Avicenna Journal of Phytomedicine (AJP)

Review Article

Pomegranate juice consumption and lipid profile: An updated systematic review and meta-analysis

Fatemeh Ghaemi[1], Maryam Emadzadeh[2], Wael Almahmeed[3], Tannaz Jamialahmadi[4], Sercan Karav[5], Amirhossein Sahebkar[1,6,7,*]

[1]*Applied Biomedical Research Center, Basic Sciences Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran*
[2]*Clinical Research Development Unit, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran*
[3]*Heart and Vascular Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates*
[4]*Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran*
[5]*Department of Molecular Biology and Genetics, Canakkale Onsekiz Mart University, Canakkale 17100, Turkey*
[6]*Centre for Research Impact & Outcome, Chitkara College of Pharmacy, Chitkara University, Rajpura, Punjab 140401, India*
[7]*Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran*

Article history:
Received: Sep 22, 2024
Received in revised form: Jun 07, 2025
Accepted: Jun 15, 2025
Epub ahead of print

**** Corresponding Author:***
Tel: +985131801239
Fax: +985138823251
amir_saheb2000@yahoo.com

Keywords:
Cholesterol
Triglyceride
Lipid
Punica granatum
Pomegranate

Abstract

Objective: Pomegranate juice (PJ) is rich in polyphenols with potential lipid-lowering effects. This study aimed to evaluate the impact of PJ consumption on blood lipid parameters through a systematic review and meta-analysis of randomized controlled trials (RCTs).

Materials and Methods: A comprehensive literature search was conducted across multiple databases to identify RCTs assessing the effects of PJ on lipid profiles in adults. A total of 17 RCTs involving 663 participants were included. Outcomes analyzed were changes in total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Subgroup and meta-regression analyses were performed based on dose, duration, and participant health status.

Results: PJ consumption was associated with significant reductions in TG (MD: −8.2 mg/dL) and LDL-C (MD: −4.8 mg/dL), and a significant increase in HDL-C (MD: +2.8 mg/dL). No overall effect was observed for TC. High heterogeneity was detected, partially explained by differences in PJ dose and population characteristics.

Conclusion: PJ may improve lipid profiles, particularly by reducing TG and LDL-C and increasing HDL-C levels. These effects appear more pronounced in populations with metabolic disorders. Future trials with standardized PJ formulations and longer durations are warranted.

Please cite this paper as:
Ghaemi F, Emadzadeh M, Almahmeed W, Jamialahmadi T, Karav S, Sahebkar A. Pomegranate juice consumption and lipid profile: An updated systematic review and meta-analysis. Avicenna J Phytomed, 2025. Epub ahead of print.

Introduction

Cardiovascular disease (CVD) is a global health concern with an increasing prevalence. Each year, nearly 18 million deaths are attributed to this non-communicable disease worldwide. In 2019, approximately 523 million people worldwide were affected by some form of CVD (Gaziano et al., 2006, Organization 2019). One of the major risk factors for CVD is an elevated concentration of blood lipids such as cholesterol and triglycerides (TGs) which are present in over 50% of adults (Boren et al., 2020, Hedayatnia et al., 2020). The accumulation of fatty deposits in the arteries, known as atherosclerosis, is associated with an increased risk of blood clots and is commonly found in individuals with CVD (Rafieian-Kopaei et al., 2014). Atherosclerosis can also cause damage to arteries in vital organs including the brain, heart, kidneys, and eyes (Mallika et al., 2007). CVD encompasses various conditions such as heart disease, stroke, peripheral arterial disease, and aortic disease (Lopez et al., 2022). Several risk factors contribute to the development of atherosclerotic cardiovascular disease, including hypertension, smoking, dyslipidemia, diabetes, obesity, and physical inactivity. Dyslipidemia is a crucial but modifiable risk factor for atherosclerotic cardiovascular disease for which, numerous drugs have been developed (Michaeli et al., 2023, Derosa et al., 2018, Sahebkar et al., 2014, Sahebkar et al., 2013, Sahebkar et al., 2013). Statins are the most widely utilized class of lipid-lowering agents which have documented efficacy in lowering low-density lipoprotein-cholesterol (LDL-C) plus a myriad of lipid-independent benefits (Bedi et al., 2016, Bahrami et al., 2018, Chruściel et al., 2016, Parizadeh et al., 2011, Sahebkar et al., 2023, Sahebkar et al., 2016). However, even with the availability of current pharmacotherapeutic agents, still a considerable number of patients do not reach therapeutic lipid goals (Ray et al., 2021, März et al., 2018). Besides, there are patients who are resistant to statin therapy or cannot tolerate these drugs (Bytyçi et al., 2022). This begs additional approaches to complement pharmacotherapy.

Over the recent decades, there has been a surge of interest to exploit the lipid-lowering effects of natural products and nutraceuticals (Asgary et al., 2013, Fogacci et al., 2019, Momtazi et al., 2017, Sahebkar et al., 2014, Sahebkar et al., 2016, Serban et al., 2016). Among various dietary interventions, Pomegranate juice (PJ) has received growing scientific attention due to its high polyphenol content, antioxidant capacity, and potential lipid-lowering effects, making it a promising candidate for cardiovascular disease prevention. Pomegranate, a deciduous shrub that produces fruit, grows between five and ten meters in height (Lansky, Newman 2007, Jurenka 2008). It is native to Iran and northern India but is cultivated worldwide (Naqvi et al., 1991). Pomegranate is known for its content of flavonoids, anthocyanins, punicic acid, ellagitannins, alkaloids, fructose, and sucrose, which contribute to its excellent antioxidant properties (Zarfeshany et al., 2014). Punicalagins, as hydrolyzable tannin, make up approximately 50% of the antioxidant potential of pomegranate juice (Naqvi et al., 1991). These compounds help prevent thickening of artery walls and reduce cholesterol and plaque buildup. Pomegranate polyphenols have been studied as potential agents for preventing and managing CVD (Vučić et al., 2019). Additionally, pomegranate polyphenols directly inhibit the oxidation of LDL cholesterol, further contributing to their beneficial effects (Aviram, Rosenblat 2012, Zarfeshany et al., 2014). Due to its high content of polyphenols and tannins, pomegranate has recently been recommended for the prevention of coronary artery disease, as it lowers blood pressure, improves blood circulation to the heart, and reduces the risk of heart attacks (Bouroshaki et al., 2010).

In this systematic review and meta-analysis of randomized controlled trials (RCTs), our objective was to investigate the effect of pomegranate juice (PJ) consumption on lipid profile.

Although previous meta-analyses, such as Sahebkar et al (2016), have evaluated the effects of pomegranate supplementation on lipid parameters, they included a limited number of studies, often combining heterogeneous forms of pomegranate (e.g. extract, capsule, and juice), and lacked detailed subgroup or meta-regression analysis. Since then, several RCTs with improved methodological quality and longer intervention durations have been published. Therefore, an updated and focused meta-analysis specifically on PJ is warranted to provide more conclusive evidence.

Materials and Methods

Search strategy

This systematic review followed the PRISMA guidelines. We conducted a thorough search of databases including PubMed, ISI Web of Science, Scopus, and the Cochrane Library, covering all studies published up to December 11, 2022. As follows, MeSH and non-MeSH terms have been merged: (Intervention OR "Intervention Study" OR "Intervention Studies" OR "controlled trial" OR randomized OR random OR randomly OR placebo OR "clinical trial" OR Trial OR "randomized controlled trial" OR "randomized clinical trial" OR RCT OR blinded OR "double blind" OR "double blinded" OR trial OR "clinical trial" OR trials OR "Pragmatic Clinical Trial" OR "Cross-Over Studies" OR "Cross-Over" OR "Cross-Over Study" OR parallel OR "parallel study" OR "parallel trial") and ("hyperlipidemia OR hyperlipidemic OR hyperlipidaemic OR hyperlipidaemia OR hypolipidemic OR hypolipidaemic OR dyslipidemia OR dyslipidemic OR hypercholesterolemia OR hypercholesterolemic OR "hypocholesterolemic" OR "hypertriglyceridemia" OR "hypotriglyceridemic" OR Triglyceride OR Triacylglycerol OR cholesterol OR Lipoprotein OR "very low density lipoprotein" OR VLDL OR "low density lipoprotein" OR LDL OR "LDL-C" OR "high density lipoprotein" OR HDL OR "HDL-C" OR "lipid profile" OR "dyslipidaemia" OR "dyslipidaemic" OR "hypercholesterolaemic" OR "hypocholesterolaemic" OR "triglycerides" OR "hypertriglyceridemia" OR "hypertriglyceridaemia" OR "hypotriglyceridemic" OR "hypotriglyceridaemic") and (pomegranate OR Punica OR “Punica granatum” OR "Punicaceae"[- Mesh]) OR "Punicaceae"[tiab])"). The search was limited to human studies published in English. Additional studies were identified by manual review of reference lists. We excluded grey literature to reduce bias and ensure data quality.

Inclusion and exclusion criteria

Eligible studies met the following criteria: (1) randomized controlled trials (RCTs) or crossover trials involving adults; (2) assessment of pomegranate juice effects on lipid parameters; and (3) reported at least one lipid-related outcome, such as total cholesterol, triglycerides, LDL-C, HDL-C, Apo A, or Apo B. Studies were excluded if they: (1) were not RCTs; (2) used pomegranate juice with other active interventions; (3) had intervention durations under one week; (4) lacked adequate outcome data; or (5) used other forms of pomegranate (e.g., extract or seed oil). To isolate the specific impact of juice, we excluded studies using alternate formulations. Variations in juice type were accounted for in subgroup analyses.

To ensure homogeneity and isolate the specific effects of PJ, we excluded studies that used other forms such as seed oil or extract. These forms contain different concentrations and types of bioactive compounds, which could confound the

results. Variations in PJ composition across studies (e.g. natural vs. concentrated juice) were addressed through subgroup and sensitivity analyses, which allowed us to explore the potential influence of dosage and intervention duration.

