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Review

Effect of pistachio on plasma lipids concentration: a meta-analysis of randomized controlled trials

[Efecto del pistacho sobre la concentración de lípidos plasmáticos:
un metanálisis de ensayos controlados aleatorios]

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Abstract: Dyslipidemia and lipoprotein metabolism disorder are involved in pathogenesis of many important diseases such as diabetes, atherosclerosis, acute pancreatitis, and malignancies. The present study aimed to evaluate the effect of pistachio on plasma lipids. Electronic databases including Scopus, Pubmed, Science Direct, and Cochrane library were searched with the keywords "lipoprotein", "blood lipid", "dyslipidemia" or "hyperlipidemia" with "Pistachio" until June 2019. Two review authors independently checked eligibility and extracted data using a standard form. Information extracted included characteristics of the patients, dose of treatment, trial duration, quality score, and trial outcomes. Four randomized clinical trials with 213 subjects worked on the effect of pistachio on blood lipids were included. Comparison of pistachio rich diet with control yielded a significant effect size of -2.6 (95% CI: -4.4 – -0.7, p=0.006) for mean reduction in total cholesterol, a significant effect size of 5.1 (95% CI: 1.8 – 8.3, p=0.002) for mean increase in HDL-cholesterol, a non-significant effect size of -0.3 (95% CI: -0.8 – 0.3, p=0.4) for mean reduction in LDL-cholesterol and a non-significant effect size of -1.3 (95% CI: -4.4 – 1.7, p=0.4) for mean reduction in triglyceride from baseline. The results demonstrated significant effect of pistachio on reducing total cholesterol and increasing HDL-cholesterol; however, its effect on lowering LDL-cholesterol and triglyceride was not significant. Further clinical trials are needed to confirm whether pistachio consumption for a certain period of time can significantly influence blood lipids.

Keywords: Pistachio; Lipoprotein; Hyperlipidemia; Hypercholesterolemia; Hypertriglyceridemia, Meta-analysis

Resumen: La dislipidemia y el trastorno del metabolismo de las lipoproteínas están implicados en la patogénesis de muchas enfermedades importantes como la diabetes, la aterosclerosis, la pancreatitis aguda y las neoplasias malignas. El presente estudio tuvo como objetivo evaluar el efecto del pistacho sobre los lípidos plasmáticos. Se realizaron búsquedas en bases de datos electrónicas, incluidas Scopus, Pubmed, Science Direct y Cochrane Library, con las palabras clave "lipoprotein", "blood lipid", "dislipidemia" o "hyperlipidemia" con "Pistachio" hasta junio de 2019. Dos autores de la revisión verificaron de forma independiente la elegibilidad y extrajeron datos utilizando un formulario estándar. La información extraída incluyó características de los pacientes, dosis de tratamiento, duración del ensayo, puntuación de calidad y resultados del ensayo. Se incluyeron cuatro ensayos clínicos aleatorios con 213 sujetos que trabajaron sobre el efecto del pistacho en los lípidos en sangre. La comparación de la dieta rica en pistacho con el control arrojó un tamaño del efecto significativo de -2,6 (IC del 95%: -4,4 - -0,7, p=0,006) para la reducción media del colesterol total, un tamaño del efecto significativo de 5,1 (IC del 95%: 1,8 - 8,3, p=0,002) para el aumento medio del colesterol HDL, un tamaño del efecto no significativo de -0,3 (IC del 95%: -0,8 - 0,3, p=0,4) para la reducción media del colesterol LDL y un efecto no significativo tamaño de -1,3 (IC del 95%: -4,4 - 1,7, p=0,4) para la reducción media de los triglicéridos desde el valor inicial. Los resultados demostraron un efecto significativo del pistacho en la reducción del colesterol total y el aumento del colesterol HDL; sin embargo, su efecto sobre la reducción del colesterol LDL y los triglicéridos no fue significativo. Se necesitan más ensayos clínicos para confirmar si el consumo de pistacho durante un cierto período de tiempo puede influir significativamente en los lípidos en sangre.

Palabras clave: Pistacho; Lipoproteína; Hiperlipidemia; Hipercolesterolemia; Hipertrigliceridemia, metanálisis

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ABBREVIATIONS

CVD: cardiovascular diseases; HDL-C: HDL cholesterol; LDL-C: low-density lipoprotein cholesterol; non–HDL-C: non–high-density lipoprotein cholesterol; TC: total cholesterol; TG: triglyceride

INTRODUCTION

Dyslipidemia and lipoprotein metabolism disorders with various etiology, is defined as increase in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), non–high-density lipoprotein cholesterol (non–HDL-C), triglyceride or some combination of them in addition to reduction of HDL cholesterol (HDL-C) (Expert Panel on Detection, 2001). Dyslipidemia is involved in pathogenesis of diabetes, atherosclerosis, acute pancreatitis, nephropathy, breast cancer, and other malignancies (Koene *et al*., 2016). Moreover, dyslipidemia is an important risk factor for cardiovascular diseases (CVD), one of the main causes of death worldwide (Yusuf *et al*., 2004). Death rates among people with CVD are rising and the number of people who will die from CVD in 2030 is estimated nearly 23.6 million (Mathers & Loncar, 2006). Management of dyslipidemia, as a preventive strategy for cardiovascular disease, may result in reduction of cardiovascular morbidity and mortality (Pan *et al*., 2016). Sometimes, conventional medicines have been successful in treating dyslipidemia but the success has been limited with some adverse effects like myopathy, rhabdomyolysis, and hepatic enzyme abnormalities (Gotto & Toth, 2016).

Via different human and animal studies, it was established that consumption of naturally derived supplements can be effective in controlling dyslipidemia. So nutritional supplements beside the other lifestyle modifications such as exercise and smoking cessation is recommended as the first intervention for treating dyslipidemia (Gotto & Toth, 2016; Bahramsoltani *et al*., 2017).

