

## Pistachio and metabolic syndrome: A review article

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### Abstract

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**Background:** Metabolic syndrome is a risk factor for cardiovascular disease (CVD) and type 2 diabetes. The most important strategy for the prevention and management of metabolic syndrome is lifestyle and nutritional changes. The aim of this review study was to survey the role of pistachio in metabolic syndrome.

**Materials and Methods:** Web of Science databases and Google Scholar were searched using keywords pistachio, metabolic syndrome, and some related criteria of metabolic syndrome.

**Results:** In this study, 15 articles were retrieve. These studies reported that pistachio has favourable nutrients such as unsaturated fatty acid, Phytochemical composition, phenolic compounds, vegetable protein, arginine, fiber, vitamins, antioxidants, and minerals. It has been shown that pistachio has an important role in reduction of metabolic syndrome and its risk factors such as abdominal obesity, visceral fat, hyperlipidemia, hypertension, and type 2 diabetes. Arginine and polyphenol compounds improve blood circulation. They suppress of appetite and reduce fat absorption. Arginine has vasodilator effects and folic acid is the main antiatherogenic factor and has a role in homocysteine metabolism.

**Conclusions:** The study data suggest that pistachios promote a healthy metabolic profile, and reverse certain deleterious consequences of metabolic syndrome. The suggested dose of pistachios for decreasing metabolic syndrome and its risk factors is 30-100 g/daily. It seems that in order to obtain the maximum dose and a definitive conclusion, a cohort clinical trail is required

**Keywords:** Pistachio, Metabolic Syndrome, Obesity, Hyperlipidemia, Hypertension, Glucose, Diabetes Mellitus.

### Introduction

Metabolic syndrome (MetS) is associated with the increased risk of cardiovascular disease (CVD), kidney disease, and type 2 diabetes. The prevalence of metabolic syndrome and type 2 diabetes are increasing in the world and in developing countries. In addition, 27% of American adults and 20-25 percent of the world population suffer from this syndrome (1). A study on the prevalence of metabolic syndrome among Iranian and French adolescents showed that the prevalence of this syndrome was higher in Iranian women than French women (55% vs.

6.6%) and High-density lipoprotein (HDL) level was particularly lower in Iranian women compared to\* French women (2). In the review by Barzin, the prevalence of MetS and its factors in the first phase compared to the third phase had increased from 13.2% to 16.4% (3). In a study in Shiraz, Iran, the prevalence of this syndrome increased by 15% with each decade of life (4). Hosseinpanah reported a four times

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increase in the incidence of metabolic syndrome and abdominal obesity in phase III of his study (5). In the South East of Iran, 1.2% of the girls had central obesity and 2% had hypertension (6). Abdominal obesity in women and men in the same area was reported as 56.9% and 16.6%, respectively (7). In addition, the prevalence of this syndrome in girls living in Rafsanjan, Iran, was 3.9% (8). Evidence demonstrates the increasing trend of this syndrome in the world and Iran. It is predicted that by 2030 the global prevalence of diabetes will increase to 50% (9-12).

One of the most important factors in the incidence and prevalence of this syndrome is unhealthy eating habits and nutrition (13). It was recently reported that genetic factors also play a role in the incidence of this syndrome. Among the important genetic factors, genes regulating lipid metabolism have been studied the most. DNA methylation and histone modification can be noted as epigenetic factors involved in the pathogenesis of metabolic syndrome (14). Given the known effects of this syndrome on public health (13), its most basic treatments are lifestyle interventions and healthy diet changes. Therefore, it is necessary to study the possible preventive effects of food and diets (1, 15).

Most studies have proven the role of certain foods, especially nuts, in the prevention of coronary heart diseases (CHD) and CVDs. The addition of nuts to the Mediterranean diet has shown positive and definitive results especially on blood lipids, cardiovascular problems, and central obesity. However, few studies have been conducted on risk factors of metabolic syndrome and type 2 diabetes (16, 17). Pistachio along with other nuts can resolve cardiovascular problems. This role depends on the special properties of pistachios. These properties are related to the high density fatty acids with one double bond monounsaturated fatty acids (MUFA), a number of double bonds with polyunsaturated fatty acids (PUFA), and small

amounts of saturated fatty acids. Moreover, pistachio has vegetarian protein and contains amino acid arginine (18). Pistachio also contains soluble and insoluble fiber, potassium, magnesium, vitamin K, a variety of tocopherols, especially  $\gamma$ -tocopherol, selenium, copper, and zinc (19).

