www.endocrinologia.org.mx

PERMANYER

Rev Mex Endocrinol Metab Nutr. 2024;11:60-73

REVISTA MEXICANA DE ENDOCRINOLOGÍA, METABOLISMO & NUTRICIÓN

REVIEW ARTICLE

The effectiveness of turmeric supplementation in reducing low-density lipoprotein cholesterol in adults

La eficacia de la suplementación con cúrcuma para reducir el colesterol unido a lipoproteínas de baja densidad en adultos

James Hesson

Department of Healthcare and Behavioral Sciences, Medical Writing Certificate Program, University of California, San Diego Extended Studies, La Jolla, California, USA

ABSTRACT

This review reports the findings of seven systematic reviews and meta-analyses evaluating the effectiveness of turmeric/curcumin as a dietary supplement in reducing LDL-cholesterol (LDL-C). PubMed was searched for publications between January 1st, 2018 and August 23th, 2023, reporting on the anticholesteremic effects of turmeric. Turmeric demonstrates antioxidant, anti-inflammatory, and anticholesteremic activity. A dosage of 850 mg/d for 10 weeks reduced LDL-C in adults over 50 years old at risk for cardiovascular disease. One study reported curcumin reduced LDL-C by a mean of 39.83 mg/dL. Yet, other reports conflicting findings on the effectiveness of turmeric supplementation, likely due to high-heterogeneity in between-study endpoints, dosage, duration, and participant characteristics. Turmeric has potential as a safe, effective, inexpensive, lipid-lowering functional food. Future studies must clarify the degree to which turmeric improves lipid indices, its mechanism of action, and the most effective form, dose, route, and duration in reducing LDL-C.

Keywords: *Curcuma longa*. Curcumin. Low-density lipoprotein cholesterol. Coronary artery disease. Functional foods.

RESUMEN

Esta revisión informa sobre los hallazgos de siete revisiones sistemáticas y metanálisis que evalúan la efectividad de la cúrcuma como suplemento dietético para reducir el colesterol-LDL (LDL-C). Se buscaron en PubMed publicaciones entre el primero de enero de 2018 y el 23 de agosto de 2023 que informaran sobre los efectos anticolesterémicos de la cúrcuma. La cúrcuma demuestra ser antioxidante, posee actividad antiinflamatoria y anticolesterémica. Una dosis de 850 mg/día redujo el C-LDL en adultos mayores de 50 años con riesgo de enfermedad cardiovascular. Un estudio informó que la curcumina redujo el C-LDL en una media de 39,83 mg/dL. Sin embargo, otros informan hallazgos contradictorios sobre la cúrcuma, probablemente debido a la alta heterogeneidad en los criterios de valoración, la dosis, la duración y las características de los participantes entre los estudios. La cúrcuma tiene potencial como alimento funcional reductor de lípidos, seguro, eficaz y económico. Los estudios futuros deben aclarar el grado en que la cúrcuma mejora los índices de lípidos, su mecanismo de acción y la forma, dosis, vía y duración más efectivas para reducir el C-LDL.

Palabras clave: *Curcuma longa*. Curcumina. Lipoproteínas de colesterol de baja densidad. Arteriopatía coronaria. Alimentos funcionales.

Correspondence:
James Hesson
E-mail: jimhesson86@gmail.com

Date of reception: 27-08-2023
Date of acceptance: 30-01-2024
DOI: 10.24875/RME.23000039

Available online: 10-06-2024
Rev Mex Endocrinol Metab Nutr. 2024;11:60-73

INTRODUCTION

Over 226,000 people died from cardiovascular disease (CVD) in Mexico in 2021, with one person dying every 2 min[1,2]. Over 56% of adults in Mexico have elevated levels of low-density lipoprotein cholesterol (LDL-C)[3,4]. Worldwide, the burden of CVD is disproportional, with nearly 80% of deaths from CVD occurring in low- and middle-income countries, along with higher rates of disability-adjusted life years[4,5].

Coronary artery disease (CAD) is the most common type of CVD[6,7] characterized by arteriosclerosis resulting from a buildup of fatty deposits that narrow the lumen of coronary arteries[8]. Risk factors for CAD include hypercholesteremia, hypertension, diabetes, smoking, being postmenopausal for women, and over 45 years old for men[9]. Lifestyle choices that increase risk for CAD include, diet, physical inactivity, overweight, obesity, and excessive alcohol consumption[10,11].

Abnormally elevated serum LDL-C is a major health concern as it plays a central role in the pathogenesis of atherosclerotic CVD (ASCVD)[9-11]. Serum LDL-C is considered a primary predictive measure of cardiovascular event risk[10]. HMG-CoA reductase inhibitors (statins) are the standard of care lipid-lowering therapy used adjunctively with lifestyle changes to treat hypercholesterolemia by reducing elevated LDL-C, total cholesterol (TC), and triglycerides (TG) levels and increasing high-density lipoprotein cholesterol levels[12].

While statins are well tolerated in most patients, due to adverse events, such as myopathy, myalgia, hepatitis, and uncomfortable cold sensations, statin intolerance has been reported in between 5 and 30% of patients according to the National Lipid Association[13]. Such patients adhere poorly to statins, discontinue or seek alternative treatments[14]. Clinicians have used a SLAP (Switch, Lower dose, Alternate dosing, Polypharmacy) management strategy to support such patients; yet, in uncommon patients with complete statin intolerance, alternatives such as ezetimibe, bempedoic acid, PCSK9 inhibitors, inclisiran novel genetic therapies, and nutraceuticals have been used to manage dyslipidemia[15].

Lifestyle changes, a first-line of therapy in improving lipid profile indices, include exercise, diet, nutraceuticals, and weight loss. Nutraceuticals and dietary supplements such as berberine, soluble fibers, plant sterols, stanols, and red yeast rice have shown effectiveness as lipid-lowering agents and are of potential value for patients with low-to-moderate hypercholesterolemia, alone or in combination with a pharmacological therapy[15]. Likewise, consuming so-called *functional foods* such as almonds, whole grains, unsaturated oils, green tea, avocados, tomatoes, and flaxseeds has been gaining attention as a safe, inexpensive means to remediate elevated LDL-C and promote a healthy diet[16]. Among these functional foods, the cooking spice turmeric has been reported to have antioxidant, anti-inflammatory, and anticancer activity in various diseases[17-19].

Turmeric is an herb (*Curcuma longa*) acclaimed to have therapeutic value. The rhizomes (roots) of the *C. longa* plant are used to derive *curcumin*, an orange-yellow-colored powder containing a molecule with the IUPAC name (1E, 6E)-1,7-bis(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene-3,5-dione)[20], considered a bioactive compound and naturally occurring phenol with pharmacological properties[20]. Similar to the functional foods mentioned previously, curcumin has potential as a safe, inexpensive dietary supplement to support cardiovascular health, which may be particularly of interest to low- and middle-income countries[21].

The precise mechanism of action (MoA) of turmeric as an antihyperlipidemic agent is unclear; however, Musazadeh et al.[22] report several possible MoAs whereby turmeric (1) reduces hepatic hydroxyl methylglutaryl CoA reductase enzyme activity, essential for cholesterol biosynthesis; (2) hampers lipogenesis enzymes (acetyl CoA carboxylase, stearoyl-CoA-desaturase 1, and fatty acid synthase), thus disrupting lipid metabolism; (3) reduces hepatic activity of acyl-CoA: cholesterol acyltransferase, an enzyme critical in producing cholesteryl esters that promote atherogenesis; (4) increases up-regulation of hepatic cholesterol 7a-hydroxylase, convertingv cholesterol to bile acids, the primary mechanism for eliminating cholesterol from the body; (5) decreases LDL receptors expression through activation of peroxisome proliferator-activated receptors g; (6) activates hormone-sensitive lipase, accompanied by reduced lipogenic enzymes.