Pistachio (*Pistacia vera* L.) from the family Anacardiaceae is one of the oldest flowering nut trees considered as part of human food since 7000 BC (DerMarderosian & Beutler, 2002). Pistachio is native to the Middle East and ancient Mediterranean civilization used seeds, nut shell, oil and resin of the plant for various therapeutic purposes (Dreher, 2012; Bozorgi *et al*., 2013). Iran, USA and Turkey are the main producers of Pistachio with a slight difference in nutritional constituents (Bulló *et al*., 2015). Pistachio contains mono and polyunsaturated fatty acids, protein and dietary fiber. In addition, this nut is a rich source of phytosterols, carotenoids, γ-tocopherol, vitamin K, phenolic compounds and certain minerals like potassium, magnesium and Iron (Dreher, 2012; Bozorgi *et al*., 2013). Important records via *in vitro* and *in vivo* studies showed that pistachio has remarkable antioxidant, anti-inflammatory, anti-tumor and anti-atherosclerosis and antimicrobial properties (Bozorgi *et al*., 2013).

Some clinical trials have reported the impact of pistachio on control of body-weight and blood pressure, insulin resistance and diabetes (Bulló *et al*., 2015). In addition, several clinical trials have determined the effect of pistachio supplements on plasma lipid markers but the results were inconsistence. Although a meta-analysis assessing the effect of nuts on lipids has been published (Del Gobbo *et al*., 2015), to the best of our knowledge, no attempt was made to meta-analyze the data of pistachio as an individual intervention. Therefore, present meta-analysis was conducted to determine the efficacy of pistachio in plasma lipid profile using data from available clinical trials to determine its role as a lipid modulator.

METHODS

Data sources and searches

A literature search was conducted on the electronic databases of Scopus, PubMed, Science Direct, and Cochrane Central Register of Controlled Trials. The search was carried out without time restriction from 1966 to June 2019 using following search strings in the title/abstract/keywords: "Pistachio AND Dyslipidemia, Pistachio AND Dyslipoproteinemia, Pistachio AND Lipoprotein, Pistachio AND blood lipids". All the relevant papers were included, irrespective of when and where they were conducted. The reference lists from earlier published review articles and the retrieved papers were manually reviewed for additional applicable studies. The initial search results were recorded for investigating whether they can be included in meta-analysis. An initial assessment was performed by two authors independently, based on the title and abstract of each article to examine the potential of inclusion in the meta-analysis. The duplicate articles and irrelevant papers were excluded. The review articles and the non-human (in vitro and animal) studies were also excluded. Included articles were randomized controlled clinical trials examining the effect of pistachio on serum lipid profile. Regarding these articles, the authors individually extracted and categorized data on the

characteristics of the patients, dose of treatment, trial duration, quality score, and trial outcomes. Figure 1 illustrates a diagram of the study selection process.

Quality assessment

To determine the quality of included studies, Jadad score was used that rates the studies in terms of description of randomization, blinding, and dropouts (withdrawals) (Jadad, 1998). The quality scale ranges from 0 to 5 from low to high. A quality score of at least 3 was considered eligible to include.

Statistical analysis

According to meta-analysis general rule, included studies were weighted by effect size, pooled and analyzed using Statsdirect software version 3.1.14. Standardized effect size and 95% confidence intervals (95% CI) were calculated using Der Simonian-Laird (for random effects) method. The Cochran Q test was used to test heterogeneity and $p<0.05$ considered significant. In case of acceptable heterogeneity or few included studies, the random effects model was used. Egger and Begg-Mazumdar tests were used to evaluate publication bias indicators in funnel plot.

RESULTS

The electronic search yielded 129 items; 20 from PubMed, 75 from Scopus, 12 from Science Direct and 22 from the Cochrane Library. Of these, 9 trials were scrutinized in full text. Five reports were considered ineligible: two investigated the effects of pistachio in diabetic and pre-diabetic patients (Hernández-Alonso *et al.*, 2014; Sauder *et al.*, 2015) and three invested different types of diet in addition to pistachio (Sheridan *et al.*, 2007; Gebauer *et al.*, 2008; Li *et al.*, 2010). Thus, 4 trials were included in the analysis representing 213 subjects (Figure No. 1). All of the included studies obtained Jadad score of 3 or more (Table No. 1). Among the studies included, 2 assessed the effect of pistachio on blood lipids in patients with metabolic syndrome (Wang *et al.*, 2012; Gulati *et al.*, 2014) and two other studies included patients with dyslipidemia or healthy volunteers (Kocyigit *et al.*, 2006; Kasliwal *et al.*, 2015).

