-20%, CHO 50-60%)	35-68 g peanuts	↓TC (10%), LDL-C (12%), total/HDL-c (0.05-0.11)
29	Rajaram et al[35]	23 (14/9)	38	Normal to mild elevation in cholesterol concentrations	RCT (CO)	4 wk	Step I (total fat 28.3% of overall energy) without pecan	72 g pecan	↓TC (6.7%), LDL-c (10.4%), TG (11.1%); ↑HDL-c (0.06 mmol/L)
30	Zibaeenezhad et al[48]	109	46.5 ± 11.4	Elevated triglycerides, total cholesterol, LDL levels Reduced HDL level	RCT	60 d	Did not receive any intervention	ASK oil	↓Triglycerides
31	Zibaeenezhad et al[49]	97	20-75	Elevated triglycerides, total cholesterol, LDL levels Reduced HDL level	RCT	30 d	Did not receive any intervention	10 mL Persian almond oil	↓TC, LDL-c

Age was presented in mean ± standard deviation or range.
Abbreviations: ↓, reduction; ↑, increase; ↔, insignificant; AAD, average American diet; ASK, *Amygdalus scoparia* kernel; CHO, carbohydrate; CO, crossover; CT, controlled trial; F, female; HDL-c, high-density lipoprotein cholesterol; HZN-S, hazelnut without skin; HZN + S, hazel nut with skin; LDL-c, low-density lipoprotein cholesterol; LF, low-fat diet; M, male; MUFA, monounsaturated fatty acids; NCEP-ATPIII, Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults; NR, not reported; PL, parallel; PRO, protein; PUFA, polyunsaturated fatty acids; RCT, randomized controlled trials; SFA, saturated fatty acid; TC, total cholesterol; TG, triglycerides; VLDL-c, very-low-density lipoprotein cholesterol; VOO, virgin olive oil.

decrease in TC, LDL, and non-HDL after consuming low and high doses. There was also an effective decrease in total/HDL and LDL/HDL ratios after ingesting pistachios at a high dose. So, the researchers have deduced consuming pistachio within a healthy diet positively minimize and enhance the plasma lipids in a dose-based mode.[18]

Cashews, Macadamias, Peanuts, and Pecans

Despite the lack of clinical outcomes related to lipid-lowering abilities of cashews, macadamias, peanuts, and pecans among individuals with increased levels of any of the following blood lipids (TG, TC, and LDL), a limited number of studies have been found confirmed that the mentioned nuts exert a favorable impact on blood lipid concentrations. In a recent study, Mah et al[29] have performed a randomized controlled trial to see whether cashews can improve lipid profile among individuals having elevations in LDL-c concentrations. They have found that the substitution of carbohydrate-rich snack (eg, potato) with a cashew-rich diet can be an effective dietary strategy to assist in the management of LDL and TC.[29] In a former research, Griel et al[27] noticed a positive alteration in lipid concentrations in patients with hypercholesterolemia, after the daily consumption of macadamia (42.5 g). A single trial was found regarding the influence of peanuts on lipid parameters in hypercholesterolemic subjects. O'Byrne et al[32] have noticed a significant reduction in LDL-c (12%), TC (10%), and total/HDL ratio after following a low-fat monounsaturated rich diet diet containing peanuts (35-68 g) when compared with low-fat diet. Concerning lipid-lowering abilities of pecans, I have found only 1 study which noticed that daily consumption of pecans (72 g) exerts a considerable decrease in TC (6.7%), LDL-c (10.4%), and TG (11.1%), as well as a significant elevation in HDL-c concentrations, and as a consequence, the consumption pecans can play an effective role as a part of cholesterol-lowering therapy in individual with high cholesterol levels.[35]

Nutritional Constituents of Nuts

The diversity in the nutritional constituents of nuts is a remarkable aspect that should be examined to explain the various impacts of their consumption on lipid parameters. Concerning lipid kinds, hazelnut, cashew, and almond nuts display an elevated ratio of MUFAs/SFAs, with affirmation in hazelnuts, which display the greatest ratio, conforming to 10:1. Walnuts present the greatest concentration of PUFAs, mostly α-linolenic acid, conforming to an overall of 47.17 g/100 g of PUFAs, whereas almonds exhibit the greatest fiber content of all the tree nuts, conforming to 12.5 g/100 g. However, peanuts contain the greatest proportion of protein and fiber in comparison with tree nuts. Suggested mechanisms for the hypocholesterolemic impact of soluble fiber include the following: (1) the fiber binds bile acids which reduces serum cholesterol and (2) bacteria in the colon ferment the fiber to yield acetate, propionate, and butyrate, which block cholesterol synthesis.[17] Besides the diverse combinations and concentrations of fatty acids, it is essential to confirm that these tree nuts also vary in bioactive compounds and micronutrients, chiefly phenolic substances in walnuts, phytosterols in peanuts, α-tocopherol in hazelnuts and almond, and carotenoids in pistachios.[13]

Strengths and Restrictions

To the best of the author's knowledge, no systematic review has been issued on the influence of nut consumption on lipid parameters among hyperlipidemic individuals. Therefore, in this study, I have performed a systematic review of clinical trials in an effort to epitomize the evidence of consuming nuts (almonds, cashews, hazelnuts, macadamia nuts, peanuts, pecans, and pistachios) on lipid parameters among hyperlipidemic individuals.

Few restrictions of this systematic review have to be mentioned. At first, most of the involved trials had a moderately few volunteers, theoretically leading to variable evaluate of therapy impacts. Another point that should be pointed out is that every trial had its own standards including follow-up intervals, medical situation, sex, various intervals of life, the use of medications, and quantity of nuts drug usage, and amount of the nut. Finally, it is well known that there are variations in constituents of same nuts in several parts of the universe and even several parts of the same country.

Conclusions

Based on the current outcomes, the authors have found that almond, walnut, pecan, and peanuts have mainly advantageous action toward TC and LDL-c, whereas hazelnut, pistachio, and walnut have mainly favorable action toward HDL-c. Trials performed up to date have regularly shown a great impact on lipid parameters in hypercholesterolemic individuals. It was also observed that all the nuts, which is included in this study, have resulted in an effective elevations in HDL-c levels. Recommendations to include tree nuts as part of a healthy diet can be addressed to positively manage lipid profile (at least within short period of time). It is probable that future studies could find other bioactive substances in nuts that would give extra advantages on human health beyond those known till now.

Author Contributions

MA, concept and idea, review manuscript, SZ, writing first draft and corections, MB, Checking statistics and quality of manuscript, proof reading

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