A major drawback of turmeric is its low absorbability and poor bioavailability, being rapidly metabolized and eliminated from the body[23]. Yet, recent attempts have boosted its bioavailability by combining it with other bioactive agents, including piperine from black pepper[24,25]. Nonetheless, the strength of the evidence demonstrating the effectiveness of turmeric in reducing LDL-C remains unclear. Most importantly, despite the aforementioned studies, no pharmaceutical has been approved by a pharmacovigilance agency, such as the US Food and Drug Administration, because over-the-counter (OTC) dietary supplements are evaluated as food and not as a drug, so they do not undergo rigorous clinical trials on safety and efficacy, leaving consumers uncertain about the efficacy, safety, quality, and purity of an OTC turmeric supplement[26].

Considering these gaps in the literature regarding the effectiveness of turmeric in reducing LDL-C and considering the potential promise, cost-savings, and convenience of consuming functional foods such as turmeric to improve cardiovascular health, a systematic search of the literature was done to further clarify turmeric's potential in reducing LDL-C.

METHODS

To consolidate high-quality evidence on the effectiveness of turmeric in reducing LDL-C, a systematic search of the literature was done in PubMed (https://www.ncbi.nlm.nih.gov) on August 23, 2023. The target population was adults, including healthy individuals and those at risk for CVD. The primary endpoint of interest for this review was mean LDL-C measured at baseline and post-intervention, reported as either mmol/L or mg/dL. The control groups ranged from foods, no treatment, or placebo. The inclusion criteria were systematic reviews and meta-analyses published between January 1, 2018, and August 23, 2023; full text, and English-language articles. The exclusion criteria were non-randomized controlled trials (RCTs), studies not reporting on LDL-C or CVD; duplicate publications; animal studies; and studies in languages other than English.

First, a search was done at PubMed, with MeSH terms listed in table 1. Second, after identifying and saving the results of two searches, the results were screened, and ineligible studies were excluded, as shown in figure 1. Third, the remaining articles were compiled into a final collection of systematic reviews and meta-analyses. These reports were then read and their findings are summarized in the Results section and table 2. PubMed filters used: meta-analysis, systematic review, published within 5 years (1/1/2018-8/23/2023), full text; age 19+ years.

RESULTS

The PubMed search provided 18 systematic reviews and meta-analyses, including one study from listing of "similar articles". Next, four duplicate studies were removed, leaving 14 for screening. From these 14 studies, seven were excluded from the screening process because they were not about CVD or did not report on LDL-C, and one study was published before 2018. All of the included studies specifically report on turmeric's effect in remediating CVD by lowering LDL-C. The findings of these studies are presented in alphabetical order by author's surname below and in table 2. The gold-standard Cochrane GRADE-Assessment[27] was adopted by three of the seven meta-analyses reviewed herein. GRADE evaluates the quality of evidence of five domains: imprecision, indirectness, risk of bias, inconsistency, and publication bias.

Ashtary-Larky et al. carried out a GRADE-assessed systematic review and meta-analysis to determine the effect of nanocurcumin supplementation on reducing risk factors for CVD[28]. Nanocurcumins are novel formulations developed to overcome the poor bioavailability profile of native curcumin, and some studies show that nanocurcumins have greater effectiveness than native curcumin in reducing LDL-C[25]. The nine RCTs of this review included 510 participants, each in subgroups characterized by Type-2 diabetes (T2DM), metabolic syndrome (MS), dyslipidemia, migraine, and non-alcoholic fatty liver disease (NAFLD); the authors did subgroup and pooled analyses of the results of these RCTs, reporting on a number of endpoints, including LDL-C, and the results are shown in table 2.

Table 1. PubMed search dates, search term syntax used, search filters, and number of articles retrieved

PubMed search date and number	Syntax entered in the database search tool	Search filters	Number of articles retrieved
August 23, 2023 #1	"Turmeric" OR "Curcuma" [Mesh] OR "curcumin" AND "Cholesterol, LDL" [Mesh]	Systematic review, meta-analysis, full text articles, publication within 5 years (1/1/2018-8/23/2023); adult	(n = 11)
August 23, 2023 #2	"Turmeric" OR "Curcuma" [Mesh] OR " low-density lipoprotein cholesterol"	Systematic review, meta-analysis, full-text articles, publication within 5 years; adult	(n = 8)

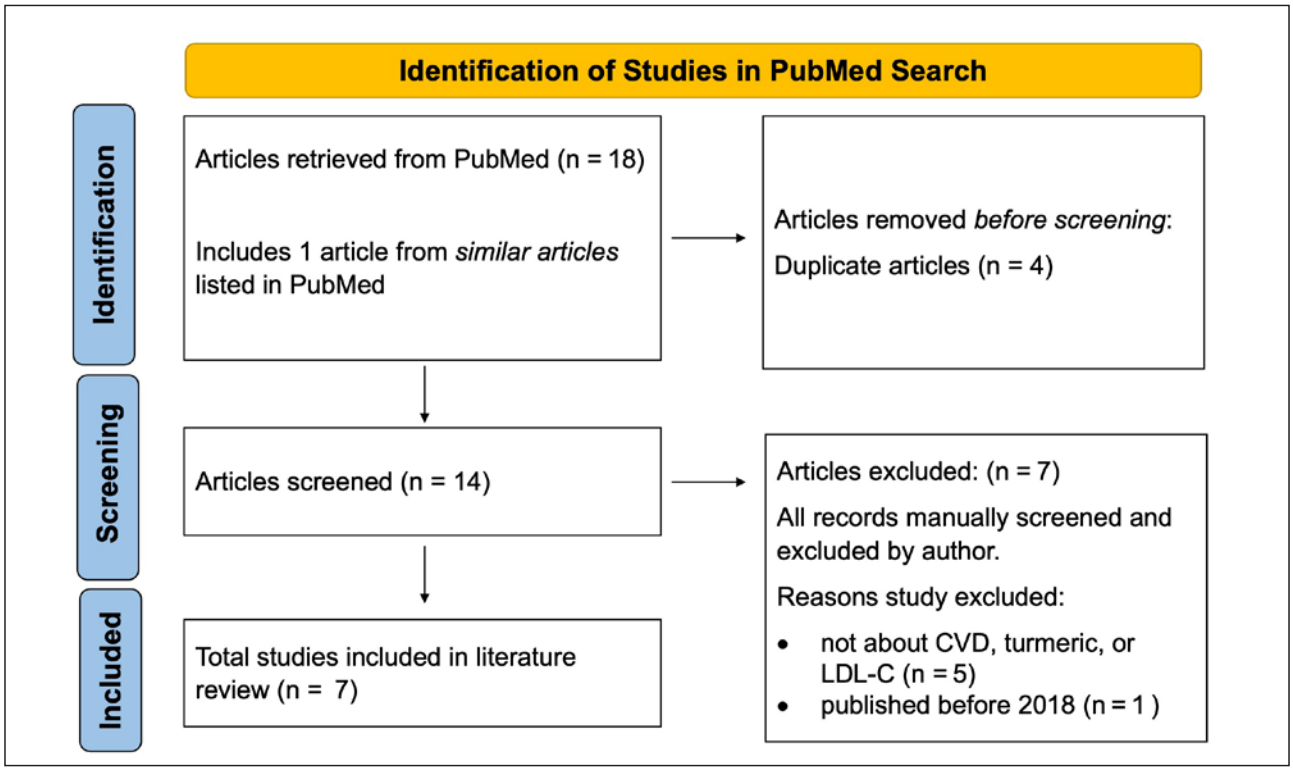

Figure 1. Flowchart of protocol for searching PubMed to identify meta-analyses and systematic reviews on the effectiveness of turmeric supplementation in reducing low-density lipoprotein cholesterol to include in a literature review.