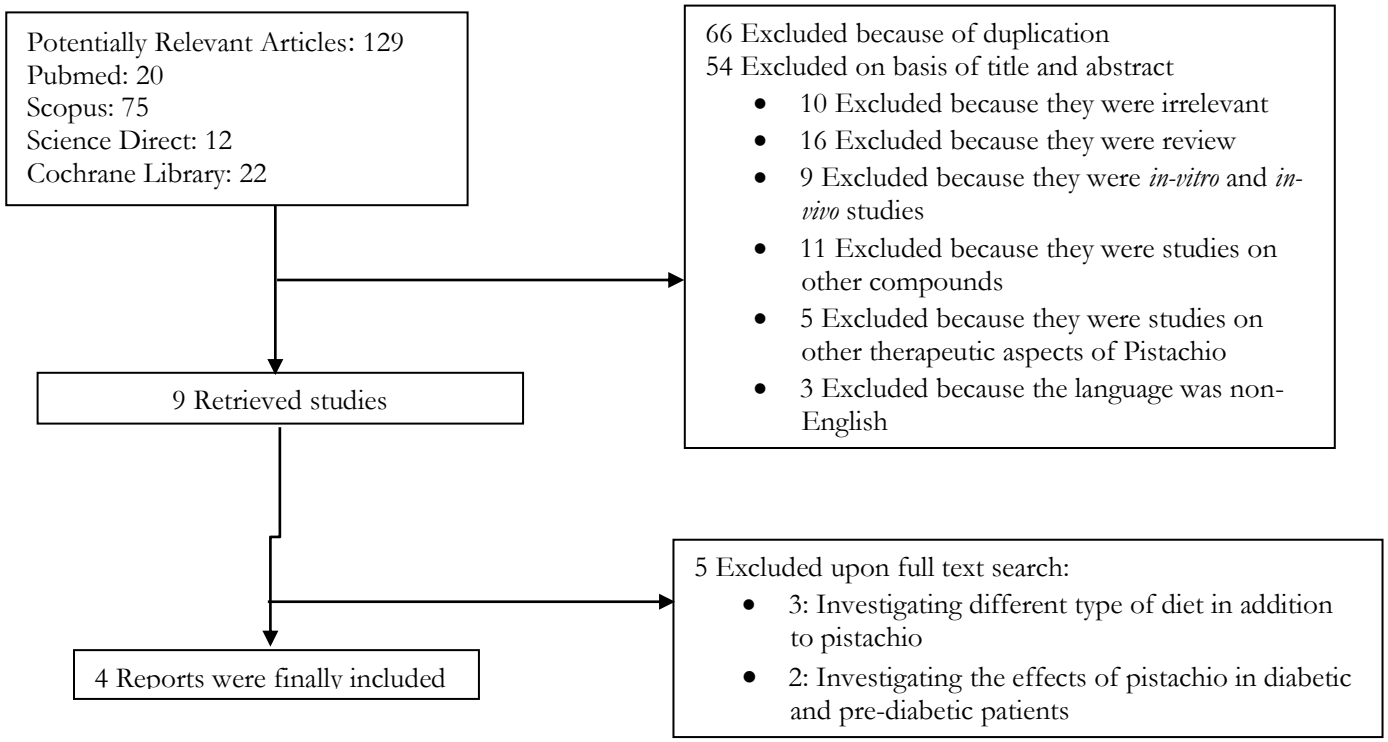

Figure No. 1
Flow diagram for study selection

Table No. 1
Characteristics of studies investigating the efficacy of pistachio in lowering plasma lipids

Study	Dose	Population					Duration	Investigated outcomes	Jaded score
		Type	M/F		Mean age				
			Pistachio	Placebo	Pistachio	Placebo			
Kasliwal *et al*., 2015	40g/day	Patients with dyslipidemia	26/3	20/7	37.7 ± 7.6	40.4 ± 8.2	3 monthes	Body mass index, Systolic BP, Diastolic BP, Fasting blood sugar, hs-CRP, Total cholesterol, Serum triacylglycerols, HDL cholesterol, LDL cholesterol, Apo-A1, Apo-B, Total/HDL-C ratio, Apo-A1/Apo-B ratio	3
Gulati *et al*., 2014	49 g/day	Metabolic syndrome	23/10	14/21	41.6 ± 8.4	43.3 ± 8.1	24 weeks	fasting blood glucose, free fatty acid; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; IAAT, intraabdominal adipose tissue; LDL-C, low-density lipoprotein cholesterol; SCAT, subcutaneous abdominal adipose tissue; TBARS, thiobarbituric acid reactive substances; TG, triglyceride; TNF, tumor necrosis factor; WC, waist circumference	2
Kocyigit *et al*., 2006	65 to 75 g/day	healthy volunteers	12/10	12/10	33.4 ± 7.2 years	32.8± 6.7	3 weeks	total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, malondialdehyde (MDA) and	2

								antioxidant potential (AOP)	
Wang *et al*., 2012	70 g/day	metabolic syndrome	12/18	13/17	51.89 ± 8.82 51.83 ± 9.37	50.66 ± 9.86	12 weeks	BMI, Fasting Glucose (mmol/L), Fasting Insulin (mU/L), Total cholesterol (mmol/L), Triglyceride (mmol/L), LDL(mmol/L), HDL (mmol/L)	3

Effect of pistachio compared to placebo on total cholesterol (TC) in patients with metabolic syndrome and healthy people

The summary for standardized effect size on mean differences on total cholesterol (TC) "ΔTC" in patients with metabolic syndrome and healthy people from 4 trials for pistachio therapy (Kocyigit *et al*., 2006; Wang *et al*., 2012; Gulati *et al*., 2014; Kasliwal *et al*., 2015) compared to placebo was -2.6 with 95% CI= -4.4 to -0.7 (p=0.006, Figure No. 2). The Cochrane Q test for heterogeneity indicated that the studies are heterogeneous (p<0.0001) and could not be combined and also publication bias, the random effects for individual and summary of effect size for standardized mean was applied. For evaluation of publication bias Egger regression of normalized effect vs. precision for all included studies for "ΔTC" in patients with metabolic syndrome and healthy people among pistachio vs. placebo therapy was -10.12 (95% CI= -18.06 to -2.18, p=0.03) and Begg-Mazumdar Kendall's test on the standardized effect vs. variance indicated tau= -0.33, p=0.38 (Figure No. 3).