Data extraction

Data collected from each study included: author, publication year, country, participant demographics (age, gender, BMI), health status, intervention details (dose and duration), study design, and changes in lipid markers (cholesterol, triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL)) pre- and post-intervention.

Quality assessment

We evaluated study quality using the Cochrane Risk of Bias tool, covering sequence generation, allocation concealment, blinding, reporting bias, and completeness of outcome data. Each domain was rated as low, unclear, or high risk. (Higgins, Green 2011, Higgins 2011). Studies rated as high risk in any domain were considered high risk overall. Sensitivity analyses were conducted to test the impact of such studies on the overall findings. This approach ensured that the main findings remained robust even when potentially biased studies were omitted.

Quantitative data synthesis

Meta-analysis was performed using Comprehensive Meta-Analysis (CMA) version 2. (Biostat, NJ). P-values <0.05 were considered statistically significant. Mean difference (MD) and 95% confidence intervals (CI) for the effect of PJ on Fasting Blood Glucose (FBG), fasting insulin and HOMA-IR were used to estimate the overall effect size in the intervention and control groups.

The following formula was used to calculate the SDs of the mean difference: SD = square root [(SD pretreatment)^2 + (SD post-treatment)^2- (2R × SD pre-treatment × SD post-treatment)], taking R = 0.8 as the correlation coefficient (Higgins 2011). When standard error (SEM) was reported, standard deviation (SD) was derived using SD = SEM × √n. For parallel and crossover studies, net changes were calculated based on differences between post- and pre-intervention values in both groups.

Heterogeneity was evaluated using Cochrane's Q and I² statistics. Subgroup analyses examined the effects of juice dose (≤300 ml/day vs. >300 ml/day), intervention duration (<2 months vs. ≥2 months), and participant health status. Meta-regression was used to explore linear trends between intervention variables and lipid changes. Funnel plots and Egger's test assessed publication bias. In this study, we considered obese people and people with metabolic syndrome as unhealthy subjects.

The choice of correlation coefficient (R=0.8) for estimating standard deviations was based on guidelines from the Cochrane Handbook (Higgins, 2011) and supported by the approach described by Wan et al. (2014), both commonly used in nutrition-related meta-analyses.

Results

Included studies

A total of 2,456 records were initially retrieved. After removing 612 duplicates and screening out 1,825 irrelevant titles and abstracts, 19 full-text articles remained for further review. Of these, two studies were excluded based on eligibility criteria, leaving 17 randomized controlled trials (RCTs) that qualified for inclusion in the final meta-analysis.(Sumner et al., 2005, Cerdá et al., 2006, González-Ortiz et al., 2011, Tsang et al., 2012, Asgary et al., 2014, Shema-Didi et al., 2014, Fuster-Muñoz et al., 2016, Kojadinovic et al., 2017, Manthou et al., 2017, Moazzen, Alizadeh 2017, Akbarpour et al., 2019, Sohrab et al., 2019, Barati Boldaji et al., 2020, Esmaeilinezhad et al., 2020, Abedini et al., 2021, Kojadinovic et al., 2021, Nemati et al., 2021) (Figure 1).

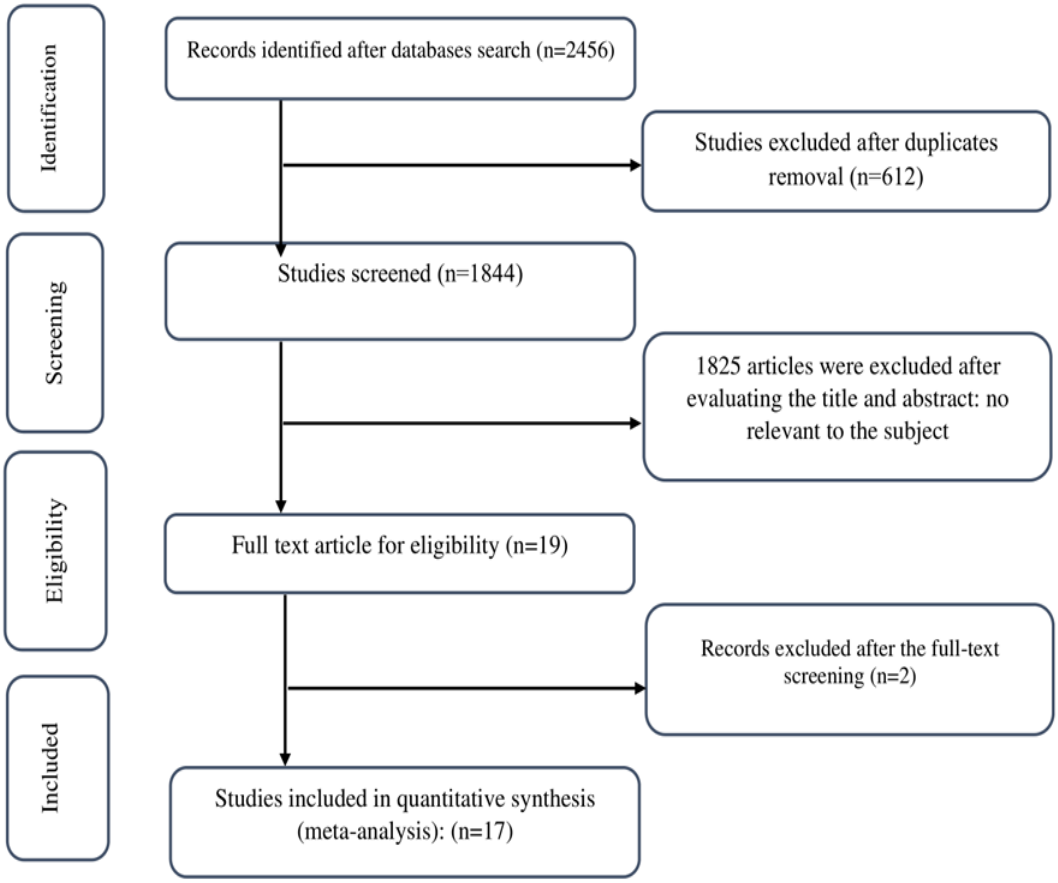


Figure 1. Flowchart of study selection for inclusion in the systematic review.

Characteristics of included studies

The 17 eligible trials included 663 participants, with 355 individuals assigned to the pomegranate juice (PJ) intervention group and 308 to the control group (each part of crossover trial was evaluated separately). The publication years ranged from 2005 to 2022. The studies were conducted across Asia (9 trials) (Asgary et al., 2014, Shema-Didi et al., 2014, Moazzen, Alizadeh 2017, Akbarpour et al., 2019, Sohrab et al., 2019, Barati Boldaji et al., 2020, Esmaeilinezhad et al., 2020, Abedini et al., 2021, Nemati et al., 2021),, Europe (6 trials)) (Cerdá et al., 2006, Tsang et al., 2012, Fuster-Muñoz et al., 2016, Kojadinovic et al., 2017, Manthou et al., 2017, Kojadinovic et al., 2021), and the Americas (2 trials) (Sumner et al., 2005, González-Ortiz et al., 2011). PJ dosages varied from 45 mL/day (Abedini et al., 2021) to 500 mL/day(Tsang et al., 2012, Manthou et al., 2017, Moazzen, Alizadeh 2017), and intervention durations ranged from 1 (Moazzen, Alizadeh 2017)to 52 weeks weeks (Shema-Didi et al., 2014). Most trials followed a parallel-group design, while four were crossover trials(Tsang et al., 2012, Manthou et al., 2017, Moazzen, Alizadeh 2017, Barati Boldaji et al., 2020). In one study, three groups were examined: a pomegranate juice (PJ, n=10), a diluted pomegranate juice group (PJD, n=11; 1:1 dilution with water) and a control group with no pomegranate juice intake (C, n=10). These were analysed as two independent comparisons. (Fuster-Muñoz et al., 2016). Participants included individuals with conditions such as type 2 diabetes(Akbarpour et al., 2019, Sohrab et al., 2019, Nemati et al., 2021),, polycystic

ovary syndrome(Esmaeilinezhad et al., 2020, Abedini et al., 2021), metabolic syndrome(Kojadinovic et al., 2017, Moazzen, Alizadeh 2017), obesity(González-Ortiz et al., 2011, Kojadinovic et al., 2021), ischemic coronary heart disease (Sumner et al., 2005), chronic obstructive pulmonary disease (Cerdá et al., 2006), hypertensive patient (Asgary et al., 2014), hemodialysis patients (Shema-Didi et al., 2014, Barati Boldaji et al., 2020), and healthy volunteers(Tsang et al., 2012, Fuster-Muñoz et al., 2016, Manthou et al., 2017). Studies included participants with Detailed information is summarized in Table 1a.

Regarding the Gonzalez Ortiz et al study, since there was no data on the gender of the subjects, we considered the participants as both sexes (González-Ortiz et al., 2011). Also, in one of the trials (Asgary et al., 2014), the effect of pomegranate juice on Apolipoprotein A (Apo A) and Apolipoprotein B (Apo B) was investigated, however, no significant changes were observed in either marker. Hence, we excluded this study because there were not enough studies reporting this effect.

Risk of Bias Assessment

Risk of bias was assessed using the Cochrane Handbook criteria(Table 1b). Many studies did not provide clear descriptions of randomization methods or allocation concealment procedures(González-Ortiz et al., 2011, Tsang et al., 2012, Asgary et al., 2014, Kojadinovic et al., 2017, Manthou et al., 2017, Moazzen, Alizadeh 2017, Akbarpour et al., 2019, Barati Boldaji et al., 2020, Nemati et al., 2021).. Blinding of participants and personnel was deemed high risk in several trials(Tsang et al., 2012, Asgary et al., 2014, Kojadinovic et al., 2017, Akbarpour et al., 2019, Sohrab et al., 2019, Barati Boldaji et al., 2020, Abedini et al., 2021, Kojadinovic et al., 2021, Nemati et al., 2021). Most of the selected studies provide sufficient information about selective reporting except for seven trials (Sumner et al., 2005, Cerdá et al., 2006, González-Ortiz et al., 2011, Asgary et al., 2014, Fuster-Muñoz et al., 2016, Manthou et al., 2017, Akbarpour et al., 2019).