Ashtary-Larky et al. report that nanocurcumin reduced LDL-C across all groups, yet in five RCTs with over 300 participants, the overall reduction was not strong (weighted mean differences [WMD]: −3.59 mg/dL; CI: −15.74, 8.56). However, in individuals with dyslipidemia, LDL-C reduction was more impressive. Subgroup analysis showed that the nanocurcumin supplementation significantly improved LDL-C in patients with LDL-C ≥ 100 mg/dL and BMI > 30, with a WMD of −13.70 (95% CI: −19.26, −8.13). Yet using the GRADE assessment, the authors downgraded the quality of evidence in these trials as very low, overall. This downgrade was based on high imprecision, inconsistency of nanocurcumin dosages among study groups, and high between-study heterogeneity (I^2 = 84.8%, $p < 0.001$) based on differences between study participants, and imprecision related to the relatively low number of study participants[28]. It should also be noted

Table 2. Summary of findings of seven meta-analyses and systematic reviews from a PubMed search on the effectiveness of turmeric in reducing LDL-C listed alphabetically by author surname

Author, date published	Study design	# of patients; disease type	Age	Gender	Race, ethnicity, country	Intervention: form, dose, route, duration, control	Primary endpoint	Safety results; adverse events	Efficacy results	Quality of evidence and limitations
Ashtary-Larky, 2021	GRADE-Assessed systematic review and meta-analysis of 9 RCTs; all parallel trials random-effects model and subgroup analysis used to determine variations by dose and baseline risk profiles	510 participants (control = 241; cases = 269) with sample sizes between 16 and 84; RCTs included participants w/ MS, NAFLD, T2DM, CVD, diabetes on hemodialysis, migraine; All study participants at risk for CVD	35-62 y	334 females; 152 males	Race: NR Ethnicity: NR, Country: Iran	Form: curcumin, nanocurcumin type NR Dose: In seven RCTs, dose was 80 mg/d nano-curcumin; In two RCTs, dose was 40 mg/d and 120 mg/d Route: oral administration Duration: 6-12 w Control group: placebo	Change in LDL-C mg/dL at baseline and postintervention reported as WMD	NR	Subgroup analyses showed nanocurcumin significantly improved LDL-C in participants with baseline LDL-C > 100 (mg/dL) and BMI > 30, with a WMD of −13.70 (95% CI: −19.26, −8.13) 5 RCTs show little change in LDL-C: WMD: −3.59 mg/dL; 95% CI: −15.74 to 8.56; p = 0.562; High between-study heterogeneity (I^2 = 84.8%, p < 0.001)	Used GRADE-Assessment to rank the quality of evidence as very low due to notable between-study heterogeneity in participant characteristics, duration, and dosages Relatively low number of participants enrolled in studies All RCTs performed in one country
Dehzad, 2023	GRADE-Assessed systematic review and meta-analysis of 64 RCTs; majority parallel trials, except for 3 crossovers random-effects model and subgroup analysis used to determine variations by dose and patients	4051 participants (control = 2006; intervention = 2045); sample sizes: 18-213 RCTs included participants who were healthy, overweight and obese, on hemodialysis, had CAD, COPD, HIV, NAFLD, PCOS, MS, T2DM, HLP, et al.	18 to 65 y	# of males and females NR	Race: NR Ethnicity: NR, Country: majority (34) of RCTs from Iran, and the rest (30) from 15 other countries.	Form: curcumin, nanocurcumin Dose: 80 mg/day (nano-curcumin) to 4000 mg/day (turmeric powder) Route: oral administration Duration: 4-24 w Control group: placebo	Mean and standard deviation change in LDL-C mg/dL at baseline and postintervention reported as WMD Included outcomes of 3 studies reporting on apolipoprotein B and apolipoprotein A	NR	LDL-C (WMD = −4.89 mg/dL; 95% CI = −5.92, −3.87; p < 0.05 High between-study heterogeneity (I^2 = 95.6% Effect observed for Apo-A, WMD = 1.58 mg/dL; 95% CI = −3.49, 6.56; I^2 = 64.4%; p < 0.05 No effect observed for Apo-B, WMD = 1.35 mg/dL; 95% CI = −9.74, 12.44; I^2 = 83.4%; p < 0.05	Used GRADE-Assessment to rank the quality of evidence for HDL-C results as low and for apolipoprotein as very low due to significant between-study heterogeneity Majority of RCTs were performed in one country

Table 2. Summary of findings of seven meta-analyses and systematic reviews from a PubMed search on the effectiveness of turmeric in reducing LDL-C listed alphabetically by author surname (continuation)

Author, date published	Study design	# of patients; disease type	Age	Gender	Race, ethnicity, country	Intervention: form, dose, route, duration, control	Primary endpoint	Safety results; adverse events	Efficacy results	Quality of evidence and limitations
Adel Mehraban, 2021	7 systematic review and meta-analyses Followed PRISMA but not registered in PROSPERO	4761 participants RCTs included participants w/ T2DM, CVD, HTN, T2DM, NAFLD, MS, HLP, HTG, MI, CHD, CKD	18-81 y	Gender only reported as "both." Number of males and females NR	Race: NR Ethnicity: NR, Country: NR	Form: curcumin, curcuminoid type NR Dose: 45-6000 mg/d Route: oral administration Duration: 1-24 w Control group: placebo, nonactive agents	Change in LDL-C mg/dL at baseline and postintervention	NR	Findings of 7 meta-analyses range from no significant change in LDL-C to a reduction of 39.83 mg/dL (95% CI: 75.02, −4.25) Most effective doses ranged from 330 to 1795 mg/d	AMSTAR scores ranged from 8 to 11 Limitations due to heterogeneity between RCTs in form, doses, ages, duration and endpoints
Musazadeh, 2022	Umbrella meta-analysis of 18 meta-analyses of RCTs RCTs from 8 different countries	10,730 participants RCTs included participants w/MS, NAFLD, T2DM, DL, and healthy	27-60 y	NR	Race: NR Ethnicity: NR, Country: majority of RCTs from Iran	Form: type of curcumin (dried drug, oil, and extracts) not distinguished or reported in most RCTs Dose: 80-1127 mg/d Route: oral administration Duration: range 2-14 w	Between-study effect size of curcumin supplementation reported as WMD	NR	Curcumin supplementation lowered LDL-C (ES: 0.49 mg/dL, 95%CI: 0.85, 0.13, p = 0.007; I^2 = 51.9%, p = 0.004). The greatest LDL-C reductions were at dosage ≤ 850 mg/d for 10 w Curcumin improved TC, TG, LDL-c, and HDL-c levels.	AMSTAR ranked RCTS from 8 to 11 on scale of 0-11. Significant publication bias reported Heterogeneity among studies very high R (I^2 = 51.9%, p Z 0.004) Type of curcumin (dried drug, oil, and extracts) not reported in most RCTs
Rafiee, 2021	Systematic review of 22 RCTs All trials parallel design Followed PRISMA reporting standards	1545 participants RCTs included participants w/T2DM, PCOS, NAFLD, CAD, DL, MS, obese or overweight, impaired glucose tolerance	16-70 y	815 females; 660 males	Race: NR Ethnicity: NR, Country: 15 RCTs done in Iran; 1 RCT each done in the United States, Thailand, Italy, Japan, China, Australia, and Taiwan	Form: curcumin, curcuminoid, curcuma extract Dose:80-2000 mg/d Route: oral administration Duration: 4-24 w Control: placebo	Change in LDL-C mg/dL at baseline and postintervention	NR	Curcumin reduced LDL-C in 6 RCTs, but 15 RCTs, the change was not significant; 1 RCT had no data for LDL-C LDL-C levels in curcumin group reduced by 0.17 versus the placebo group (95% CI: −0.43 −0.09; p = 1.27; p = 0.2) Half of RCTs showing improved LDL-C had formulations with high bioavailability	Jadad Scale ranked quality of evidence of in 21 RCTs as high, and low quality in 1 RCT Limitations in RCTs related to heterogeneity of dosage, duration, formulations Did not report mean LDL-C changes in mg/dL or mmol/L; only reports LDL-C increased or decreased, not addressing primary endpoint of interest of this review