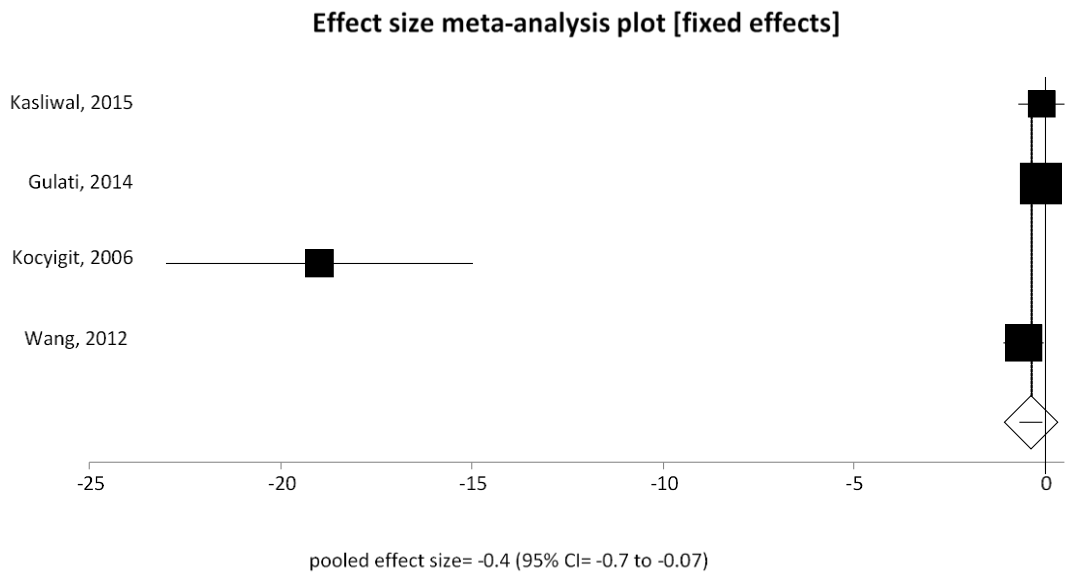

Figure No. 2
Individual and pooled effect size for the outcome of "ΔTC" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients and healthy people

Effect of pistachio compared to placebo in total LDL in patients with metabolic syndrome and healthy people

The summary for standardized effect size on mean differences of LDL "ΔLDL" in patients with metabolic syndrome and healthy people from 4 trials for pistachio therapy (Kocyigit *et al*., 2006; Wang *et al*., 2012; Gulati *et al*., 2014; Kasliwal *et al*., 2015) compared to placebo was -0.3 with 95% CI= -0.8 to 0.3 (p=0.4, Figure No. 4). The Cochrane Q test for heterogeneity indicated that the studies are heterogeneous (p=0.005) and could not be combined, thus the random effects for individual and summary of effect size for standardized mean was applied. For evaluation of publication bias Egger regression of normalized effect vs. precision for all included studies for "ΔLDL" in patients with metabolic

syndrome and healthy people among pistachio vs. placebo therapy was -9.5 (95% CI= -46.3 to 27.3, *p*=0.38) and Begg-Mazumdar Kendall's test on the standardized effect vs. variance indicated tau= -0.67, *p*=0.08 (Figure No. 5).

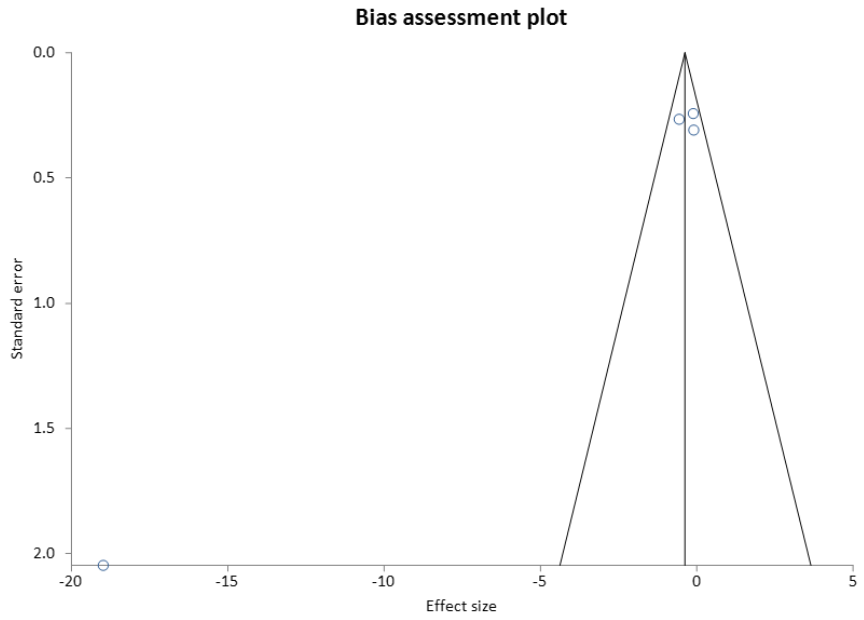

Figure No. 3
Publication bias indicators for the outcome of "ΔTC" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients and healthy people

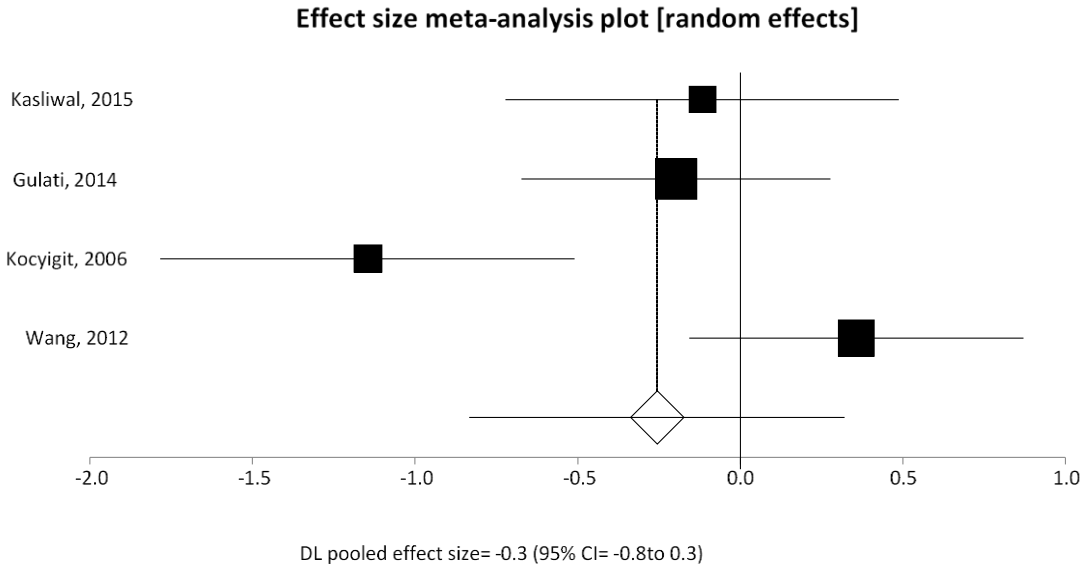

Figure No. 4
Individual and pooled effect size for the outcome of "ΔLDL" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients and healthy people