Although studies with high or unclear risk of bias were not excluded, their influence was tested through leave-one-out sensitivity analyses to evaluate the robustness of the pooled estimates. Most studies adequately reported outcome data and addressed incomplete data, though some had concerns with selective reporting or lack of information on blinding of outcome assessors.

Effect of PJ consumption on TC

The final result of the meta-analysis with 15 trials (323 cases and 280 control subjects) showed that PJ consumption had no significant effect on serum TC levels**.** Subgroup analysis by dosage revealed a significant reduction in total cholesterol (TC) with intake of >300 ml/day PJ (MD= -4 mg/dl, 95 % CI -7.7, -0.4, P = 0.03) (Figure 2A) (Table 1c).

Effect of PJ consumption on TG

Determination of whether PJ consumption affects TG status in 17 treatment arms (323 cases and 280 control subjects) indicated a significant reduction in TG levels (MD: -8.2 mg/dl, 95% CI: -16.3 to -0.12, P = 0.04). Subgroup analysis based on duration, dose of PJ intake, and health status of participants revealed that PJ consumption had significant effects on TG reduction in studies conducted on unhealthy participants (MD = -11.9, 95% CI: -20.3 to -3.5, P = 0.006) and those following the consumption of ≤300 ml/d PJ (MD: -12.9 mg/dl, 95 % CI -21.3, -4.5, P = 0·003).

A stronger triglyceride-lowering effect of pomegranate juice was observed in studies with intervention durations of two months or less, based on subgroup analysis (MD: -19.25 mg/dl, 95 % CI -27.6, -10.9; P <0.001) (Figure 2B) (Table 1c).

Table 1. (a) Characteristic of the studies included in meta-analysis; (b) Quality assessment of the included studies; (c) Result of subgroup analysis of pomegranate juice on lipid profile in adults.

(a) Characteristic of included studies in meta-analysis

Studies		year	Country	Study Design	Participant	Sex	Sample size		Trial Duration (Week)	Age		Means BMI		Intervention	
							IG	CG		IG	CG	IG	CG	PJ dose (ml/day)	Control group
1	Abedini, M.	2021	Iran	parallel, R	PCOS	F	22	22	8	24.76 ±1.13	25.57 ±1.09	29.65 ±0.70	31.86 ±1.15	45	NI
2	Akbarpour (A)	2019	Iran	parallel, R	T2DM	F	10	10	8	45-55	NR	23.97±4.50	24.9±2.33	100	NI
3	Akbarpour (B)	2019	Iran	parallel, R	T2DM	F	10	10	8	45-55	NR	25.65±2.9	24.97±3.46	100	NI
4	Asgari	2013	Iran	parallel, R	hypertensive patients	Both	11	10	2	58.91± 5.06	46.90 ± 12.36	26.79±3.47	27.95 ± 4.14	150	placebo
5	Barati-Boldagi	2019	Iran	Cross over	Hemodialysis patients	Both	22	19	8	47.8 ±13.3	NR	23.93±4.77	23.88±4.77	100	NI
6	B Cerda	2006	Spain	parallel, R	COPD	M	15	15	5	60.00±10.90	63.40±8.90	31.40±4.80	30.60±5.80	400	placebo
7	E. Fuster-Muñoz(A)	2015	Spain	parallel, R	athletes	M	10	10	3	33.3± 9.0	35.2 ±8.5	NR	NR	200	NI
8	E. Fuster-Muñoz(B)	2015	Spain	parallel, R	athletes	M	10	11	3	33.3± 9.0	37.5 ±11.4	NR	NR	200	NI
9	Esmaeilinezhad,(A)	2019	Iran	parallel, R	PCOS	F	22	21	8	29.30 ± 7.46	30.60± 7.43	26.25 ± 2.93	26.77 ± 1.70	2 L/ week (285 daily)	NI
10	Esmaeilinezhad,(B)	2019	Iran	parallel, R	PCOS	F	22	21	8	30.04 ± 6.39	29.52 ± 5.82	25.75 ± 2.45	26.29 ± 1.70	2 L/ week (285 daily)	placebo
11	González Ortiz	2011	Mexico	parallel, R	obese adult volunteers	Both	10	10	4	36.3± 8.3	38.3 ± 10.4	35.2± 3.1	33.8± 4.1	120	placebo
12	Kojadinovic-1	2017	Serbia	parallel, R	metabolic syndrome	F	12	11	6	40-60	40-60	32.17±3.56	26.50±6.63	300	NI
13	Kojadinovic-2	2021	Serbia	parallel, R	Overweight Patients with Dyslipidemia	Both	12	12	2	54.42 ± 6.26	52.38 ± 13.31	28.96±3.62	27.78±2.38	300	NI
14	Manthou	2017	Greece	Cross over	healthy subjects	Both	5	5	2	31.8±6.6		NR	NR	500	NI
15	Moazzen	2017	Iran	Cross over	metabolic syndrome	Both	16	16	1	51.57 ± 10.04	NR	NR	NR	500	placebo
16	Nemati(A)	2022	Iran	parallel, R	T2DM	M	9	10	8	41.33 ± 1.50	41.81 ± 1.88	32.69 ± 1.30	33.34 ± 1.51	240	placebo
17	Nemati(B)	2022	Iran	parallel, R	T2DM	M	9	10	8	43.22±2.48	42.60±1.89	34.55 ± 3.14	32.28 ± 1.78	240	placebo
18	Shema-Didi, L.	2014	Israel	parallel, R	hemodialysis (HD) patients	Both	66	35	52	66.5 ± 11.8	NR	NR	NR	100	placebo
19	Sohrab	2019	Iran	parallel, R	T2DM	Both	30	30	6	54.6 ± 8.4	55.3 ± 8.5	27.1 ± 3.5	26.4 ± 3.6	200	NI
20	Sumner	2005	USA	parallel, R	CHD	Both	26	19	12	69 ± 11	69 ± 9	28 ± 6	29 ± 5	240	placebo
21	Tsang	2012	UK	Cross over	healthy subjects	Both	14	14	4	40–65	NR	26.7 ± 3.3	NR	500	placebo

(b) Quality assessment of included studies

studies	Random sequence generation	Allocation concealment	Selective reporting	Other sources of bias	Blinding (participants and personnel)	Blinding (outcome assessment)	Incomplete outcome data
Abedini	L	L	L	L	H	U	L
Akbarpour	U	U	H	U	H	H	L
Asgary	U	U	H	H	H	H	L
Barati boldagi	U	U	L	L	H	H	L
B Cerda	U	L	H	L	L	U	L
E. Fuster-Muñoz	U	L	H	U	L	L	L
Esmaeilinezhad	L	L	L	L	L	L	L
González Ortiz	U	U	H	U	L	U	L
Kojadinovic-1	U	U	L	U	H	H	L
Kojadinovic-2	U	L	L	U	H	H	L
Manthou	U	U	H	L	U	U	L
Moazzen	U	U	L	L	L	U	L
Nemati	U	U	L	U	H	U	L
Shema didi	U	L	L	U	L	U	L
Sohrab	L	L	L	U	H	U	L
Sumner	L	U	H	L	L	L	L
Tsang	U	U	L	U	H	U	L

(c) Result of subgroup analysis of pomegranate juice on lipid profile in adults

	Number of treatment arms	Difference in means (95%CI)	p	I^2 (%)
Subgroup analyses of pomegranate juice supplementation on TC				
Overall effect	157	-0.15 (-5.65, 5.34)	0.95	72%
Duration (month)				
2 months<	9	2.13 (-5.45, 9.71)	0.6	69%
2 months≥	8	-2.6 (-11.9, 6.8)	0.6	78%
Intervention dose (ml/day)				
≤300	13	0.6 (-7.6, 8.8)	0.9	77%
>300	4	-4 (-7.7, -0.4)	0.03	5.8%
Health status				
Healthy	3	-1.71 (-9.23, 5.79)	0.65	12%
Unhealthy	14	0.3 (-6.28, 6.9)	0.9	76%
Subgroup analyses of pomegranate juice supplementation on TG				
Overall effect	17	-8.2(-16.3, -0.12)	0.04	68%
Duration (month)				
<2 months	9	6 (-0.3, 12.3)	0.06	0
2 months≥	8	-19.25 (-27.6, -10.9)	0.001<	55%
Intervention dose (ml/day)				
≤300	13	-12.9 (-21.3, -4.5)	0.003	57%
>300	4	5.7 (-1.44, 12.9)	0.11	0
Health status				

Healthy	3	6.45 (-1.6, 14.5)	0.11	0
Unhealthy	14	-11.9 (-20.3, -3.5)	< 0.006	60%
Subgroup analyses of pomegranate juice supplementation on HDL				
Overall effect	21	2.8 (0.9, 4.72)	0.003	88%
Duration (month)				
2 months<	11	-0.1 (-1.7, -0.3)	0.006	0
2 months≥	10	6.25 (3.9, 8.6)	<0.001	82%
Intervention dose (ml/day)				
≤300	17	3.5 (1.6, 5.5)	<0.001	83%
>300	4	-1.08 (-1.9, -0.3)	0.007	0
Health status				
Healthy	5	0.4 (-1.7, 2.5)	0.7	0
Unhealthy	16	3.5 (1.3, 5.7)	0.002	91%
Subgroup analyses of pomegranate juice supplementation on LDL				
Overall effect	19	-4.8 (-9.4, -0.16)	0.04	86%
Duration (month)				
2 months <	9	-1.8 (-6, 23)	0.4	23%
2 months≥	10	-5.8 (-12.3, -0.7)	0.08	91%
Intervention dose (ml/day)				
≤300	15	-6 (-11, -0.5)	0.03	86%
>300	4	0.2 (-3.8, 4.2)	0.9	17%
Health status				
Healthy	3	-4.8 (-11.6, 2.1)	0.1	0
Unhealthy	16	-4.9 (-10, 0.2)	0.06	89%

IG, intervention group; CG, control group; R, randomized; NR, not reported; F, Female; M, Male; NR, not reported; NI, No Intervention; PCOS, polycystic ovary syndrome; T2DM, type 2 diabetes mellitus; COPD, chronic obstructive pulmonary disease; CHD, ischemic coronary heart disease. In the age column, either the mean ± standard deviations are reported, or the age range of the individuals. L, low risk of bias; H, high risk of bias; U, unclear risk of bias.TC: total cholesterol, TG: Triglyceride, HDL: High density lipoprotein, LDL: Low density lipoprotein.