Table 2. Summary of findings of seven meta-analyses and systematic reviews from a PubMed search on the effectiveness of turmeric in reducing LDL-C listed alphabetically by author surname (continuation)

Author, date published	Study design	# of patients; disease type	Age	Gender	Race, ethnicity, country	Intervention: form, dose, route, duration, control	Primary endpoint	Safety results; adverse events	Efficacy results	Quality of evidence and limitations
Saeedi et al., 2022	Systematic review and meta-analysis of 16 RCTs 11 RCTs were randomized double-blind placebo-control trial Followed PRISMA reporting standards	1288 participants RCTs included participants w/DL	18-70 y	NR	Race: NR Ethnicity: NR, Country: seven RCTs done in Iran; one each done in Mexico, Germany, Iraq, Pakistan, and Taiwan, and two done in Australia	Form: (curcumin-phospholipid) Dose:294-2400 mg/d Route: oral administration Duration:11 d to 12 w	Change in LDL-C mg/dL at baseline and postintervention	NR	5 RCTs report LDL-C improved postintervention; 7 RCTs report no statistically significant difference in LDL-C; 1 RCT reports no difference in sdLDL in participants with dyslipidemia treated w/ curcuminoid Pooled odds ratio showed LDL-C levels in curcumin group reduced by 0.17 versus placebo group (95% CI: 0.43-0.09; Z = 1.27; p = 0.2)	Did not report mean LDL-C changes in mg/dL or mmol/L; only reports LDL-C increased or decreased, not addressing primary endpoint of interest of this review One study did not clearly state study design.
Schoeneck et al., 2020	GRADE-Assessed meta-analysis of 6 RCTs, combining crossover and parallel trials	436 participants RCTs included participants w/ HG, MS, NAFLD, T2DM, DL, pre-HTN, risk factors for CVD	18-60 y	In four RCTs, 235 females; 217 males. In two RCTs gender NR	Race: NR Ethnicity: NR, Country: two RCTs done in Iran; two in India; one each in Thailand, Pakistan, Taiwan	Form and dose: 2.3 g/d turmeric powder in two RCTs, and 600 mg/d turmeric extract in four of six RCTs Route: oral administration Duration:8 w Control: placebo	Change in LDL-C mg/dL at baseline and postintervention, reported as WMD	NR	LDL-C reduced by −6.3 mg/dL (−0.35 mmol/L) (95%CI: −0.48 to −0.22, p < 0.0001)	Used GRADE-Assessment to rank the quality of evidence on turmeric RCTs as moderate due to indirectness Risk of bias ranked low

ACD: atherosclerotic cardiovascular disease; CAD: cardiovascular artery disease; CVD: cardiovascular disease; CHD: congestive heart disease; CKD: chronic kidney disease; DL: dyslipidemia; HDL-C: high-density lipoprotein cholesterol; HG: hyperglycemia; HLP; hyperlipidemia; HTG; hypertriglyceridemia; MI: myocardial infarction; HTN: hypertension; LDL-C: low-density lipoprotein cholesterol; mg/dL: milligrams per deciliter; MS: metabolic syndrome; NAFLD: non-alcoholic fatty liver disease; NR: not reported; PCOS: Polycystic ovary syndrome; RCT: randomized controlled trial; sdLDL: small dense low-density lipoprotein; SD: standard deviation; SE: size effect; TC: total cholesterol; TG: triglycerides; T2DM: type-2 diabetes mellitus; WMD: weighted mean difference; w: week; d: day; COPD: chronic obstructive pulmonary disease.

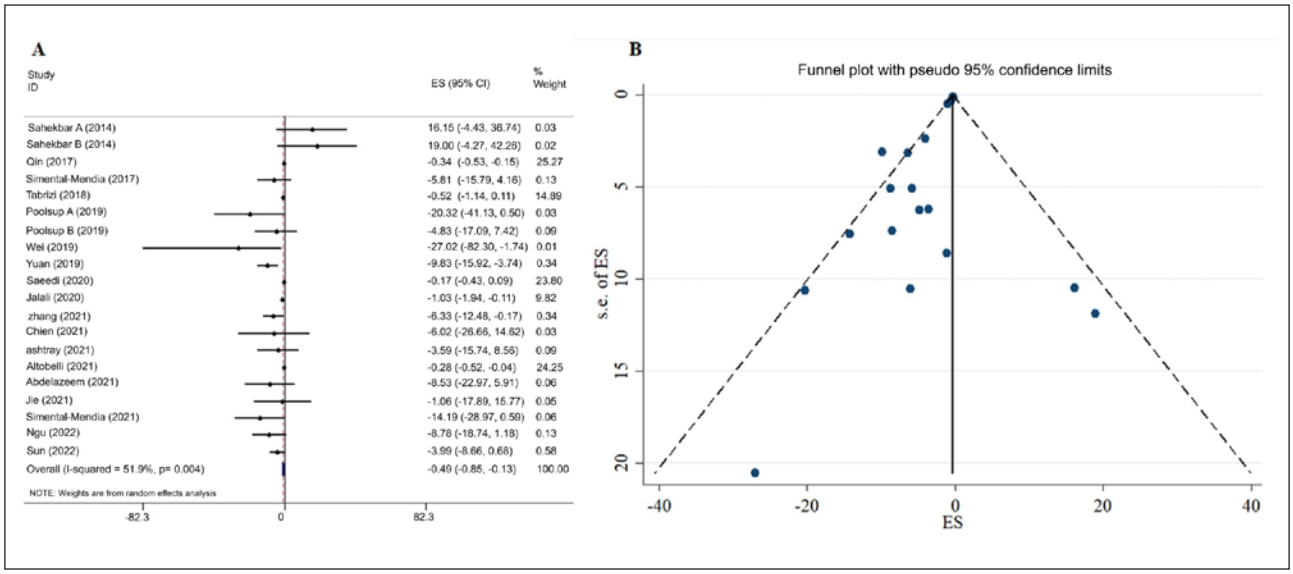

Figure 2. A: detailing the mean difference and 95% confidence intervals; **B:** displaying publication bias in the studies reporting and the pooled mean differences in effect size of curcumin supplementation on low-density lipoprotein cholesterol levels between intervention and control groups in 18 studies (Musazadeh, 2022). ES: effect size. *Reprinted from curcumin as a novel approach in improving lipid profile: an umbrella meta-analysis. Nutrition, metabolism, and cardiovascular diseases. Volume 32, Issue 11, November 2022, Pages 2493-2504, with permission from Elsevier.*

that the confidence intervals in the analysis and sub-analyses were wide, further reducing the quality of the level of this evidence. Consequently, while this study reports promising findings—nanocurcumins reduced LDL-C in patients with dyslipidemia—the low quality of evidence of these trials may render these findings unsettled and open to question, with the true effect possibly different from the estimate of the effect.

Searching PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar, Dehzad et al. carried out a GRADE-Assessed systematic review and meta-analysis on 64 RCTs that enrolled 4,051 participants to determine the effect of curcumin supplementation on reducing risk factors for CVD[29]. The RCTs included participants who were healthy, overweight and obese, on hemodialysis, had CAD, Chronic obstructive pulmonary disease (COPD), HIV, NAFLD, polycystic ovary syndrome (PCOS), MS, T2DM, hyperlipidemia (HLP) and other illnesses. The authors report that curcumin supplementation improved TG, TC, LDL-C, and high-density lipoprotein cholesterol (HDL-C) indices. Regarding the outcome of primary interest, curcumin reduced LDL-C, WMD = −4.89 mg/dL; 95% CI: −5.92, −3.87; $p < 0.001$. Yet, the authors stress that the literature regarding whether turmeric supplementation improves the lipid profile is contradictory, with some studies reporting improvements similar to their findings and while others did not.