Phytochemicals found in pistachio include phytosterols (1) which contain sitosterol, stigmasterol, campesterol, ellagic acid, quercetin, isoflavonoids, tocotrienol, carotenoids, polyphenolic compounds, including phenolic acids (antioxidant), proanthocyanidins, flavonoids, Lutein, anthocyanins, luteolin, chlorophyll, kaempferol, and rutin (20).

In the year 2003, the Food and Drug Administration (FDA) recommended a daily consumption of 43 grams (5.1 ounce) of pistachios as part of a low-fat diet (21). In previous studies, the consumption of 25 grams of pistachios almost 5 times a week was recommended (20-24). Pistachio is an ancient and native plant of the Middle East. According to the Food and Agricultural Organization (FAO) database, United States of America is the second largest producer of pistachios after Iran and it supplied 21% of the world's pistachio in 2010 (22).

Due to the properties of nuts and their proven positive effects on the prevention of CHD and CVD, this study aimed to review the studies conducted on the effects of pistachios on metabolic syndrome risk factors. It was hoped that the reviewing of these texts would provide better solutions for the prevention of metabolic syndrome or some of its risk factors. Pistachio is one of the most important products of Rafsanjan and by creating a clearer picture of the role of pistachios and its properties may be useful in people at risk for MetS and Diabetic patients .

## Material and Methods

Research Strategy: For this review study, relevant articles in English and Farsi were

obtained from databases of MEDLINE (www.pubmed.com; National Library of Medicine) and Cochrane (www.cochrane.org/reviews; The Cochrane Collaboration), Google Scholar search engine (https://scholar.google.com), and Persian-language databases of Scientific Information Database (<http://www.sid.ir>) and Magiran (<http://www.magiran.com>).

The search was undertaken using the keywords of "metabolic syndrome and pistachio", and "metabolic syndrome and nuts". The keywords related to other metabolic syndrome factors included "impaired fasting glucose or diabetes and pistachios", "dyslipidemia and pistachio", "hypertension and pistachios", and "central obesity and nuts". After reviewing the abstracts obtained, those which were consistent with the study criteria were selected and the full article of the relevant abstracts was obtained. Manual research was also conducted on the references of the obtained articles.

#### Data collection

The author's name, year of publication, study design (randomized clinical trial, crossover clinical trial, and semi-empirical), participants' dietary intake type, duration of intervention, the pistachio/day consumption dosage, and the duration of follow-up were determined. The characteristics of the participants were being healthy or sick, or having one of the risk factors for metabolic syndrome (dyslipidemia, hypercholesterolemia, hypertension, impaired fasting glucose, and obesity). The inclusion criteria consisted of studies which were conducted exclusively on the effects of pistachio on humans and metabolic syndrome or its risk factors. The exclusion criteria included studies on other nuts or the combination of pistachio with other nuts, and studies on animals. The survey was conducted without a time limit.

About 1259 articles were originally found. Articles which included interventions on almonds, walnuts, peanuts, hazelnuts, and

combination of other nuts with pistachios were excluded. Among the remaining studied, 15 articles were found, which were directly related to pistachios and measurement of indices of fasting glucose, lipid profile, blood pressure, obesity, and other risk factors.

## Results

In the present study, 15 studies conducted on the effects of pistachios on metabolic syndrome or its factors were reviewed (19,25-36,38). The results of these studies are shown in table 1. As seen in this table, the number of the study subjects ranged from a minimum of 17 to maximum of 90 people, and the intervention duration from 3 weeks to 24 months. Among them, 4 clinical trials were cross-sectional studies with washout duration of 8 hours in one study and 2 to 4 weeks in other studies. Moreover, 2 studies were quasi-experimental studies (23, 37).

### **Pistachios and metabolic syndrome**

Among the reviewed studies, 3 were on individuals with metabolic syndrome, 2 on individuals with diabetes, and 1 on individuals with prediabetes. The amount of pistachio consumed in these studies ranged from 45-90 g. In all 5 studies pistachio had positive effects on the assessed variables. In other words, the beneficial effects of this nut were shown on cardiometabolic profile or metabolic syndrome. In a study conducted on individuals with diabetes, systolic ambulatory blood pressure showed visible improvement, especially during bedtime.