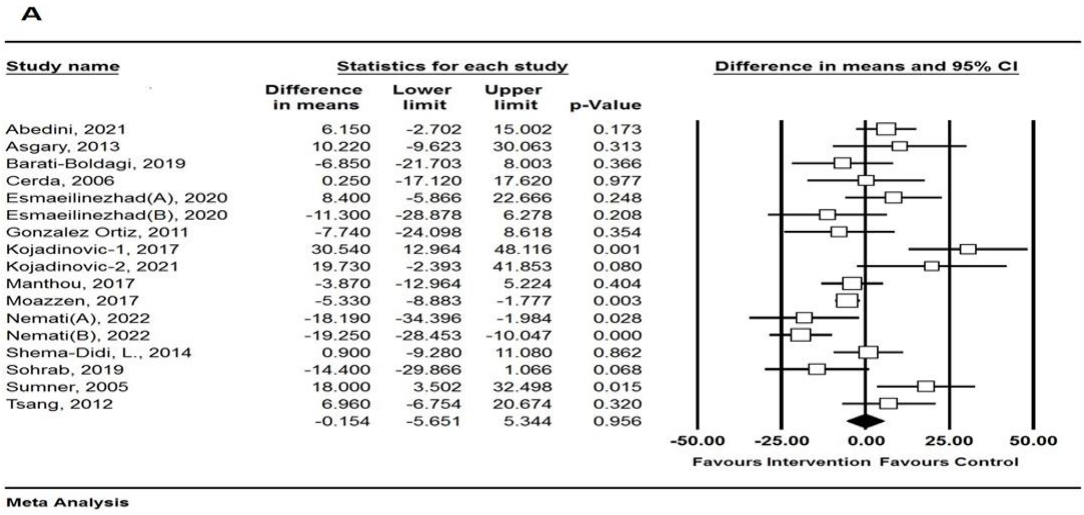
Effect of PJ consumption on HDL-C

Overall, 17 studies with a total sample size of 355 in the intervention group and 316 in the placebo group for HDL-C were included in the analysis (Sumner et al., 2005, Cerdá et al., 2006, González-Ortiz et al., 2011, Tsang et al., 2012, Asgary et al., 2014, Shema-Didi et al., 2014, Fuster-Muñoz et al., 2016, Kojadinovic et al., 2017, Manthou et al., 2017, Moazzen, Alizadeh 2017, Akbarpour et al., 2019, Sohrab et al., 2019, Barati Boldaji et al., 2020, Esmaeilinezhad et al., 2020, Abedini et al., 2021, Kojadinovic et al., 2021, Nemati et al., 2021). PJ consumption significantly affects HDL-C (MD = 2.8 mg/dl; 95% CI: 0.9 to 4.72; p = 0.003) (Figure 2C). After subgroup analysis, the beneficial effects of PJ on improvement of HDL levels remained significant on consumption of ≤300 ml/day and whether the duration of intervention was more than 2 months. Moreover, the HDL-C improving effects was shown on unhealthy individuals (Table 1c). Moreover, the subgroup analysis revealed that PJ consumption reduced HDL-C when a high dose of PJ (>300 ml/day) was used or in studies that used a short duration (< 2 months) compared with longer duration. In other subgroups, consumption of PJ increased HDL-C (Figure 2C).

Effect of PJ consumption on LDL-C

The final result of the meta-analysis with 19 treatment arms (343 cases and 300 control subjects) indicated a significant reduction in LDL-C levels (MD: -4.8 mg/dl, 95% CI: -9.4 to -0.16, p = 0.04). In the subgroup analysis based on the administered dosage, LDL-C significantly decreased following the consumption of ≤300 ml/day PJ (MD= -6 mg/dl, 95 % CI -11, -0.5, p = 0·03). Further subgroup analyses did not reveal any additional findings (Figure 2D).

As shown in Table 1c, high I^2 values are evident among certain outcomes. After conducting subgroup analysis, it was observed that high I^2 values persist among the unhealthy subgroup, studies with ≤300 ml/day, and studies with an intervention duration of 2 months or longer. Upon closer examination of Table 1a, it was discovered that among the 10 studies with interventions lasting less than 2 months, 50% involved healthy individuals, athletes, or obese volunteers. Conversely, all participants in the seven studies with interventions lasting longer than 2 months were unhealthy and consumed doses of <300 ml per day. Doses exceeding 300 ml per day were consistently 500 ml/day (and 400 ml/day in one study), while doses ≤300 ml/day varied from 45 to approximately 6 times more than that (300 ml/day).



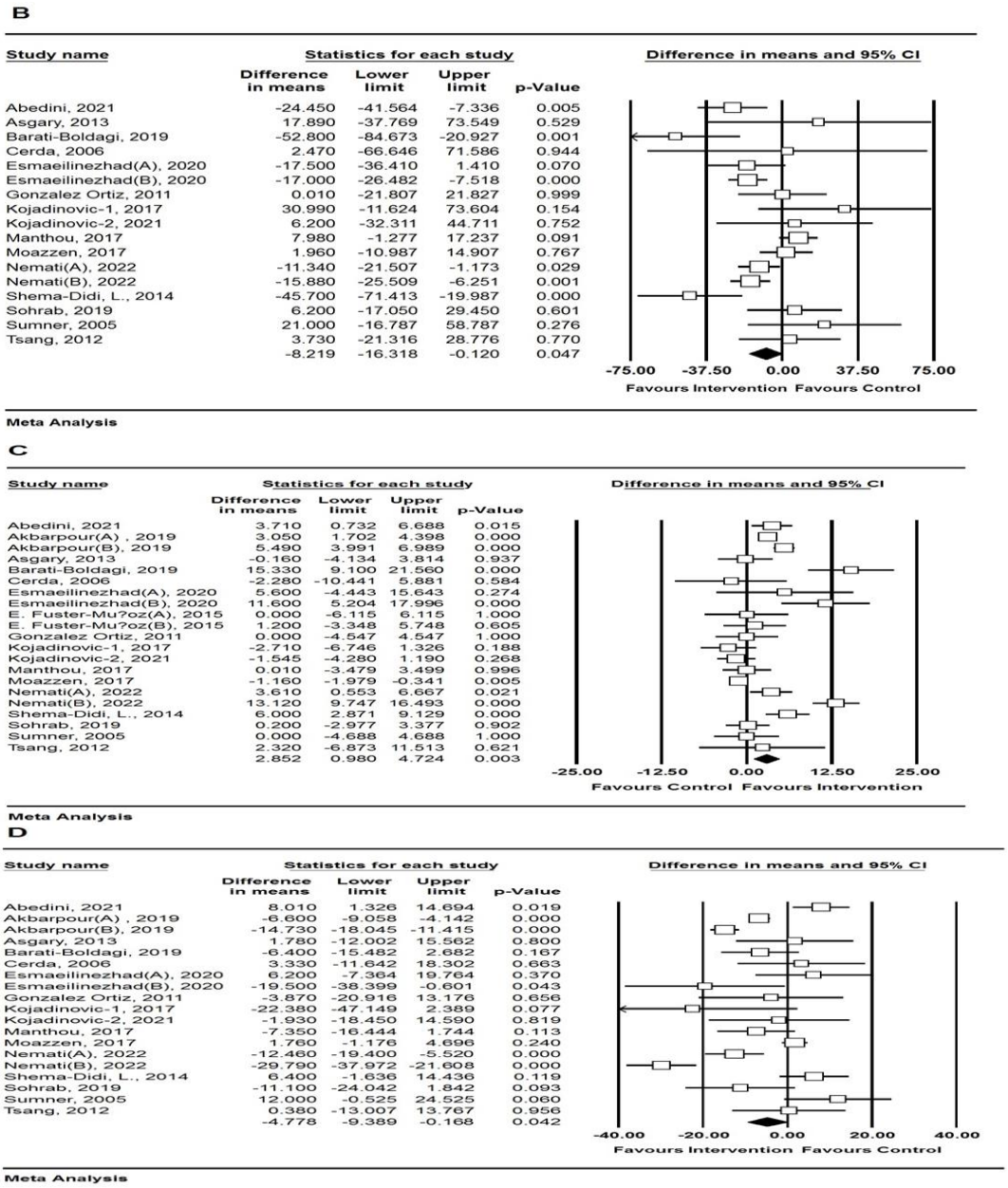


Figure 2. Forest plot detailing mean difference and 95% confidence intervals (CIs) for the effect of pomegranate juice on A) Total Cholesterol (TC); B) Triglyceride (TG); C) High-density lipoprotein (HDL); and D) low-density lipoprotein (LDL).

Sensitivity analysis

The impact of each individual study on the overall effect size was assessed through a leave-one-out sensitivity analysis. Excluding individual trials did not substantially alter the overall effects of pomegranate juice (PJ) on total cholesterol (TC) or high-density lipoprotein (HDL). However, the overall effect on triglycerides (TG) was significantly influenced by the exclusion of studies by Abedini (Abedini et al., 2021)barati, Barati-Boldagi (Barati Boldaji et al., 2020), , Esmaeilinezhad (A and B)(Esmaeilinezhad et al., 2020), and Nemati (A and B) (Nemati et al., 2021) and Shema-Didi ((Shema-Didi et al., 2014). Moreover, removing the studies conducted by Akbarpour (A) and (B) (Akbarpour et al., 2019), Barati-Boldagi (Barati Boldaji et al., 2020), Esmaeilinezhad (B) (Esmaeilinezhad et al., 2020), Kojadinovic-1 (Kojadinovic et al., 2017), Manthou (Manthou et al., 2017) , Nemati(A) and (B) (Nemati et al., 2021), and Sohrab (Sohrab et al., 2019) resulted in changing the overall effect of PJ on LDL (Figure 3).