Of all the meta-analyses reviewed here, the one by Dehzad et al. was the only one to incorporate RCTs that considered the effect of curcumin on apolipoproteins. The authors report that while curcumin improved TG and HDL-C levels, unexpectedly, no meaningful change in apolipoproteins (Apo-A and Apo-B) was observed, concluding that the exact MoA and degree to which curcumin affects circulating apolipoproteins remains poorly understood. Subgroup analysis for nanocurcumin showed no significant improvement of LDL-C. Dehzad et al. also report that subgroup analysis showed higher rates of LDL-C reduction observed in the trials from Iran compared to trials in other countries: Iran, WMD −11.40 (−12.74, −10.07) versus other countries, WMD 0.13 (−0.03, 0.23)[29].

A systematic review of seven meta-analyses was done by Adel Mehraban et al. to assess the effectiveness of curcumin in treating dyslipidemia[30]. As shown in table 2, the pooled results of these studies showed that curcumin reduced LDL-C by a mean of 39.83 mg/dL, reduced total cholesterol by 25.13 mg/dL, and reduced

triglycerides by 33.65 mg/dL, and increased HDL-C by 4.31 mg/dL. The turmeric daily doses that were effective in reducing LDL-C and increasing HDL-C ranged from 330 to 1795 mg/dL across all studies, while the doses that were effective in reducing triglycerides ranged from 1000 to 1795 mg/dL[30]. Adel Mehraban et al. report a wide range of results including no significant effect in one RCT and a notable reduction of LDL-C by 39.83 mg/dL in a systematic review by Jalali et al.[31]. Due to the high heterogeneity ($I^2 > 50\%$) between trials, these findings should be interpreted with caution.

Musazadeh et al.[22], carried out an umbrella meta-analysis using a random-effects model to assess the findings of multiple meta-analyses reporting on the role of curcumin in improving lipid profile indices. An umbrella review is a review of systematic reviews and meta-analyses, the highest quality of evidence available in medical research[32]. The authors reviewed 19 meta-analyses and systematic reviews and concluded that curcumin improves TC, TG, LDL-C, and HDL-C levels and confirmed its antihyperlipidemic properties. Pooling the data of 10 730 study participants in 18 studies and 20 related effect sizes (ES), Musazadeh et al. report that curcumin supplementation improved LDL-C overall with a moderate effect size of 0.49 (ES: 0.49 mg/dL, 95% CI: 0.85, 0.13, $p = 0.007$), as shown in the forest plot in figure 2. In subgroup analyses, Musazadeh et al.[22] found that curcumin supplementation at 850 mg/day for over 10 weeks reduced LDL-C in adults over 50 years with CAD, showing a large effect size of 1.48 (ES: 1.48 (3.25, 0.30). We assumed the authors are applying Cohen's d model, widely used in meta-analyses, in which an effect size from 0.2 to 0.5 is considered small, and 0.5-0.8 is considered medium, and > 0.8 is considered large when measuring the differences in standard deviations between the means of the intervention and control groups in these 18 studies. The ES were also calculated as WMD to accommodate for differences among studies.

Musazadeh et al. also found that the subgroup sensitivity analyses showed that the effect of curcumin supplementation in reducing LDL-C was not dependent on any single study. Yet, the authors also found high heterogeneity among the studies ($I^2 = 51.9\%$, $p = 0.004$) as shown in table 2. Between-study heterogeneity could be attributed to variations in sample size, mean age, study population ethnicity, duration of intervention, differences in dosages, and type of effect size. The authors of the study acknowledge that while some systematic reviews found no change in key lipid parameters after curcumin supplementation, other systematic reviews found clinically meaningful improvements in lipid profile indices[22]. The authors conclude that the differences in findings between these studies are due to the aforementioned high heterogeneity among the RCTs[22]. The authors call for future studies to further clarify dosage, duration, and MoA whereby turmeric supplementation remediates the lipid profile. They propose curcumin supplementation be considered as an adjuvant or alternative treatment for improving key lipid profile parameters[22].

Rafiee et al., 2021, carried out a systematic review of 22 RCTs from eight countries, comprising 1545 participants grouped by T2DM, PCOS, NAFLD, dyslipidemia, MS, obese, overweight, and glucose tolerance impairment[33]. All study participants were at risk for CVD. The authors summarize values for TC, TG, HDL, and LDL-C in all RCTs, as shown in table 2, and conclude that curcumin supplementation significantly reduced at least one of these lipid profile indicators in over 60% of the RCTs. However, the findings regarding LDL-C are equivocal on the effectiveness of curcumin in improving lipid profile in those at risk for CAD. The authors found that curcumin reduced LDL-C in 6 RCTs, but in 15 RCTs, the change was not statistically significant, and one RCT had no reported data for LDL-C, as shown in Table 2. These mixed findings may be related to between-study heterogeneity seen in variations in curcumin formulations or the wide range of dosages among study groups, ranging from 80 mg to 2000 mg/day[33].

Rafiee et al. report that some of the most promising findings in improving lipid profile risk factors came from RCTs using curcumin supplements with high bioavailability. Considering this, two of the studies[34,35] reported by Rafiee et al., 2021, that used novel curcumin formulations are reviewed here. Jazayeri-Tehrani et al. performed an RCT to determine if curcumin plays a role in treating NAFLD[34]. The novelty of this study is in its use of a polymeric nanoparticle formulation designed to overcome the low stability and bioavailability of curcumin. According to the authors, nanocurcumin with polylactic-co-glycolic acid nanoparticles

increased curcumin bioavailability by 22-fold. The authors report that nanocurcumin compared to placebo decreased LDL-C from 135.6 mg/dL (SD 17.6) (mg/dL) at baseline to 114.6 mg/dL (SD 20.5) at the end of the study, with a mean difference of −21.0 mg/dL and a narrow confidence interval (95% CI: −22.2 to −19.7) ($p < 0.001$). These results show an average weighted mean of 21 mg/dL reduction of LDL-C in the intervention group[34].

Saeedi et al. carried out a systematic review and meta-analysis of 14 RCTs to determine the effectiveness of curcumin in improving blood lipid profiles in individuals with dyslipidemia[35]. Five of the RCTs reported improvements in LDL-C from turmeric supplementation post-intervention, whereas seven studies reported no meaningful improvement in LDL-C (Table 2). One study using curcuminoid supplementation reported no change in small dense low-density lipoprotein (sdLDL) after 4 weeks. Overall, LDL-C levels in all curcumin groups were reduced by 0.17 versus placebo groups (95% CI: −0.43 −0.09; $Z = 1.27$; $p = 0.2$)[35].

Schoeneck et al. (2021) reported findings from a GRADE-assessed meta-analysis of 108 systematic reviews, identifying 20 functional foods showing moderate to large effects in reducing LDL-C, and surprisingly, unfiltered coffee caused a moderate to large increase in LDL-C[36]. Reporting on findings of a systematic review by Qin et al.[37] on turmeric, Schoeneck et al. conclude that compared to the other foods in their study, turmeric was relatively strong in reducing LDL-C, but they downgraded the quality of the evidence-based on indirectness because Qin et al. provided turmeric in different forms (powder, extract, dispersion), which made it challenging to determine the dose and form of turmeric spice to which the results corresponded. Hence, the authors call for further studies to clarify the dosage of turmeric in reducing LDL-C as well as studies to clarify the MoA whereby turmeric reduces LDL-C. Table 2 shows the findings of 6 RCTs from a systematic review on turmeric; the primary outcome of interest was LDL-C in mmol/L (mmol/L were converted to mg/dL). In four of six of the RCTs, turmeric reduced LDL-C by −0.35 mmol/L, (95% CI: −0.48 to −0.22) or −6.3 mg/dL postintervention[36].

Because the seven systematic reviews and meta-analyses in this review refer to dozens of RCTs, it is not feasible to review and assess the findings of each one here. Yet, to represent some of the diversity of these studies, several RCTs are summarized below including those that combined or compared turmeric with a hypocaloric diet, zinc supplementation, aerobic training, turmeric-fortified bread, phytosterols, coenzyme Q10, curcuminoid supplementation, and a statin medication, in patients who were healthy, pre-diabetic, or had PCOS.