### **The effects of pistachios on blood lipids and measurement of antioxidants**

The effects of pistachios on dyslipoproteinemia were investigated in 8 other studies. In all of these studies, blood lipids and lipoproteins, and in some of them, the amount of antioxidants and oxidizing substances were measured before and after the intervention. As can be seen in table 1, the positive effects of pistachios on these factors

were reported. Only in one study, no changes were observed in body mass index (BMI) and blood pressure, but the lipid profile improved as a result of pistachios consumption. In men with erectile dysfunction, pistachios improved lipid profile and also resolved this disorder.

### Pistachios and obesity

A study was conducted on obese individuals and the results showed that pistachios can cause weight loss and reduce triglycerides, but have no effect on cholesterol, insulin, glucose, and HDL serum cholesterol (Table 1).

**Table 1: pistachios' effect on metabolic syndrome and the factors of this syndrome in clinical interventions**

	Author	Year	N	The study population	Study duration	Study conclusion	Study design	References
1	Kendal	2014	30	Having metabolic syndrome	5-10 weeks 5 meals	Postprandial sugar reduction and increased peptides similar to glucagon	Clinical trial	27
2	Gulati	2014	60	Having metabolic syndrome	24 weeks Addition of pistachios to diet along with exercising	Improved metabolic profiles such as waist circumference, fasting glucose, total cholesterol, LDL, hs-CRP, TNF- $\alpha$ , FFAs, TBARS, and adiponectin compared to the control group	Clinical trial	34
3	Wang	2012	90	Metabolic syndrome without diabetes mellitus	4 weeks One group with 40 g and the other group with 70 g of pistachios	Reduced in glucose challenge test results, no change in triglycerides in the group with the higher dose of pistachios and no difference in the two groups, no change in body size or BMI, and waist-to-hip measurement	Clinical trial	26
4	-Sauder KA	2014	30	Diabetes	4 weeks with 2 weeks 20% washout of energy in pistachio diet with moderate fat	Reduced peripheral resistance, increased cardiac output Improved heart rate, reduced systolic ambulatory blood pressure with the greatest reduction during sleep time ( $5.7 \pm 2$ mmHg). Improved risk factors in well-controlled diabetes	crossover clinical trial	28
5	<u>Hernández-Alonso</u>	2014	54	Prediabetes	(57 g pistachios) 4 months 4 week washout period separated from the study duration	Reduction in fasting glucose, insulin resistance and other risk markers, such as fibrinogen, oxidized LDL, and platelet factor 4. Interleukin-6 mRNA and resisting gene expression, and an increase in glucagon-like peptide-1	crossover clinical trial	35
6	Sheridan	2007	15	Individuals with moderate hypercholesterolemia	4 weeks 15% energy from pistachios, 2-3 ounce per day	A significant reduction in TC/HDL-C, LDL-C/HDL-Cho, Increase in HDL-Cho No change in BMI, and blood pressure	crossover clinical trial	29
7	Kay	2010	28	Individuals with moderate hypercholesterolemia	4 weeks Used 2 pistachio dosages (1) 32-63 g (2) 63-125 g	Increased lutein, alpha-tocopherol, and beta-carotene, Reduced oxidized LDL	Clinical trial	19
8	Gebauer	2008	28	Dyslipidemia with high LDL	4 weeks with two doses of pistachios (1) 32-63 g/day (2) 63-126 g/day	Improved CVD risk factors such as dose-related LDL-cholesterol, total cholesterol, apolipoprotein B, apolipoprotein B/ apolipoprotein A and especially esteroil desaturase activity	Clinical trial	31
9	Holligan	2014	18	Healthy	One serving of pistachios	Reduced LDL and increased HDL	Clinical trial	36