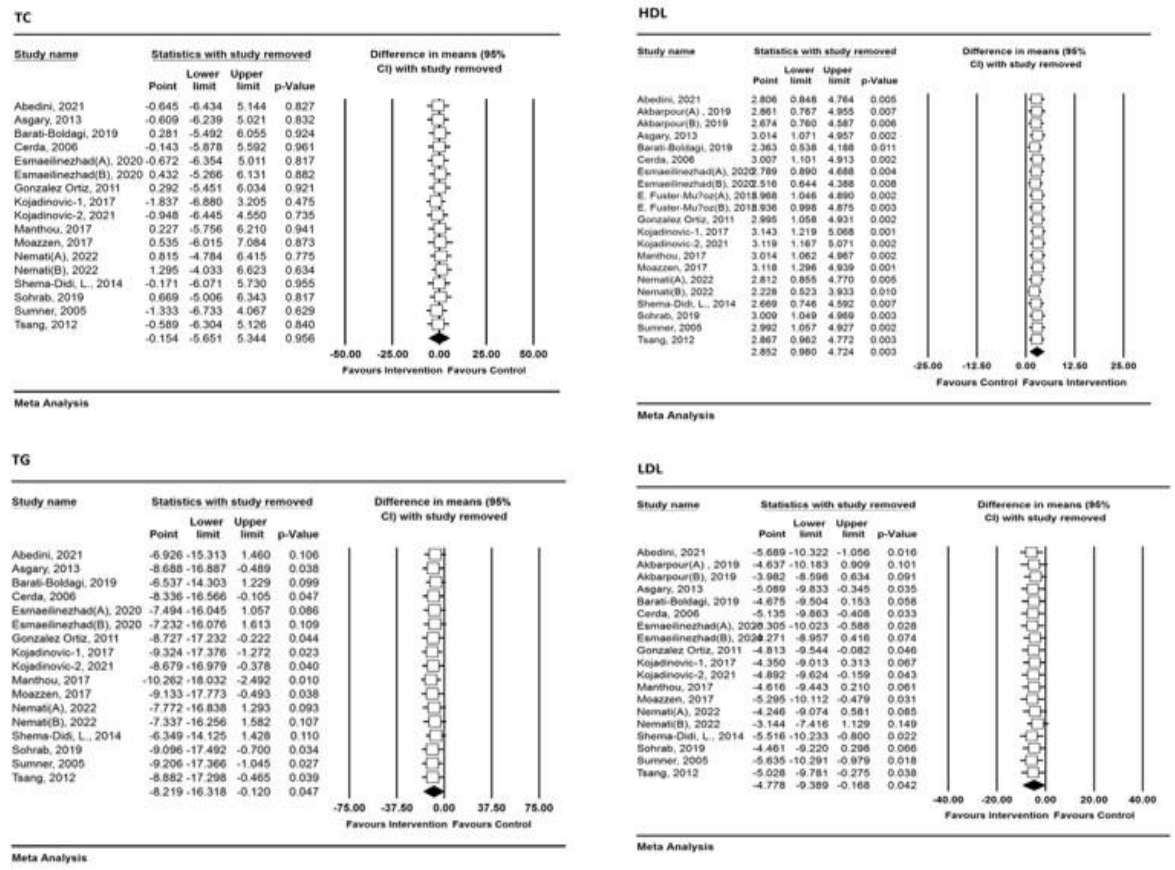


Figure 3. Leave-one-out sensitivity analysis for the impact of pomegranate juice consumption on Total Cholesterol (TC); Triglyceride (TG); High-density lipoprotein (HDL); and low-density lipoprotein (LDL).

Almost all of the studies that changed the previous significant results had intervention durations of two months or more and low-dose interventions (≤300 ml/day). This suggests that the significant results could be due to high doses in the short term.

Meta-regression

To assess potential linear relationships between the dose and duration of intervention and changes in lipid profile, meta regression analysis were conducted. As a result, meta-regression analysis did not show a significant association between PJ dose (p=0.16) and duration with changes in TC (p=0.27). However, the effect of PJ on TG, HDL and LDL concentration was associated with dose of intervention ($p < 0.001$) (Figure 4 and 5a). Also, it was shown that longer duration correlates with higher HDL and lower levels of LDL and TG. Note that even by removing the study conducted by Shema-Didi et al. (Shema-Didi et al., 2014), which was outlier in terms of the duration of intervention, the results did not change in meta-regression analysis.

Publication bias

Based on a funnel plot and Egger`s test, there was no evidence of publication bias in studies evaluating the effect of PJ on TC (p=0.18), TG (p=0.75), HDL (p=0.13) and LDL (p=0.80). Figure 5b depicts the funnel plot for TC.

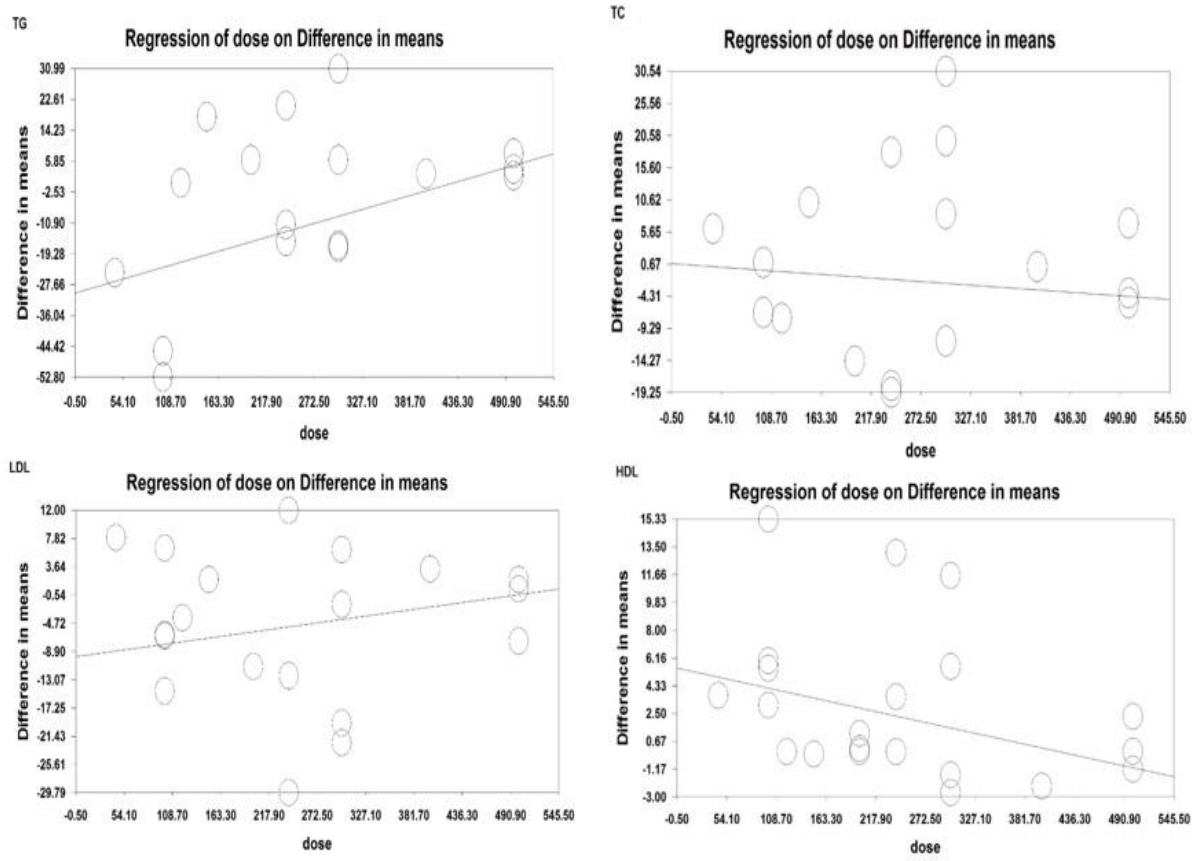
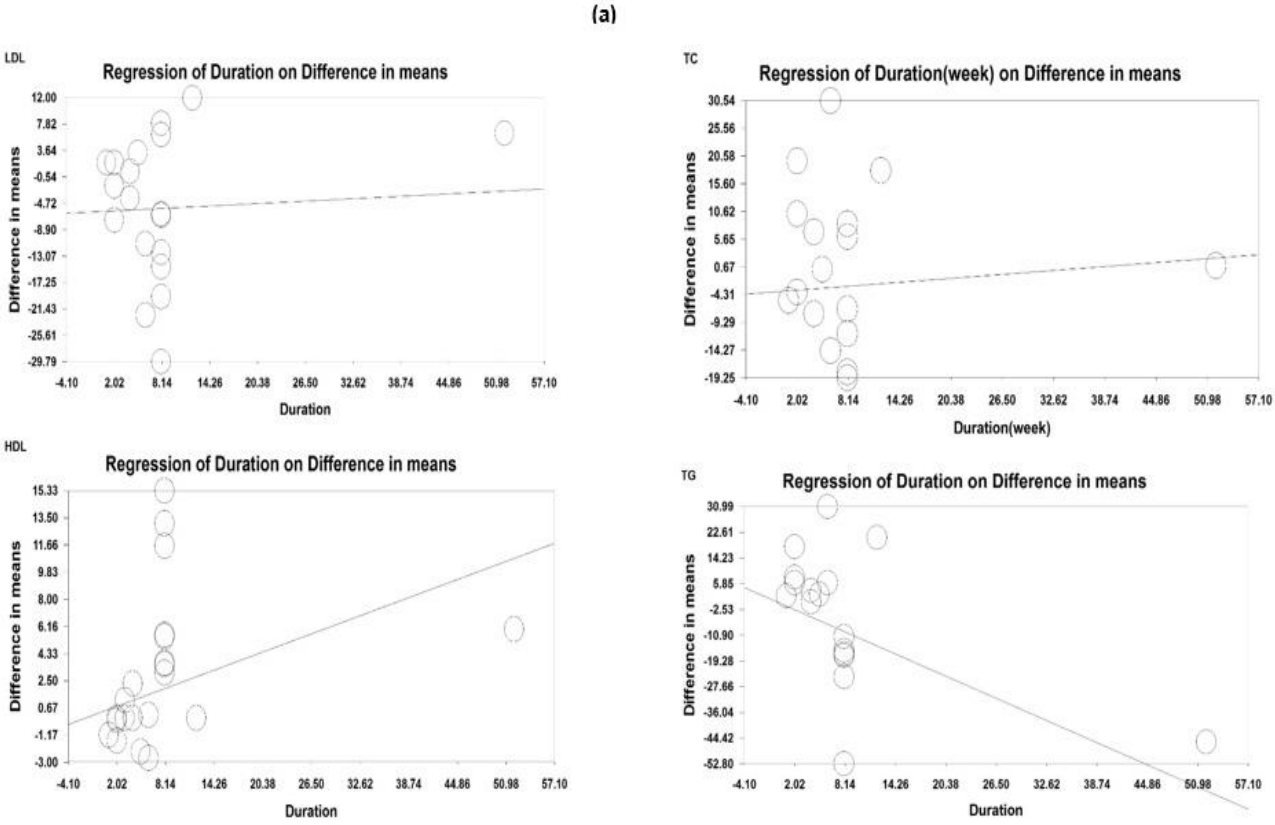


Figure 4. Meta-regression plots of the association between mean changes in plasma lipid concentrations and dose of pomegranate juice consumed per day.