Karandish et al. 2022 report that LDL-C was reduced in pre-diabetic adults on a hypocaloric diet treated with curcumin (−16.89 mg/dL), curcumin and zinc supplementation (−17.93 mg/dL)[38]. Likewise, Dolati et al. (2022) found that curcumin and aerobic training combined improved lipid profiles greater than aerobic training or curcumin alone, with LDL-C decreased by a percent of 19.17% in the curcumin and aerobic training group[39]; Ferguson et al. (2019) report that bread fortified with curcumin combined with phytosterols reduced LDL-C by 8.8% (−0.44 ± 0.06 mmol/L) compared to placebo; thus potentially identifying a simple, inexpensive preventative strategy for sustaining heart health[40]. Yet, curcumin alone in fortified bread resulted in no meaningful improvement in LDL-C, contradicting earlier findings by the same group[41].

Conversely, other novel RCTs report less promising results. Sangouni et al. (2020) found that combining coenzyme Q10 and curcumin did not improve LDL-C levels in individuals with MS[42]. Likewise, Saeedi et al. (2022) report that curcuminoid supplementation did not improve sdLDL levels[35]. Furthermore, one curcumin supplement formulation did not perform as well as a comparative statin in reducing LDL-C (Laffin et al., 2023)[43], and, Ghanbarzadeh-Ghashti et al. reported no difference in curcumin supplementation in the lipid profile of patients with PCOS[44].

Finally, Funamoto et al. carried out an RCT investigating the effects of curcumin supplementation on glucose tolerance and LDL-C in patients with impaired glucose tolerance or non-insulin-dependent diabetes[45]. Addressing curcumin's poor bioavailability, a novel drug delivery system was developed. Natural curcumin comprises large granules; consequently, this supplement was designed to take advantage of nanosized particles with a coating making it highly absorbable in the intestinal tract. In a previous study

of patients with COPD, the authors reported that this novel formulation reduced α1-Antitrypsin-low-density lipoprotein, an oxidized low-density lipoprotein known to promote atherosclerosis[45]. However, in this study of patients with impaired glucose tolerance or non-insulin-dependent diabetes mellitus, LDL-C did not differ between patients administered treatment or placebo for 6 months. While the treatment reduced oxidized LDL, it did not show any beneficial effects in reducing LDL-C; the authors speculate that the small sample size and short duration time may have affected this outcome[45].

DISCUSSION

The goal of this review was to consolidate recent high-quality evidence on the effectiveness of turmeric in reducing LDL-C in adults. The primary endpoint of interest was mean LDL-C reported as either mmol/L or mg/dL, measured before and after turmeric supplementation. A PubMed search provided seven systematic reviews and meta-analyses whose findings are summarized in the results section and in table 2. The implications of these results are discussed below.

Turmeric has shown antioxidant, anti-inflammatory, and anticholesteremic activity in preclinical studies[17-19]. Recent research has attempted to clarify the most effective formulation, route, duration, and dosage of turmeric needed to improve the lipid profile in humans. Adel Mehraban et al. and Musazadeh et al.[22,30] report some of the highest reductions in LDL-C levels after turmeric supplementation. In the most comprehensive meta-analysis in this literature review, including over 10,000 participants in 19 RCTs, Musazadeh et al.[22] report that a turmeric supplement dosage of 850 mg/d for 10 weeks was most effective in reducing LDL-C, particularly in adults over 50 years old and those at risk for CVD. Recent studies have reported on novel formulations aiming to improve on the poor bioavailability of turmeric. For example, Jazayeri-Tehrani et al. reported that nanocurcumin is more effective than native curcumin in reducing LDL-C[34]. In one RCT reported by Jazayeri-Tehrani et al., a nanocurcumin increased curcumin bioavailability by 22-fold and decreased LDL-C from 135.6 mg/dL (SD 17.6) at baseline to 114.6 mg/dL (SD 20.5) at end of study, with an average WMD of 21 mg/dL reduction of LDL-C[34].

The findings from a number of meta-analyses reviewed herein could represent a minimal clinically important difference (MCID) in managing lipid profiles. For example, Adel Mehraban et al. report a mean reduction of LDL-C by 39.83 mg/dL in a systematic review[31]. The guidelines of the American College of Cardiology identify LDL-C levels of ≤ 100 mg/dL as optimal for maintaining cardiovascular health in individuals without other risk factors for ASCVD. In individuals with LDL-C above 100 mg/dL at low-to-moderate risk for CAD, a reduction for 39.83 mg/dL in LDL-C would be a meaningful improvement in reducing their LDL-C to a healthy range of < 100 mg/dL[46,47].

While statins are a powerful standard-of-care treatment for lowering elevated levels of LDL-C (≥ 190 mg/dL), for patients with low-to-moderate levels of LDL-C at risk for CVD, lifestyle changes could improve lipid profile indices, including exercise, diet, nutraceuticals, and weight loss. Consuming functional foods such as avocados, almonds, and turmeric, for example, have shown low-to-moderate efficacy in reducing LDL-C[15]. This review summarized promising research on how consuming turmeric spice can a be safe, simple, and inexpensive primary and secondary preventive approach to improve cardiovascular health[36,40]. Overall, findings from a number of RCTs suggest that turmeric may have a positive effect as an adjuvant dietary supplement along with change of lifestyle practices among patients at low-to-moderate risk of CAD.

Likewise, a review by Panahi et al. compares the efficacy of statins and curcumin in treating hypercholesterolemia and HLP[48]. As reported earlier, the MoA involved in curcumin reducing LDL-C is complex, operating simultaneously at a number of sites in the intestine and liver. Yet, interestingly Panahi et al.[48] provide a detailed review of the metabolic and cellular MoA of curcumin and statins, and point out that they both target the same specific nuclear receptors and enzymes while reducing LDL-C. The authors note that while statins are more efficient in lowering LDL-C, for some patients, they have adverse effects. The authors

suggest that for such patients, a combination of a statin and curcumin could synergistically lower LDL-C to a desirable level, while requiring a lower dosage of the statin, which could reduce the risk of adverse effects, such as extreme muscle pain[48].

Yet, despite a number of systematic reviews, meta-analyses, and RCTs that report positive outcomes of turmeric in improving the lipid profile parameters in individuals at risk for CAD, questions remain about the precise lipid-lowering potential of turmeric supplementation. Three of the seven meta-analyses reported here[27-29,36,49] used the rigorous Cochrane GRADE approach[27] to evaluate the quality of evidence of studies based on publication bias, imprecision, indirectness, risk of bias, and inconsistency. Based on these domains, the authors of these three meta-analyses downgraded the quality of evidence of a number of RCTs investigating turmeric's effectiveness in improving cardiovascular health. Furthermore, it should be stressed that all of the systematic reviews and meta-analyses in this review reported some level of uncertainty and conflicting findings on the effectiveness of turmeric supplementation in reducing LDL-C. This uncertainty was commonly attributed to the high between-study heterogeneity among many RCTs, with many having a wide range of study endpoints and participant characteristics, and a lack of standardized measures, dosage, and duration. The lack of standardized measures alone can illustrate the challenge of understanding some of the findings. For example, physicians typically provide patients a summary of lipid profile measures such as LDL-C in mg/dL or in mmol/L. While one of the primary endpoints of the PubMed search for this literature review was to find systematic reviews, meta-analyses, and RCTs reporting on mean LDL-C in mg/dL or mmol/L before and after turmeric intervention, some of the systematic reviews and RCTs did not provide these standard measures, making their findings less usefulin a clinical context.Despite the fact that dozens of RCTs have investigated the effectiveness of turmeric as a lipid-lowering agent, such reporting inconsistencies should raise questions about the overall reliability, validity, and value of some of the findings of these studies.