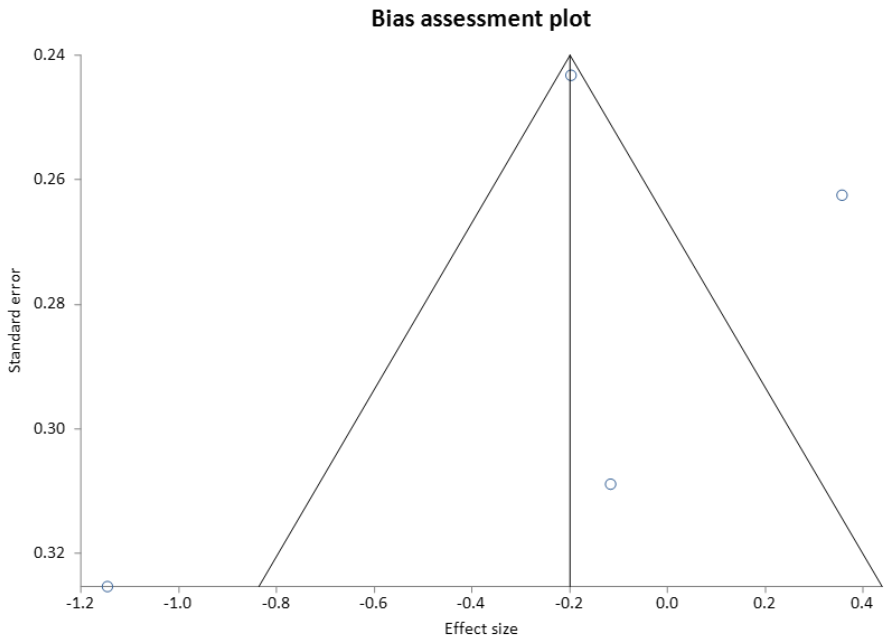

Figure No. 5
Publication bias indicators for the outcome of "ΔLDL" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients and healthy people

Effect of pistachio compared to placebo on total HDL in patients with metabolic syndrome and healthy people

The summary for standardized effect size on mean differences of HDL "ΔHDL" in patients with metabolic syndrome and healthy people from 3 trials for pistachio therapy compared to placebo (Kocyigit *et al.*, 2006; Gulati *et al.*, 2014; Kasliwal *et al.*, 2015;) was 5.1 with 95% CI= 1.8 to 8.3 (p=0.002, Figure No. 6). The Cochrane Q test for heterogeneity indicated that the studies are heterogeneous (p<0.0001) and could not be combined, thus the random effects for individual and summary of effect size for standardized mean was applied. For evaluation of publication bias Egger regression of normalized effect vs. precision for all included studies for "ΔHDL" in patients with metabolic syndrome and healthy people among pistachio vs. placebo therapy could not be calculated because of too few strata.

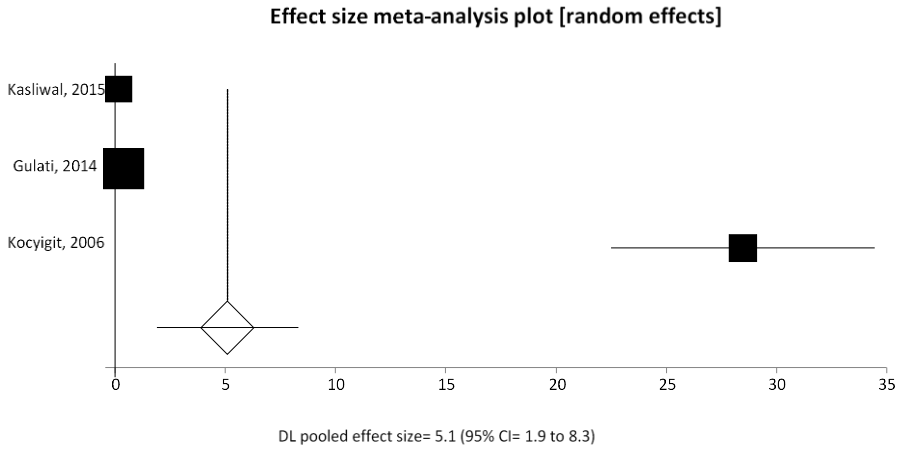

Figure No. 6
Individual and pooled effect size for the outcome of "ΔHDL" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients and healthy people

Effect of pistachio compared to placebo n total TG in patients with metabolic syndrome and healthy people

The summary for standardized effect size on mean differences of TG "ΔTG" in patients with metabolic syndrome and healthy people from 4 trials for pistachio therapy compared to placebo (Kocyigit *et al.*, 2006; Wang *et al.*, 2012; Gulati *et al.*, 2014; Kasliwal *et al.*, 2015) was -1.3 with 95% CI= -4.4 to 1.7 (p=0.4, Figure No. 7). The Cochrane Q test for heterogeneity indicated that the studies are heterogeneous (p<0.0001) and could not be combined, thus the random effects for individual and summary of effect size for standardized mean was applied. For evaluation of publication bias Egger regression of normalized effect vs. precision for all included studies for "ΔTG" in patients with metabolic syndrome and healthy people among pistachio vs. placebo therapy was -2.8 (95% CI= -46.3 to 40.7, p=0.81) and Begg-Mazumdar Kendall's test on the standardized effect vs. variance indicated tau= 0, p= 0.75 (Figure No. 8).