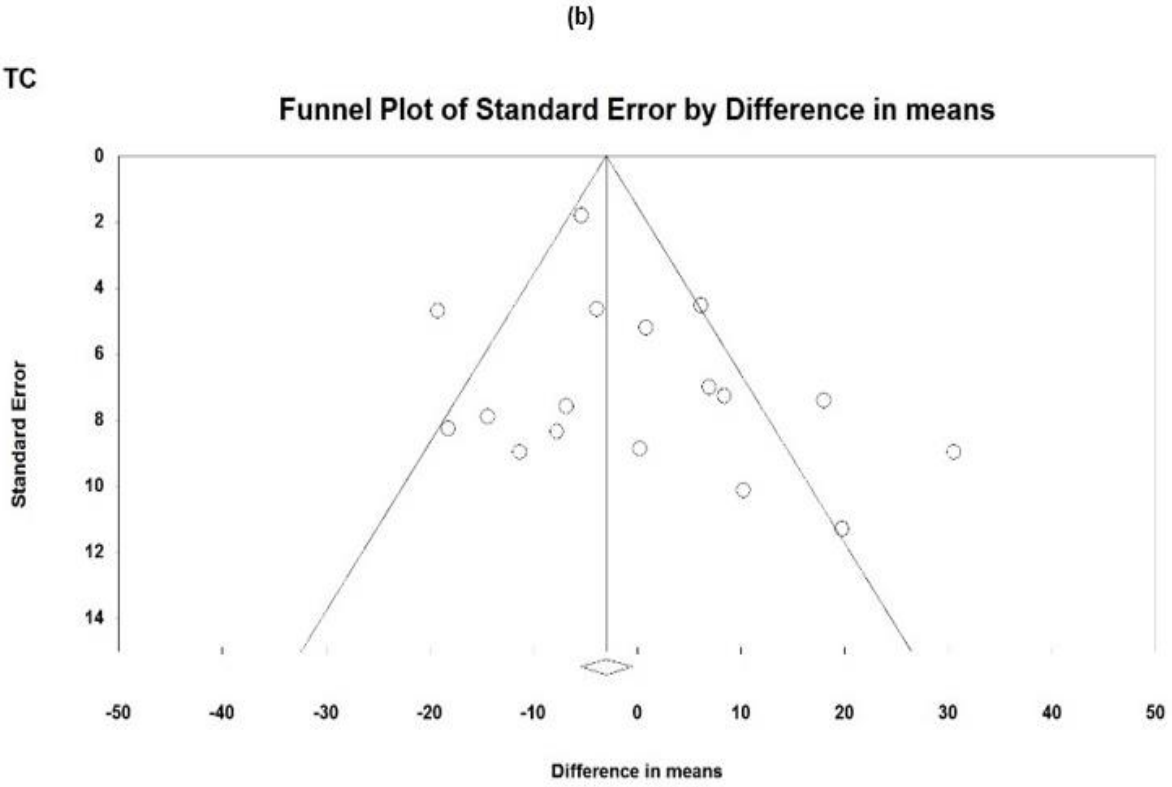


Figure 5. (a) Meta-regression plots of the association between mean changes in plasma lipid concentrations and duration of supplementation with pomegranate juice. (b) Funnel plots detailing publication bias in the studies reporting the impact of pomegranate juice on total cholesterol

Discussion

This updated meta-analysis includes 17 studies evaluating the effects of pomegranate juice (PJ) consumption on lipid profiles. The findings suggest that PJ intake is associated with significant reductions in low-density lipoprotein (LDL) and triglyceride (TG) levels. Additionally, PJ consumption has a significant positive effect on high-density lipoprotein (HDL) concentration, while no significant change was observed in total cholesterol (TC) levels. The underlying mechanisms through which PJ influences lipid metabolism remain unclear and warrant further investigation.

Human clinical trials have provided evidence that PJ may exert lipid-lowering effects through multiple mechanisms. Aviram et al. (2004) demonstrated that daily PJ consumption significantly enhanced paraoxonase-1 (PON1) activity and reduced LDL oxidation in healthy individuals, supporting its antioxidative and antiatherogenic properties. Similarly, Sohrab et al. (2019) showed that PJ improved lipid profiles and reduced inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP) in patients with type 2 diabetes. These findings suggest that PJ may modulate lipid metabolism via antioxidative and anti-inflammatory pathways in humans. A study by Hosseini et al. suggests that PJ may lower cholesterol levels by inhibiting HMG-CoA reductase, an enzyme responsible for cholesterol synthesis (Hosseini et al., 2013). In a randomized clinical trial, PJ intake for 12 weeks improved lipid profiles in patients with type 2 diabetes, resulting in reductions in TC and LDL-C (Sohrab et al., 2019). Furthermore, a study conducted on healthy adults showed that consuming natural polyphenol-rich PJ after resistance exercise can improve lipid profiles and reduce LDL-cholesterol (Ammar et al., 2020). It is worth noting that

discrepancies among the included trials may be attributed to factors such as small sample sizes, variations in supplementation duration, and differences in dosage and form of pomegranate used.

Concentrated pomegranate juice (CPJ) has the potential to affect TG and HDL-C levels by increasing serum paraoxonase activity which is an antioxidant enzyme found in the HDL complex. This enzyme plays a role in protecting blood lipids from oxidation. The polyphenol content in CPJ, including compounds like punicalagin, gallic acid, and ellagic acid, binds to HDL (Aviram et al., 2004, Sohrab et al., 2019). PJ can increase the activity of PON1 through mechanisms such as reducing fat peroxides or directly affecting the enzyme itself (Estrada-Luna et al., 2018). As a result, PJ has the ability to reduce cholesterol absorption, increase cholesterol excretion, and modulate key enzymes involved in cholesterol metabolism, such as HMG-CoA reductase and acyltransferase (Esmaillzadeh et al., 2006, Sohrab et al., 2019). PJ also stimulates macrophages to release HDL, which helps prevent HDL depletion (Kaplan et al., 2001).

Moreover, PJ may influence blood lipids by up-regulating various enzymes and factors involved in lipid metabolism, including hormone-sensitive lipase, fatty acid synthase, pyruvate kinase, acetyl-CoA carboxylase 1, sterol regulatory element-binding protein-1C (SREBP-1C), and adiponectin (Medjakovic and Jungbauer 2013). Pomegranate's ability to regulate the expression of genes involved in lipogenesis and fatty acid oxidation in the liver, along with its capacity to increase PON1 expression and activity, which prevents LDL oxidation in HDL particles, are factors that contribute to its anti-atherogenic and lipid-lowering effects (Estrada-Luna et al., 2018). Additionally, PJ may suppress cholesterol synthesis in macrophages and degradation of oxidized LDL (Fuhrman et al., 2005). The hypocholesterolemic effects of certain polyphenols, particularly procyanidins with a high molecular weight, are attributed to reduced cholesterol absorption in the intestine. Differences between studies may arise from variations in the polyphenol contents of different pomegranate cultivars (Ogino et al., 2007).

Several studies have suggested that the down-regulation of acetyl-CoA carboxylase prevents the accumulation of TG in the liver (Zang et al., 2006, Ogino et al., 2007). Furthermore, polyphenols found in pomegranate, such as gallic acid, as well as other phytochemicals like punicic acid, have been found to reduce TC, triacylglycerol, and LDL-cholesterol concentrations in obese mice (Jang et al., 2008, Hontecillas et al., 2009). Although the precise mechanism of action of PJ is not fully understood, it is believed to involve peroxisome proliferator-activated receptors (PPARs) which play a role in regulating lipid metabolism (Hsu, Huang 2007). Punicic acid and gallic acid found in pomegranates can activate PPAR-α which in turn, activates genes involved in lipid metabolism (Viladomiu et al., 2013).

This meta-analysis has certain limitations that should be acknowledged. Firstly, some of the clinical studies included in the analysis had small sample sizes, which may affect the generalizability of the findings. Additionally, the lack of standardization in PJ preparations across studies introduces variability in potency and composition. Moreover, variations in participant characteristics, such as age, sex, health status, and dietary/lifestyle factors might have introduced confounding factors that can influence the results. Finally, the presence of potential publication bias is an inherent limitation to meta-analyses which should be considered upon interpretation of findings. Our results partially align with those of Sahebkar et al. (2016), who reported modest effects of pomegranate supplementation on LDL-C and HDL-C, but no significant effect on TG. In contrast, our updated meta-analysis, which includes more recent trials and focuses exclusively on PJ (rather than combining capsules and extracts), identified a significant reduction

in TG levels. Moreover, our use of meta-regression and detailed subgroup analyses allowed a more nuanced interpretation of intervention effects.