Other global shortcomings of studies on RCTs on the efficacy of turmeric in improving cardiovascular health relate to publication bias and overlapping and redundancy in reported studies. Publication bias results from the high rate of failure to report on non-statistically significant findings, which skews the overall data and findings. While publication bias is a universal issue affecting all scientific publications, Musazadeh et al.[22] reported high rates of publication bias in the RCTs in their review of 22 meta-analyses on turmeric, shown in figure 2. Because a number of studies have reported very positive findings of curcumin supplementation, this review also provides a much-needed counterbalance to publication bias by reporting on shortcomings and unanswered questions in some of the RCTs on turmeric. Another concern about the findings reported here is related to the overlapping and redundancy of RCTs reported across all seven meta-analyses; many of the systematic reviews herein reported on some of the same studies. Hence, generalizing about the collective and cumulative power of the findings of these systematic reviews and meta-analyses would be problematic and muddled due to this overlapping and redundancy.

An additional limitation that should be improved in future RCTs would be selecting only study participants with hypercholesteremia and not a mix of other disorders. Furthermore, future studies should account for differences in study participants' weight as this effects dosage and absorption. Likewise, because many of the RCTs included did not clearly report on the type of curcumin (powder, oil, and extract), greater clarity and consistency are needed in this regard. Finally, future studies on turmeric would benefit from including greater diversity in the race and ethnicity of study participants. While the RCTs reported herein were done in nine different countries, over half of these studies on turmeric have been carried out in one country, Iran. Finally, the RCTs did not extensively focus on safety issues related to turmeric, which should be included in future studies.

CONCLUSION

Turmeric spice has potential as a safe, effective, inexpensive, lipid-lowering functional food, but

considering the Cochrane GRADE approach, a stronger quality of evidence is need to confirm this. Turmeric may also play a role as a lipid-lowering agent in patients with low-to-moderate hypercholesterolemia or as an adjuvant for complete statin-intolerant patients. While promising findings have been reported on turmeric's role in ameliorating cardiovascular health, contradictory findings have also been reported. Consequently, further studies are needed to standardize reporting, confirm effectiveness, evaluate safety, and decrease between-study heterogeneity. Future studies must clarify and verify the degree to which turmeric supplementation may improve lipid indices, the MoA whereby turmeric reduces LDL-C, as well as the most effective form, dose, route, and duration of turmeric supplementation in reducing LDL-C.

ACKNOWLEDGMENTS

I would like to acknowledge Donna Simcoe, MS, MS, MBA, CMPP, adjunct faculty at the University of California San Diego Extended Studies for providing an editorial review of the draft manuscript. I also wish to thank Anne Brouha, MD, for critical feedback on the final draft of this manuscript, and Ana Laura Hernandez, MS, research professional in cardiology, for confirming the consistency between the Spanish and English abstract.

FUNDING

This research has not received any specific grants from agencies in the public, commercial, or for-profit sectors.

CONFLICTS OF INTEREST

The author declares that he has no conflicts of interest.

ETHICAL DISCLOSURES

Protection of human and animal subjects. The author declares that no experiments were performed on humans or animals for this study.

Confidentiality of data. The author declares that no patient data appear in this article.

Right to privacy and informed consent. The author declares that no patient data appear in this article.

Use of artificial intelligence for generating text. The author declares that he has not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

REFERENCES

1. World Health Organization. Cardiovascular Diseases (CVDs); 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)
2. Cardiology ACo. Advancing Cardiovascular Health in Mexico Roundtable: Outcome Report; 2021. Available from: https://www.acc.org//-/media/non-clinical/files-pdfs-excel-ms-word-etc/2022/11/i22228-advancing-cardiovascular
3. The American Heart Association. New Effort to Standardize Cardiovascular Care in Mexico, Address Gaps in Care; 2022. Available from: https://newsroom.heart.org/news/new-effort-to-standardize-cardiovascular-care-in-mexico-address-gaps-in-care
4. Vaduganathan M, Mensah GA, Turco JV, Fuster V, Roth GA. The global burden of cardiovascular diseases and risk: a compass for future health. J Am Coll Cardiol. 2022;80:2361-71.
5. Mensah GA, Roth GA, Fuster V. The global burden of cardiovascular diseases and risk factors: 2020 and beyond. J Am Coll Cardiol. 2019;74:2529-32.
6. Staff AHAe. What is Cardiovascular Disease? American Heart Association; 2023. Available from: https://www.heart.org/en/health-topics/consumer-healthcare/what-is-cardiovascular-disease
7. Prevention CfDCa. Heart Disease Facts: National Center for Chronic Disease Prevention and Health Promotion, Division for Heart Disease and Stroke Prevention; 2022. Available from: https://www.cdc.gov/heartdisease/facts.htm
8. Steadman's Online. Coronary Artery Disease: Steadman's Online Medical Dictionary; 2023. Available from: https://stedmansonline.com/lww/term/mlrC1500025195/575202/coronary-artery-disease
9. Staff American Heart Association e. Coronary Artery Disease: American Heart Association; 2023. Available from: https://www.heart.org/en/health-topics/consumer-healthcare/what-is-cardiovascular-disease/coronary-artery-disease
10. Jung E, Kong SY, Ro YS, Ryu HH, Shin SD. Serum cholesterol levels and risk of cardiovascular death: a systematic review and a dose-response meta-analysis of prospective cohort studies. Int J Environ Res Public Health. 2022;19:8272.
11. Tsao CW, Aday AW, Almarzooq ZI, Anderson CA, Arora P, Avery CL, et al. Heart disease and stroke statistics-2023 update: a report from the American heart association. Circulation. 2023;147:e93-621.
12. Bansal AB, Cassagnol M. HMG-CoA reductase inhibitors. In: StatPearls. Treasure Island, FL: StatPearls Publishing LLC; 2023.
13. Cheeley MK, Saseen JJ, Agarwala A, Ravilla S, Ciffone N, Jacobson TA, et al. NLA scientific statement on statin intolerance: a new definition and key considerations for ASCVD risk reduction in the statin intolerant patient. J Clin Lipidol. 2022;16:361-75.