				individuals with high LDL	per day with 30% fat and other diet containing 34% fat with two servings of pistachios	in the two servings of pistachios diet, Increased amount of beta-sitosterol in both groups of pistachios		
10	Kocyigit	2006	67	Healthy individuals	3 weeks pistachios replacement for 20% of daily energy	Reduction in total cholesterol, ratio of cholesterol to HDL, the MDA (oxidative stress reduction), and ratio of LDL to HDL	Clinical trials	30
11	Sari	2010	32 Man	Normolipidemic individuals	At first 4 weeks of Mediterranean diet and 4 weeks adding pistachios to the Mediterranean diet	Reduced cholesterol, LDL-C, triglycerides and fasting glucose, and total cholesterol ratio to HDL and LDL to HDL Improved endothelial function reduces IL-6, MDA Increased superoxide dismutase no effect on CRP, and aTNF	Quasi-experimenta 1	32
12	Edwards	1999	10	Individuals with moderate hypercholesterol emia	20% of energy from pistachios for 3 weeks	Lower cholesterol, decreased cholesterol ratio to HDL and triglycerides Increased HDL No change in body weight and blood pressure	crossover clinical trial	33
13	Li Z	2010		Obese subjects	12 weeks 53 g of pistachios	Weight loss and reduced triglycerides No impact on cholesterol, the good cholesterol, insulin, and glucose		25
14	-M Aldemir	2011	17 Married man	Individuals with erectile dysfunction	three weeks 100 g of pistachios	Decreased triglycerides, LDL cholesterol Increased HDL cholesterol Improved International Index of Erectile Function (IIEF) and penile color Doppler ultrasound (PCDU)	Quasi-experimenta 1	37
15	Parham	2014	48	Individuals with Diabetes	25 g of pistachios twice a day 12 weeks 8 hours of washout	Reduced HbA1c (-0.4%), fasting glucose (14 mg/d), blood pressure, and BMI	crossover clinical trial	38

**LDL: Low-density lipoprotein; HDL: High-density lipoprotein; CRP: C-reactive protein; BMI: Body mass index; TNF- $\alpha$ : Tumor necrosis factor- $\alpha$ ; FFAs: Free fatty acids; TBARS: Thiobarbituric acid reactive substances; MDA: Malondialdehyde; CVD: Cardiovascular disease; aTNF: anti tumor necrosis factor**

### Discussion

This investigation showed the positive effects of pistachios on individuals with metabolic syndrome, diabetes, dyslipidemia, obesity, and healthy subjects and normolipidemic individuals. The positive effects of pistachios on this syndrome, dyslipidemia disorders, and ultimately, prevention of CVD can be attributed to the special properties of this nut. It contains nutrients, which play an important role in the treatment and prevention of metabolic syndrome and its risk factors. Pistachios, compared to walnuts and almonds that have fatty acids, have

less fat and energy and more of other nutrients including potassium, vitamin K, phytosterols, phenolic acid, lutein, gamma-tocopherol, xanthophyll, and carotenoids (1, 18).

Furthermore, the distribution of fatty acids have an impact on the nutritional and physical properties of pistachios. Triglycerides and fatty acids in its structure affect, especially from a physical viewpoint, melting point and oxidation. In terms of nutritional benefits of pistachios, fatty acid patterns and the arrangement of the triglyceride structure can have a significant

impact on the lipid profile, chylomicrons size, and sterol ester metabolism. These effects lead to a reduction in CVD. Fatty acids in pistachios include palmitic, stearic, oleic, linoleic, and linolenic acids which are the fatty acids in carbon with the unsaturated second position. It has low amounts of palmitic acid which has the greatest impact on the incidence of heart disease. In addition, its amount of oleic acid is inversely related to linoleic acid. Meaning that by reduction of each of these two, the other value increases and the amount of these two fatty acids always remains constant. Iranian pistachios have a higher nutritional value than other countries. This is related to environmental conditions and storage. However, genetic factors and technology is also important. The results of the study by Mohammadi showed that Owhadi pistachios, compared to other varieties in Iran, have better nutritional properties because of the existence of linoleic acid in the second carbon position. Therefore, the Iranian pistachio can have beneficial effects on lipid profile, chylomicrons size, sterol ester metabolism, and prevention of MetS and cardiovascular problems (23).