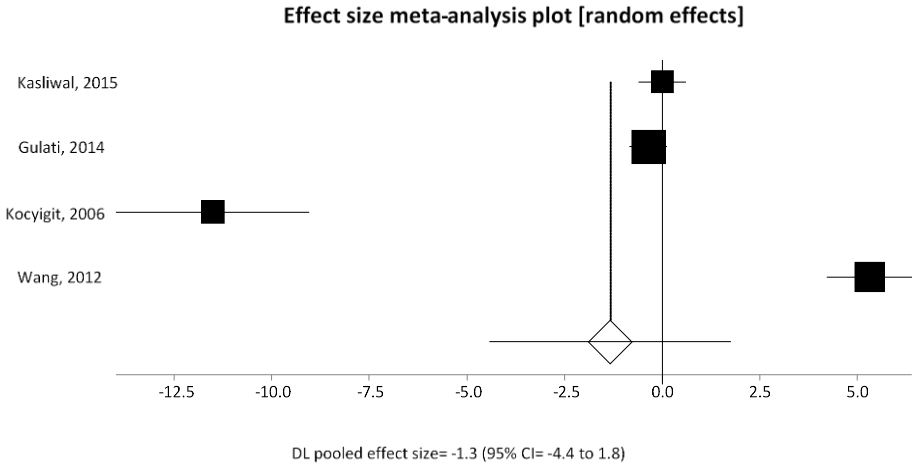

Figure No. 7

Individual and pooled effect size for the outcome of "ΔTG" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients and healthy people

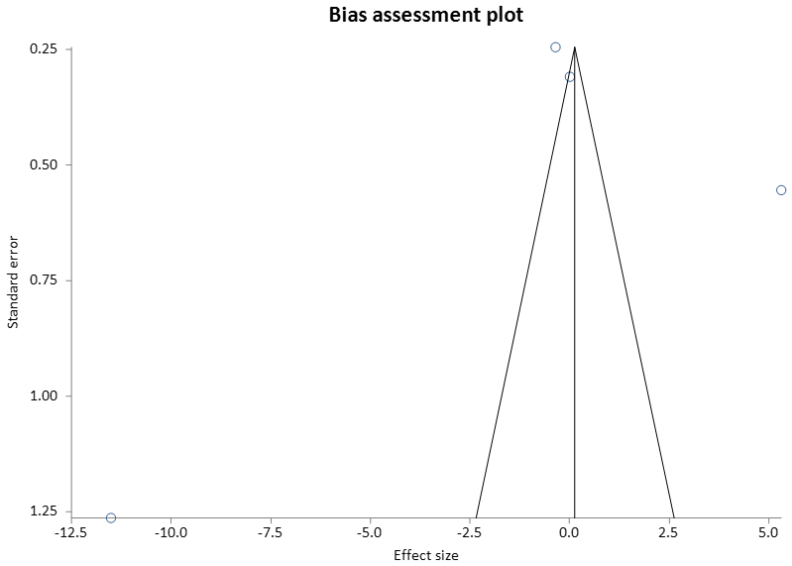

Figure No. 8

Publication bias indicators for the outcome of "ΔTG" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients and healthy people

Effect of pistachio compared to placebo on total cholesterol (TC) in patients with metabolic syndrome

The summary for standardized effect size on mean differences of total cholesterol (TC) "ΔTC" in patients with metabolic syndrome from 3 trials for pistachio therapy compared to placebo (Kocyigit *et al*., 2006; Wang *et al*., 2012; Gulati *et al*., 2014; Kasliwal *et al*., 2015) was -0.26 with 95% CI= -0.57 to 0.04 (p=0.09, Figure No. 9). The Cochrane Q test for heterogeneity indicated that the studies are heterogeneous (P= 0.4) and could be combined, but because of few included studies the random effects for individual and summary of effect size for standardized mean was applied. For evaluation of publication bias Egger regression of normalized effect vs. precision for all included studies for "ΔTC" in patients with metabolic syndrome among pistachio vs. placebo therapy could not be calculated because of too few strata.

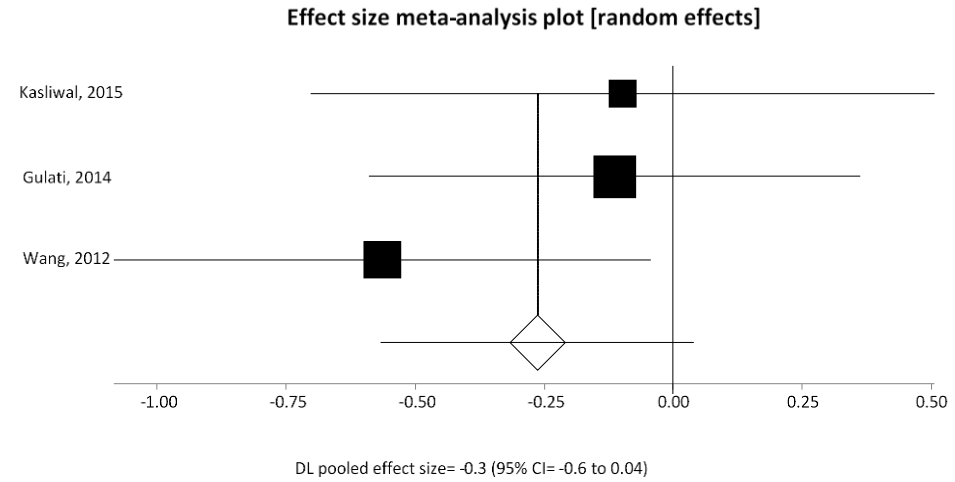

Figure No. 9
Individual and pooled effect size for the outcome of "ΔTC" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients

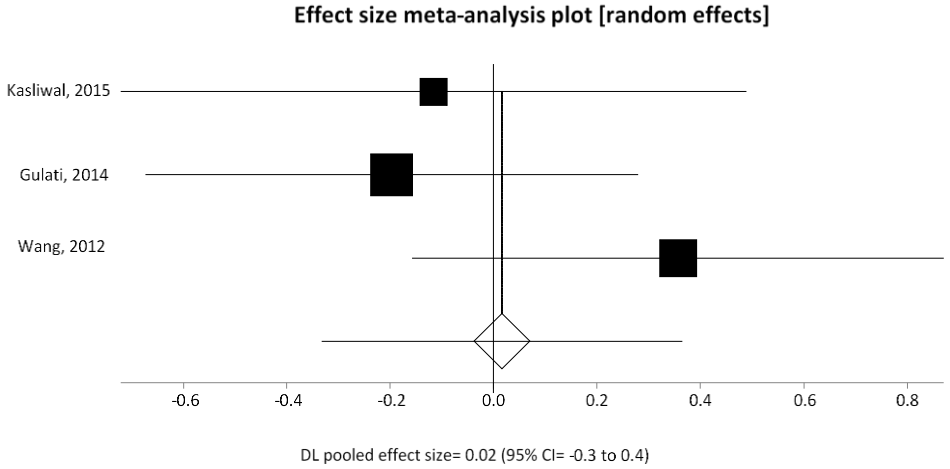

Figure No. 10
Individual and pooled effect size for the outcome of "ΔLDL" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients

Effect of pistachio compared to placebo on total LDL in patients with metabolic syndrome

The summary for standardized effect size on mean differences of LDL "ΔLDL" in patients with metabolic syndrome and healthy people from 3 trials for pistachio therapy compared to placebo (Wang *et al*., 2012; Gulati *et al*., 2014; Kasliwal *et al*., 2015) was 0.02 with 95% CI= -0.33 to 0.37 (p=0.9, Figure No. 10). The Cochrane Q test for heterogeneity indicated that the studies are heterogeneous (p=0.3) and could be combined, but because of few included studies the random effects for individual and summary of effect size for standardized mean was applied. For evaluation

of publication bias, Egger regression of normalized effect vs. precision for all included studies for "ΔLDL" in patients with metabolic syndrome among pistachio vs. placebo therapy could not be calculated because of too few strata.

Effect of pistachio in comparison to placebo therapy in total HDL in patients with metabolic syndrome

The summary for standardized effect size on mean differences of HDL "ΔHDL" in patients with metabolic syndrome from 2 trials for pistachio therapy compared to placebo (Wang *et al.*, 2012; Gulati *et al.*, 2014) was 0.3 with 95% CI =-0.07 to 0.6 (p= 0.1, Figure No. 11). The Cochrane Q test for heterogeneity indicated that the studies are heterogeneous (p=0.6) and could be combined, but because of few included studies the random effects for individual and summary of effect size for standardized mean was applied. For evaluation of publication bias Egger regression of normalized effect vs. precision for all included studies for "ΔHDL" in patients with metabolic syndrome among pistachio vs. placebo therapy could not be calculated because of too few strata.

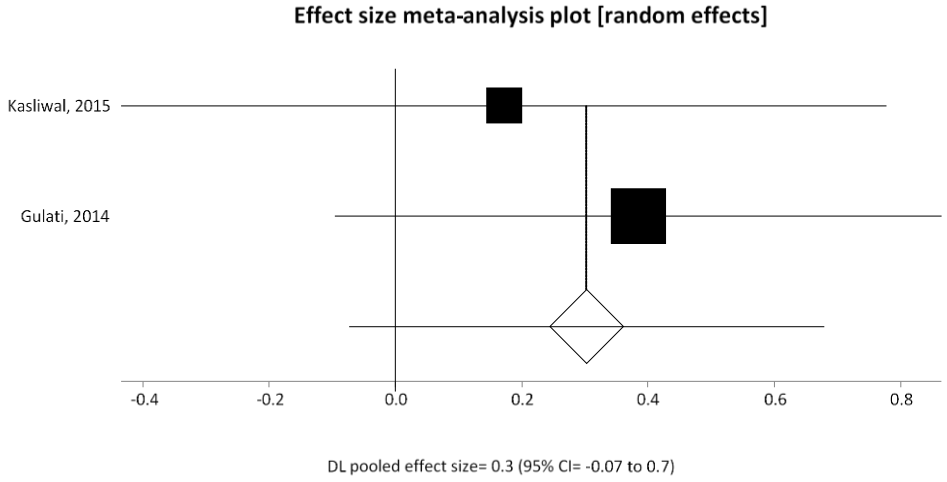

Figure No. 11
Individual and pooled effect size for the outcome of "ΔHDL" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients

Effect of pistachio compared to placebo on total TG in patients with metabolic syndrome

The summary for standardized effect size on mean differences of TG "ΔTG" in patients with metabolic syndrome from 4 trials for pistachio therapy compared to placebo (Kocyigit *et al.*, 2006; Wang *et al.*, 2012; Gulati *et al.*, 2014; Kasliwal *et al.*, 2015) was 1.6 with 95% CI= -0.98 to 4.18 (p=0.2, Figure No. 12). The Cochrane Q test for heterogeneity indicated that the studies are heterogeneous (p<0.0001) and could not be combined, thus the random effects for individual and summary of effect size for standardized mean was applied. For evaluation of publication bias Egger regression of normalized effect vs. precision for all included studies for "ΔTG" in patients with metabolic syndrome among pistachio vs. placebo therapy could not be calculated because of too few strata.

DISCUSSION

The aim of this systematic review and meta-analysis is to determine the effects of Pistachio on plasma lipid concentration. The present study provides the most reliable evidence from randomized clinical trials exploring the effect of pistachio on blood lipids in 213 subjects. Two studies have been carried out in India and two other studies were performed in China and Turkey. All studies have been conducted on adults whose average age exceeds thirty years. Two trials were performed for three months, one for 6 months and one for three weeks. In healthy people, pistachio has been added to their regular diet, but in patients with metabolic syndrome, a standard diet with or without pistachio was evaluated. The present meta-analysis shows remarkable effects of pistachio on lowering total cholesterol and enhancing high-density lipoprotein cholesterol (HDL). However, no significant effect was observed for lowering LDL and TG. Animal studies about pistachio effect on lipoproteins are rare. In one animal study, Aksoy and co-workers administered Pistachio to rats as 20% of caloric intake for 10 weeks. Significant increase in HDL was observed in pistachio treated rats but triglyceride and LDL cholesterol were not changed. Increasing the dose up to 40% of caloric intake didn't show considerable alteration that can be associated with more calorie intake or increasing amount

of saturated and polyunsaturated fatty acids (Aksoy *et al.*, 2007).