In conclusion, based on the available RCTs, the current systematic review and meta-analysis suggest that PJ consumption may have beneficial effects on lipid profile. However, it is important to note that further research is warranted.

A large prospective randomized trial utilizing a standardized PJ preparation and an adequate sample size is needed to confirm the potential beneficial effect of PJ on lipid profile. Furthermore, such a study could explore the possible synergistic effects of PJ when used in conjunction with lipid-lowering medications and anti-diabetic drugs. Future research should aim to conduct high-quality RCTs using standardized PJ formulations with well-characterized polyphenol content. Studies targeting specific populations—such as individuals with type 2 diabetes, metabolic syndrome, or familial hypercholesterolemia—are needed. Furthermore, trials should evaluate longer intervention durations, examine dose–response relationships, and explore mechanistic biomarkers such as CRP, IL-6, and expression of genes relevant to lipid metabolism.

Acknowledgment

The authors of this research sincerely appreciate all the employees and staff of Mashhad University of Medical Sciences who supported us in conducting this research.

Conflicts of interest

The authors have declared that there is no conflict of interest.

References

Abedini, M., Ghasemi-Tehrani, H., Tarrahi, M. J., Amani, R. (2021). The effect of concentrated pomegranate juice consumption on risk factors of cardiovascular diseases in women with polycystic ovary syndrome: A randomized controlled trial. Phytother Res. 35 (1), 442-451.

Akbarpour, M., Shoorabeh, F. F., Faraji, F. (2019). Effect of eight weeks of resistance training with supplementation of pomegranate juice on oxidative/ antioxidant factors and lipid profiles in women with type 2 diabetes. Knowl. Health Basic Med. Sci. 14 (3), 52-58.

Ammar, A., Trabelsi, K., Bailey, S. J., Turki, M., Bragazzi, N. L., Boukhris, O., El Abed, K., Bouaziz, M., Ayadi, F., Driss, T. (2020). Effects of natural polyphenol-rich pomegranate juice supplementation on plasma ion and lipid profiles following resistance exercise: a placebo-controlled trial. Nutr Metab. 17 (1), 1-12.

Asgary S, Kelishadi R, Rafieian-Kopaei M, Najafi S, Najafi M, Sahebkar A. Investigation of the lipid-modifying and antiinflammatory effects of cornus mas L. supplementation on dyslipidemic children and adolescents. Pediatr. Cardiol. 2013;34(7):1729-35.

Asgary, S., Sahebkar, A., Afshani, M. R., Keshvari, M., Haghjooyjavanmard, S., Rafieian-Kopaei, M. (2014). Clinical evaluation of blood pressure lowering, endothelial function improving, hypolipidemic and anti-inflammatory effects of pomegranate juice in hypertensive subjects. Phytother Res. 28 (2), 193-199.

Aviram, M., Rosenblat, M. (2012). Pomegranate protection against cardiovascular diseases. Evid. Based Complement. Alternat. Med. 2012.

Aviram, M., Rosenblat, M., Gaitini, D., Nitecki, S., Hoffman, A., Dornfeld, L., Volkova, N., Presser, D., Attias, J., Liker, H. (2004). Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation. Clin Nutr. 23 (3), 423-433.

Bahrami A, Parsamanesh N, Atkin SL, Banach M, Sahebkar A. Effect of statins on toll-like receptors: a new insight to pleiotropic effects. Pharmacol Res. 2018;135:230-8.

Barati Boldaji, R., Akhlaghi, M., Sagheb, M. M., Esmaeilinezhad, Z. (2020). Pomegranate juice improves cardiometabolic risk factors, biomarkers

of oxidative stress and inflammation in hemodialysis patients: a randomized crossover trial. J Sci Food Agric. 100 (2), 846-854.

Bedi, O., Dhawan, V., Sharma, P.L. et al. Pleiotropic effects of statins: new therapeutic targets in drug design. Naunyn-Schmiedeberg's Arch Pharmacol 389, 695–712 (2016).

Boren, J., Chapman, M. J., Krauss, R. M., Packard, C. J., Bentzon, J. F., Binder, C. J., Daemen, M. J., Demer, L. L., Hegele, R. A., Nicholls, S. J. (2020). Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and therapeutic insights: a consensus statement from the European Atherosclerosis Society Consensus Panel. Eur. Heart J. 41 (24), 2313-2330.

Bouroshaki, M. T., Sadeghnia, H. R., Banihasan, M., Yavari, S. (2010). Protective effect of pomegranate seed oil on hexachlorobutadiene-induced nephrotoxicity in rat kidneys. Ren. Fail. 32 (5), 612-617.

Cerdá, B., Soto, C., Albaladejo, M., Martinez, P., Sanchez-Gascon, F., Tomás-Barberán, F., Espin, J. (2006). Pomegranate juice supplementation in chronic obstructive pulmonary disease: a 5-week randomized, double-blind, placebo-controlled trial. Eur J Clin Nutr. 60 (2), 245-253.

Chruściel P, Sahebkar A, Rembek-Wieliczko M, Serban MC, Ursoniu S, Mikhailidis DP, et al. Impact of statin therapy on plasma adiponectin concentrations: A systematic review and meta-analysis of 43 randomized controlled trial arms. Atheroscler. 2016;253:194-208.

Derosa G, Sahebkar A, Maffioli P. The role of various peroxisome proliferator-activated receptors and their ligands in clinical practice. J Cell Physiol. 2018;233(1):153-61.

Esmaeilinezhad, Z., Barati-Boldaji, R., Brett, N. R., de Zepetnek, J. O. T., Bellissimo, N., Babajafari, S., Sohrabi, Z. (2020). The effect of synbiotics pomegranate juice on cardiovascular risk factors in PCOS patients: a randomized, triple-blinded, controlled trial. J Endocrinol Invest. 43 (4), 539-548.

Esmaillzadeh, A., Tahbaz, F., Gaieni, I., Alavi-Majd, H., Azadbakht, L. (2006). Cholesterol-lowering effect of concentrated pomegranate juice consumption in type II diabetic patients with hyperlipidemia. Int J Vitam Nutr Res. 76 (3), 147-151.

Estrada-Luna, D., Martínez-Hinojosa, E., Cancino-Diaz, J., Belefant-Miller, H., López-Rodríguez, G., Betanzos-Cabrera, G. (2018). Daily supplementation with fresh pomegranate juice increases paraoxonase 1 expression and activity in mice fed a high-fat diet. Eur J Nutr. 57, 383-389.

Fogacci F, Banach M, Mikhailidis DP, Bruckert E, Toth PP, Watts GF, et al. Safety of red yeast rice supplementation: A systematic review and meta-analysis of randomized controlled trials. Pharmacol Res. 2019;143:1-16.

Fuhrman, B., Volkova, N., Aviram, M. (2005). Pomegranate juice inhibits oxidized LDL uptake and cholesterol biosynthesis in macrophages. J Nutr Biochem. 16 (9), 570-576.

Fuster-Muñoz, E., Roche, E., Funes, L., Martínez-Peinado, P., Sempere, J., Vicente-Salar, N. (2016). Effects of pomegranate juice in circulating parameters, cytokines, and oxidative stress markers in endurance-based athletes: A randomized controlled trial. J. Nutr. 32 (5), 539-545.

Gaziano, T., Reddy, K. S., Paccaud, F., Horton, S., Chaturvedi, V. (2006). Cardiovascular disease. Disease Control Priorities in Developing Countries. 2nd edition.

González-Ortiz, M., Martínez-Abundis, E., Espinel-Bermúdez, M. C., Pérez-Rubio, K. G. (2011). Effect of pomegranate juice on insulin secretion and sensitivity in patients with obesity. Ann Nutr Metab. 58 (3), 220-223.

Haghighatdoost, F., Hariri, M. (2018). Effect of resveratrol on lipid profile: An updated systematic review and meta-analysis on randomized clinical trials. Pharmacol Res. 129, 141-150.

Hedayatnia, M., Asadi, Z., Zare-Feyzabadi, R., Yaghooti-Khorasani, M., Ghazizadeh, H., Ghaffarian-Zirak, R., Nosrati-Tirkani, A., Mohammadi-Bajgiran, M., Rohban, M., Sadabadi, F. (2020). Dyslipidemia and cardiovascular disease risk among the MASHAD study population. Lipids Health Dis. 19, 1-11.

Higgins, J. P., Green, S. (2011). Cochrane handbook for systematic reviews of interventions 5.1. 0. The cochrane collaboration. 2011.

Higgins, J. P. T. a. G., S 2011. Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration. Version 5.1.0.

Hontecillas, R., O'Shea, M., Einerhand, A., Diguardo, M., Bassaganya-Riera, J. (2009). Activation of PPAR γ and α by punicic acid ameliorates glucose tolerance and suppresses obesity-related inflammation. J Am Coll Nutr. 28 (2), 184-195.

Hosseini, S. E., Rezaei, E., Mehrabani, D., Tavakoli, F. (2013). Effect of pomegranate juice on lipid profile in streptozotocin-induced diabetic adult male rats. J Exp Anim Biol. 2, 13-20.

Hsu, S.-C., Huang, C.-j. (2007). Changes in liver PPARα mRNA expression in response to two levels of high-safflower-oil diets correlate with changes in adiposity and serum leptin in rats and mice. J Nutr Biochem. 18 (2), 86-96.

Jang, A., Srinivasan, P., Lee, N. Y., Song, H. P., Lee, J. W., Lee, M., Jo, C. (2008). Comparison of hypolipidemic activity of synthetic gallic acid–linoleic acid ester with mixture of gallic acid and linoleic acid, gallic acid, and linoleic acid on high-fat diet induced obesity in C57BL/6 Cr Slc mice. Chem Biol Interact. 174 (2), 109-117.

Jurenka, J. (2008). Therapeutic applications of pomegranate (Punica granatum L.): a review. Altern Med Rev. 13 (2).