Moreover, soluble and insoluble fiber can effect the treatment of hypercholesterolemia and prevent obesity and constipation (19). These important properties of pistachios have placed it among the most important nutritional standards in the prevention of chronic diseases. Regular consumption of pistachios does not cause weight gain, but reduces weight and BMI. Its energy is mostly excreted in the stool and a small amount of its energy is absorbed. In some interventions, the amount of measured fat in the stool was higher than normal during the intervention compared to before the intervention. Pistachio consumption can even prevent the increase in the distribution of body fat or obesity (23). Moderate consumption of pistachios may affect satiety, saturation, and satisfaction, and therefore, reduce energy consumption and help

with weight control (18). Pistachios can be used as a controlled snack for individuals with caloric restriction and can help in weight loss (25). Intake of Pistachio can cause insulin providence, lowered postprandial blood glucose and increased postprandial glucagon like peptide( GLP) (26). The antioxidants in pistachios reduce oxidizing agents such as malondialdehyde (MDA) and oxidized low-density lipoprotein (LDL) and prevent the formation of free radicals (27). Free radicals play an important role in the incidence of chronic diseases such as CVD, metabolic syndrome, and type 2 diabetes. In every 100 grams of pistachio there is 3-9 mg of vitamin E. Vitamin E ( $\alpha$ -tocopherol) is recognised as an essential lipophilic antioxidant in the diet protecting lipoproteins and making fundamental changes in lipid profile (18, 20). Therefore, it plays an important role in the prevention of CHDs. Moreover, through vasodilatation, inhibition of platelet aggregation, and prevention of adhesion it prevents atherosclerosis and angina (27). Vitamin E is effective in maintaining cell integrity and preventing diseases associated with free radicals (diabetes, metabolic syndrome, and cardiovascular complications) (20).

Arginine in pistachio causes the production of mediums such as nitric oxide. This oxide acts as a vasodilator and an antiplatelet. Lack of nitric oxide is associated with endothelial dysfunction and increased risk of heart disease. Therefore, pistachios can play a crucial role as a vasodilator substance in diets (18). Controlled pistachio consumption in diets of diabetic adults improves at least one main risk factor meaning blood pressure (28).

In the study by Gulati, in addition to exercising, the intervention group received pistachios (29). Compared to the control group, they had improved metabolic profiles such as waist circumference, fasting glucose, total cholesterol, adiponectin. They also showed improvements in

terms of LDL cholesterol, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), free fatty acids (FFAs), C-reactive protein (CRP), and thiobarbituric acid reactive substances (TBARS) (29).

Therefore, intervention with pistachios along with exercise can have beneficial effects on cardiovascular and metabolic profiles or MetS (29). According to the profile of nutrients in pistachios and the conducted clinical trials, adding pistachios to the diet of individuals with diabetes or metabolic syndrome or at risk of metabolic syndrome improves these risk factors. Therefore, including pistachios to the diet is a health strategy for improvement of cardiovascular and metabolic health (25).

In 2010, the US food guide recommended pistachio consumption in order to reduce the symptoms of metabolic syndrome, diabetes, and cardiovascular problems (18). Although the abovementioned studies have shown the positive effects of pistachios, some studies (16, 25, 29, 33) reported the lack of positive effect on BMI, glucose, and cholesterol. This may be due to heterogeneity between studies, the duration of study, the dose of pistachios, quantity and quality of carbohydrates, the type and quantity of fat, the gender of the participants, or subjects without disease and metabolic syndrome.

It is recommended that future studies be conducted on pistachio intervention with higher doses of pistachios, longer duration, larger sample size, subjects with similar conditions, healthy subjects or subjects with a risk factor, similar diets in terms of carbohydrate and fat quantity, type of activity, gender, and other possible mechanisms associated with nutrients of nuts and non-nutrient chemicals found in pistachios (16). In addition, the effects of higher doses of pistachios on the important indicator of blood sugar control (HbA1c) should be examined for a longer period of time to determine whether the acute beneficial effects of pistachios can last for longer durations.

## Conclusion

The results of the reviewed studies showed the positive effects of pistachios on adults with diabetes, metabolic syndrome, dyslipidemia, obesity, and healthy and normolipidemic adults. Although in 3 studies there were no changes in BMI, blood pressure, and glucose, in all 3 studies, the lipid profiles had improved. It seems that for the prevention and treatment of MetS and its risk factors, pistachio intake with dosage of 30-100 grams/ day can be useful. For a definite conclusion and determination of the maximum dosage, more clinical trials are needed.

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