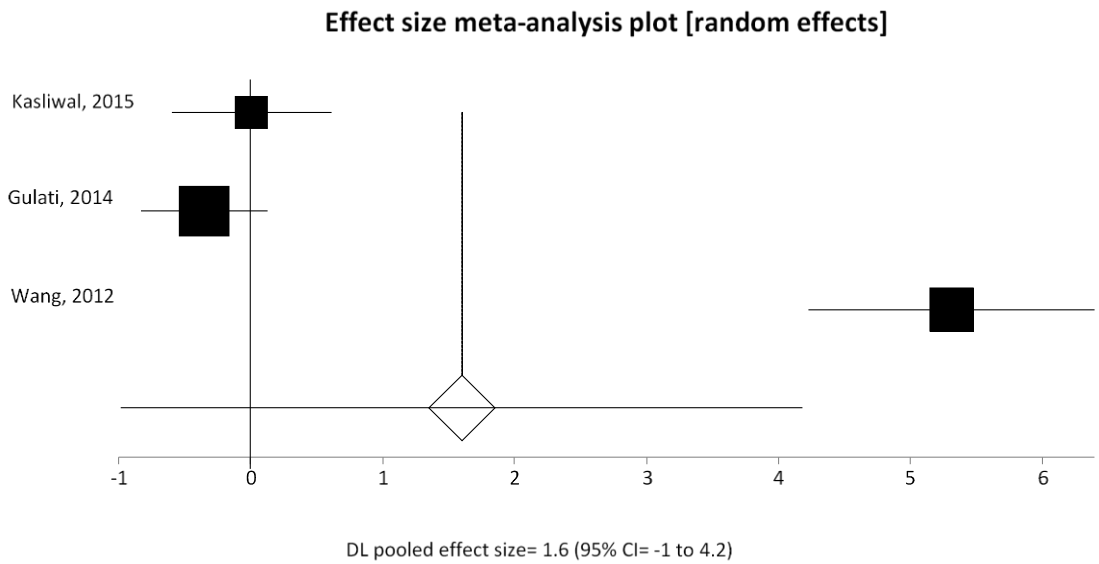

Figure No. 12
Individual and pooled effect size for the outcome of "ΔTG" in the studies considering pistachio comparing to placebo therapy in metabolic syndrome patients

There are various studies about pistachio phytochemicals and their potential efficacy for reducing blood lipids. Pistachio seed oil content is about 50-60%. Oleic acid (C18:1) is the main monounsaturated fatty acid and linoleic acid (C18:2) is the main polyunsaturated fatty acid of pistachio oil (Bozorgi *et al.*, 2013; Bulló *et al.*, 2015). Different mechanisms like up-regulation of the LDL receptor and enhancement of CYP7 activity have been determined for the ability of unsaturated fatty acids for lowering LDL and increasing HDL (Fernandez & West, 2005). The main phytosterols identified in pistachio oil include β-sitosterol, campesterol, Δ 5-avenasterol, stigmasterol, brassicasterol and cholesterol (Bozorgi *et al.*, 2013). Lipid lowering property of phytosterols is mainly related to their similarity in structure with cholesterol, which allows them to compete with cholesterol for binding to micelles in intestine and resulted in reduction of cholesterol absorption. In addition, easier hydrolysis of phytosterols lead to the reduced solubility of cholesterol in missiles and more cholesterol fecal excretion (Gupta *et al.*, 2011). Pistachio contains phenolic compounds like gallic acid, catechin, epicatechin, resveratrol, naringenin, quercetin and luteolin. The cholesterol lowering effects of gallic acid, catechin, and epicatechin have been confirmed. These compounds delayed cholesterol absorption via inhibition of pancreatic cholesterol esterase, bile acids binding and less solubilization of cholesterol in micelles (Ngamukote *et al.*, 2011). Likewise, resveratrol has demonstrated cholesterol-lowering activity through different mechanisms such as increasing the synthesis and efflux of bile acids, reducing cholesterol synthesis and increasing cholesterol efflux (Shao *et al.*, 2016). In addition, pistachio contains a considerable amount of fiber. Eating a handful of pistachio nuts provides approximately 10% of recommended daily fiber intake for healthy adults (Kasliwal *et al.*, 2015). Some mechanisms are determined for cholesterol lowering property of fiber like inhibition of hepatic fatty acid synthesis, binding to cholesterol or bile acids during micelles formation and improvement of intestinal motility (Brown *et al.*, 1999). The present meta-analysis showed no remarkable impact of pistachio on TG and LDL. As noted earlier, pistachio phytosterols can reduce blood lipids but treatment period enhancement or increasing the dose can be resulted in rising levels of saturated and polyunsaturated fatty acids. In case of pistachio phenolic constituents, some parameters like storage, condition and processing procedure can affect the amount and quality of these compounds (Serrano *et al.*, 2009). So these cases may be involved in negative result of this study. The present study has some limitations; the most important of them is few numbers of high quality studies found and a small number of patients included. Moreover, included studies were heterogeneous in terms of characteristics of subjects, pistachio dose, and duration of treatment.

CONCLUSION

This meta-analysis showed a considerable effect of pistachio on reducing total cholesterol and increasing high-density lipoprotein cholesterol (HDL). However, no significant effect was observed for lowering LDL and TG. Further clinical

trials are needed to confirm whether pistachio consumption for a certain period of time can significantly influence blood lipids.

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