14. Bosco G, Di Giacomo Barbagallo F, Spampinato S, Lanzafame L, Di Pino A, Piro S, et al. Management of statin intolerant patients in the era of novel lipid lowering therapies: a critical approach in clinical practice. J Clin Med. 2023;12:2444.
15. Cicero AF, Fogacci F, Stoian AP, Vrablik M, Al Rasadi K, Banach M, et al. Nutraceuticals in the management of dyslipidemia: which, when, and for whom? Could nutraceuticals help low-risk individuals with non-optimal lipid levels? Curr Atheroscler Rep. 2021;23:57.
16. Perez-Martinez P, Ros E, Botet JP, Civeira F, Pascual V, Garces C, et al. Functional foods and nutraceuticals in the treatment of hypercholesterolemia: statement of the Spanish society of arteriosclerosis 2023. Clin Investig Arterioscler. 2023;25:248-61.
17. Avila-Galvez MA, Gonzalez-Sarrias A, Martinez-Diaz F, Abellan B, Martinez-Torrano AJ, Fernandez-Lopez AJ, et al. Disposition of dietary polyphenols in breast cancer patients' tumors, and their associated anticancer activity: the particular case of curcumin. Mol Nutr Food Res. 2021;65:e2100163.
18. Nelson KM, Dahlin JL, Bisson J, Graham J, Pauli GF, Walters MA. The essential medicinal chemistry of curcumin. J Med Chem. 2017;60:1620-37.
19. Dehzad MJ, Ghalandari H, Nouri M, Askarpour M. Antioxidant and anti-inflammatory effects of curcumin/turmeric supplementation in adults: a GRADE-assessed systematic review and dose-response meta-analysis of randomized controlled trials. Cytokine. 2023;164:156144.
20. Information NCfB. PubChem Compound Summary for CID 969516, Curcumin. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/curcumin
21. Sohn SI, Priya A, Balasubramaniam B, Muthuramalingam P, Sivasankar C, Selvaraj A, et al. Biomedical applications and bioavailability of curcumin-an updated overview. Pharmaceutics. 2021;13:2102.
22. Musazadeh V, Roshanravan N, Mohammadizadeh M, Kavyani Z, Dehghan P, Mosharkesh E. Curcumin as a novel approach in improving lipid profile: an umbrella meta-analysis. Nutr Metab Cardiovasc Dis. 2022;32:2493-504.
23. Pan-On S, Dilokthornsakul P, Tiyaboonchai W. Trends in advanced oral drug delivery system for curcumin: a systematic review. J Control Release. 2022;348:335-45.
24. Hirose A, Kuwabara Y, Kanai Y, Kato C, Makino Y, Yoshi F, et al. Comparative pharmacokinetics of new curcumin preparations and evidence for increased bioavailability in healthy adult participants. Int J Clin Pharmacol Ther. 2022;60:530-8.
25. Kothaplly S, Alukapally S, Nagula N, Maddela R. Superior bioavailability of a novel curcumin formulation in healthy humans under fasting conditions. Adv Ther. 2022;39:2128-38.
26. Administration UFaD. FDA 101: Dietary Supplements; 2022. Available from: https://www.fda.gov/consumers/consumer-updates/fda-101-dietary-supplements
27. Cochrane. GRADE Approach. Cochrane Training; 2013. Available from: https://training.cochrane.org/grade-approach
28. Ashtary-Larky D, Rezaei Kelishadi M, Bagheri R, Moosavian SP, Wong A, Davoodi SH, et al. The effects of nano-curcumin supplementation on risk factors for cardiovascular disease: a GRADE-assessed systematic review and meta-analysis of clinical trials. Antioxidants (Basel). 2021;10:1015.
29. Dehzad MJ, Ghalandari H, Amini MR, Askarpour M. Effects of curcumin/turmeric supplementation on lipid profile: a GRADE-assessed systematic review and dose-response meta-analysis of randomized controlled trials. Complement Ther Med. 2023;75:102955.
30. Adel Mehraban MS, Tabatabaei-Malazy O, Rahimi R, Daniali M, Khashayar P, Larijani B. Targeting dyslipidemia by herbal medicines: a systematic review of meta-analyses. J Ethnopharmacol. 2021;280:114407.
31. Jalali M, Mahmoodi M, Mosallanezhad Z, Jalali R, Imanieh MH, Moosavian SP. The effects of curcumin supplementation on liver function, metabolic profile and body composition in patients with non-alcoholic fatty liver disease: a systematic review and meta-analysis of randomized controlled trials. Complement Ther Med. 2020;48:102283.
32. Choi GJ, Kang H. Introduction to umbrella reviews as a useful evidence-based practice. J Lipid Atheroscler. 2023;12:3-11.
33. Rafiee S, Bagherniya M, Askari G, Sathyapalan T, Jamialahmadi T, Sahebkar A. The effect of curcumin in improving lipid profile in patients with cardiovascular risk factors: a systematic review of clinical trials. Adv Exp Med Biol. 2021;1291:165-77.
34. Jazayeri-Tehrani SA, Rezayat SM, Mansouri S, Qorbani M, Alavian SM, Daneshi-Maskooni M, et al. Nano-curcumin improves glucose indices, lipids, inflammation, and Nesfatin in overweight and obese patients with non-alcoholic fatty liver disease (NAFLD): a double-blind randomized placebo-controlled clinical trial. Nutr Metab (Lond). 2019;16:8.
35. Saeedi F, Farkhondeh T, Roshanravan B, Amirabadizadeh A, Ashrafizadeh M, Samarghandian S. Curcumin and blood lipid levels: an updated systematic review and meta-analysis of randomised clinical trials. Arch Physiol Biochem. 2022;128:1493-502.
36. Schoeneck M, Iggman D. The effects of foods on LDL cholesterol levels: a systematic review of the accumulated evidence from systematic reviews and meta-analyses of randomized controlled trials. Nutr Metab Cardiovasc Dis. 2021;31:1325-38.
37. Qin S, Huang L, Gong J, Shen S, Huang J, Ren H, et al. Efficacy and safety of turmeric and curcumin in lowering blood lipid levels in patients with cardiovascular risk factors: a meta-analysis of randomized controlled trials. Nutr J. 2017;16:68.
38. Karandish M, Mozaffari-Khosravi H, Mohammadi SM, Cheraghian B, Azhdari M. Curcumin and zinc co-supplementation along with a loss-weight diet can improve lipid profiles in subjects with prediabetes: a multi-arm, parallel-group, randomized, double-blind placebo-controlled phase 2 clinical trial. Diabetol Metab Syndr. 2022;14:22.
39. Dolati S, Namiranian K, Amerian R, Mansouri S, Arshadi S, Azarbayjani MA. The effect of curcumin supplementation and aerobic training on anthropometric indices, serum lipid profiles, c-reactive protein and insulin resistance in overweight women: a randomized, double-blind, placebo-controlled trial. J Obes Metab Syndr. 2020;29:47-57.
40. Ferguson JJ, Wolska A, Remaley AT, Stojanovski E, MacDonald-Wicks L, Garg ML. Bread enriched with phytosterols with or without curcumin modulates lipoprotein profiles in hypercholesterolaemic individuals. A randomised controlled trial. Food Funct. 2019;10:2515-27.
41. Ferguson JJ, Stojanovski E, MacDonald-Wicks L, Garg ML. Curcumin potentiates cholesterol-lowering effects of phytosterols in hypercholesterolaemic individuals. A randomised controlled trial. Metabolism. 2018;82:22-35.
42. Sangouni AA, Taghdir M, Mirahmadi J, Sepandi M, Parastouei K. Effects of curcumin and/or coenzyme Q10 supplementation on metabolic control in subjects with metabolic syndrome: a randomized clinical trial. Nutr J. 2022;21:62.
43. Laffin LJ, Bruemmer D, Garcia M, Brennan DM, McErlean E, Jacoby DS, et al. Comparative effects of low-dose rosuvastatin, placebo, and dietary supplements on lipids and inflammatory biomarkers. J Am Coll Cardiol. 2023;81:1-12.
44. Ghanbarzadeh-Ghashti N, Ghanbari-Homaie S, Shaseb E, Abbasalizadeh S, Mirghafourvand M. The effect of curcumin on metabolic parameters and androgen level in women with polycystic ovary syndrome: a randomized controlled trial. BMC Endocr Disord. 2023;23:40.
45. Funamoto M, Shimizu K, Sunagawa Y, Katanasaka Y, Miyazaki Y, Kakeya H, et al. Effects of highly absorbable curcumin in patients with impaired glucose tolerance and non-insulin-dependent diabetes mellitus. J Diabetes Res. 2019;2019:8208237.
46. Wilson PW, Polonsky TS, Miedema MD, Khera A, Kosinski AS, Kuvin JT. Systematic review for the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of cardiology/American heart association task force on clinical practice guidelines. J Am Coll Cardiol. 2019;73:3210-27.
47. Gupta K, Kakar TS, Jain V, Gupta M, Al Rifai M, Slipczuk L, et al. Comparing eligibility for statin therapy for primary prevention under 2022 USPSTF recommendations and the 2018 AHA/ACC/ multi-society guideline recommendations: from national health and nutrition examination survey. Prog Cardiovasc Dis. 2022;75:78-82.
48. Panahi Y, Ahmadi Y, Teymouri M, Johnston TP, Sahebkar A. Curcumin as a potential candidate for treating hyperlipidemia: a review of cellular and metabolic mechanisms. J Cell Physiol. 2018;233:141-52.
49. Dehzad MJ, Ghalandari H, Amini MR, Askarpour M. Effects of curcumin/turmeric supplementation on liver function in adults: a GRADE-assessed systematic review and dose-response meta-analysis of randomized controlled trials. Complement Ther Med. 2023;74:102952.