Kaplan, M., Hayek, T., Raz, A., Coleman, R., Dornfeld, L., Vaya, J., Aviram, M. (2001). Pomegranate juice supplementation to atherosclerotic mice reduces macrophage lipid peroxidation, cellular cholesterol accumulation and development of atherosclerosis. J Nutr. 131 (8), 2082-2089.

Kojadinovic, M., Glibetic, M., Vucic, V., Popovic, M., Vidovic, N., Debeljak-Martacic, J., Arsic, A. (2021). Short-Term Consumption of Pomegranate Juice Alleviates Some Metabolic Disturbances in Overweight Patients with Dyslipidemia. J Med Food. 24 (9), 925-933.

Kojadinovic, M. I., Arsic, A. C., Debeljak-Martacic, J. D., Konic-Ristic, A. I., Kardum, N. D., Popovic, T. B., Glibetic, M. D. (2017). Consumption of pomegranate juice decreases blood lipid peroxidation and levels of arachidonic acid in women with metabolic syndrome. J Sci Food Agric. 97 (6), 1798-1804.

Kosmas, C. E., Rodriguez Polanco, S., Bousvarou, M. D., Papakonstantinou, E. J., Peña Genao, E., Guzman, E., Kostara, C. E. (2023). The triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio as a risk marker for metabolic syndrome and cardiovascular disease. Diagn. 13 (5), 929.

Lansky, E. P., Newman, R. A. (2007). Punica granatum (pomegranate) and its potential for prevention and treatment of inflammation and cancer. J Ethnopharmacol. 109 (2), 177-206.

Libby, P. (2002). Atherosclerosis: the new viewSci Am. 286 (5), 46-55.

Lopez, E. O., Ballard, B. D., Jan, A. 2022. Cardiovascular disease. StatPearls [Internet], StatPearls Publishing.

Mallika, V., Goswami, B., Rajappa, M. (2007). Atherosclerosis pathophysiology and the role of novel risk factors: a clinicobiochemical perspective. Angiology. 58 (5), 513-522.

Manthou, E., Georgakouli, K., Deli, C. K., Sotiropoulos, A., Fatouros, I. G., Kouretas, D., Haroutounian, S., Matthaiou, C., Koutedakis, Y., Jamurtas, A. Z. (2017). Effect of pomegranate juice consumption on biochemical parameters and complete blood count. Exp Ther Med. 14 (2), 1756-1762.

März W, Dippel F-W, Theobald K, et al. Utilization of lipid-modifying therapy and low-density lipoprotein cholesterol goal attainment in patients at high and very-high cardiovascular risk: real world evidence from Germany. Atheroscler. 2018;268:99–107.

Medjakovic, S., Jungbauer, A. (2013). Pomegranate: a fruit that ameliorates metabolic syndrome. Food Funct. 4 (1), 19-39.

Michaeli, D.T., Michaeli, J.C., Albers, S. et al. Established and Emerging Lipid-Lowering Drugs for Primary and Secondary Cardiovascular Prevention. Am J Cardiovasc Drugs 23, 477–495 (2023).

Moazzen, H., Alizadeh, M. (2017). Effects of

Pomegranate Juice on Cardiovascular Risk Factors in Patients with Metabolic Syndrome: a Double-Blinded, Randomized Crossover Controlled Trial. Plant Foods Hum Nutr. 72 (2), 126-133.

Momtazi AA, Banach M, Pirro M, Katsiki N, Sahebkar A. Regulation of PCSK9 by nutraceuticals. Pharmacol Res. 2017;120:157-69.

Naqvi, S., Khan, M., Vohora, S. (1991). Anti-bacterial, anti-fungal and anthelmintic investigations on Indian medicinal plants. Fitoterapia. 62 (3), 221-228.

Nemati, S., Tadibi, V., Hoseini, R. (2021). How combined aerobic training and pomegranate juice intake affect lipid profile? A clinical trial in men with type 2 diabetesBiomed. Hum. Kinet. 13 (1), 147-154.

Ogino, Y., Osada, K., Nakamura, S., Ohta, Y., Kanda, T., Sugano, M. (2007). Absorption of dietary cholesterol oxidation products and their downstream metabolic effects are reduced by dietary apple polyphenols. Lipids. 42, 151-161.

Organization, W. H. (2019). Cardiovascular diseases. 2017. Geneva: WHO.

Parizadeh SMR, Azarpazhooh MR, Moohebati M, Nematy M, Ghayour-Mobarhan M, Tavallaie S, et al. Simvastatin therapy reduces prooxidant-antioxidant balance: Results of a placebo-controlled cross-over trial. Lipids. 2011;46(4):333-40.

Rafieian-Kopaei, M., Setorki, M., Doudi, M., Baradaran, A., Nasri, H. (2014). Atherosclerosis: process, indicators, risk factors and new hopes. Int J Prev Med. 5 (8), 927.

Ray KK, Molemans B, Schoonen WM, et al. EU-wide cross-sectional observational study of lipid-modifying therapy use in secondary and primary care: the DA VINCI study. Eur J Prev Cardiol. 2021;28:1279–89.

Sahebkar, A., Simental-Mendia, L. E., Giorgini, P., Ferri, C., Grassi, D. (2016). Lipid profile changes after pomegranate consumption: A systematic review and meta-analysis of randomized controlled trials. Phytomedicine. 23 (11), 1103-1112.

Sahebkar A, Chew GT, Watts GF. Recent advances in pharmacotherapy for hypertriglyceridemia. Prog Lipid Res. 2014;56(1):47-66.

Sahebkar A, Watts GF. New LDL-cholesterol lowering therapies: Pharmacology, clinical trials, and relevance to acute coronary syndromes. Clin Ther. 2013;35(8):1082-98.

Sahebkar A, Watts GF. New therapies targeting apoB metabolism for high-risk patients with inherited dyslipidaemias: What can the clinician expect? Cardiovasc Drugs Ther. 2013;27(6):559-67.

Sahebkar A, Foroutan Z, Katsiki N, Jamialahmadi T, Mantzoros CS. Ferroptosis, a new pathogenetic mechanism in cardiometabolic diseases and cancer: Is there a role for statin therapy? Metabolism. 2023;146.

Sahebkar A, Serban C, Ursoniu S, Mikhailidis DP, Undas A, Lip GYH, et al. The impact of statin therapy on plasma levels of von Willebrand factor antigen: Systematic review and meta-analysis of Randomised placebo-controlled trials. Thromb Haemost. 2016;115(3):520-32.

Sahebkar A. Curcuminoids for the management of hypertriglyceridaemia. Nature Reviews Cardiology. 2014;11

Sahebkar A, Serban MC, Gluba-Brzózka A, Mikhailidis DP, Cicero AF, Rysz J, et al. Lipid-modifying effects of nutraceuticals: An evidence-based approach. J. Nutr.. 2016;32(11-12):1179-92.

Serban MC, Sahebkar A, Dragan S, Stoichescu-Hogea G, Ursoniu S, Andrica F, et al. A systematic review and meta-analysis of the impact of Spirulina supplementation on plasma lipid concentrations. Clin Nutr. 2016;35(4):842-51.

Shema-Didi, L., Kristal, B., Sela, S., Geron, R., Ore, L. (2014). Does Pomegranate intake attenuate cardiovascular risk factors in hemodialysis patients? Nutr J. 13, 18.

Shema-Didi, L., Kristal, B., Sela, S., Geron, R., Ore, L. (2014). Does Pomegranate intake attenuate cardiovascular risk factors in hemodialysis patients? Nutr J. 13, 1-8.

Sohrab, G., Roshan, H., Ebrahimof, S., Nikpayam, O., Sotoudeh, G., Siasi, F. (2019). Effects of pomegranate juice consumption on blood pressure and lipid profile in patients with type 2 diabetes: A single-blind randomized clinical trial. Clinical nutrition ESPEN. 29, 30-35.

Sohrab, G., Roshan, H., Ebrahimof, S., Nikpayam, O., Sotoudeh, G., Siasi, F. (2019). Effects of pomegranate juice consumption on blood pressure and lipid

profile in patients with type 2 diabetes: A single-blind randomized clinical trial. Clin Nutr ESPEN. 29, 30-35.

Sumner, M. D., Elliott-Eller, M., Weidner, G., Daubenmier, J. J., Chew, M. H., Marlin, R., Raisin, C. J., Ornish, D. (2005). Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. Am J Cardiol. 96 (6), 810-814.

Thannoun, A. M., Tayib, M. M. (2014). Effect of pomegranate juice consumption on lipid profile in healthy and hypercholesterolemic rats. J. Agric. 42 (1), 280-292.

Tsang, C., Smail, N. F., Almoosawi, S., Davidson, I., Al-Dujaili, E. A. (2012). Intake of polyphenol-rich pomegranate pure juice influences urinary glucocorticoids, blood pressure and homeostasis model assessment of insulin resistance in human volunteers. J Nutr Sci. 1, e9.

Tuzcu, E. M., Kapadia, S. R., Tutar, E., Ziada, K. M., Hobbs, R. E., McCarthy, P. M., Young, J. B., Nissen, S. E. (2001). High prevalence of coronary atherosclerosis in asymptomatic teenagers and young adults: evidence from intravascular ultrasound. Circ J. 103 (22), 2705-2710.

Viladomiu, M., Hontecillas, R., Lu, P., Bassaganya-Riera, J. (2013). Preventive and prophylactic mechanisms of action of pomegranate bioactive constituents. Evid Based Complement Alternat Med. 2013.

Vučić, V., Grabež, M., Trchounian, A., Arsić, A. (2019). Composition and potential health benefits of pomegranate: a review. Curr Pharm Des. 25 (16), 1817-1827.

Zang, M., Xu, S., Maitland-Toolan, K. A., Zuccollo, A., Hou, X., Jiang, B., Wierzbicki, M., Verbeuren, T. J., Cohen, R. A. (2006). Polyphenols stimulate AMP-activated protein kinase, lower lipids, and inhibit accelerated atherosclerosis in diabetic LDL receptor–deficient mice. Diabetes. 55 (8), 2180-2191.

Zarfeshany, A., Asgary, S., Javanmard, S. H. (2014). Potent health effects of pomegranate. Adv Biomed Res3.