

### Health and Nutrition Research Reference Guide

This Guide is intended to provide a quick reference to global human research on nuts generally and pistachios in particular. It is written for use by health professionals, with nutritionists and dietitians in mind and it is not intended for consumers. Animal studies looking at specific mechanistic aspects of the role of pistachios on health are also available, however these are not included within this guide.



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#### **Pistachios and Mortality**

'Epidemiological and/or clinical trials have suggested that nut consumption has a beneficial impact on health outcomes such as hypertension, diabetes, CVD, cancer, other inflammatory conditions and total mortality.'<sup>1</sup> A systematic review of 20 prospective cohort studies (Mayhew 2016) showed a 19% reduction in all-cause mortality with nut consumption.<sup>2</sup>

In a study published in the November 2013 issue of the New England Journal of Medicine, the association of nut consumption with total and cause-specific mortality was examined among 76,464 women in the Nurses' Health Study and 42,498 men in the Health Professionals Follow-up Study. Consumption of nuts was inversely associated with total mortality in both men and women, independent of other predictors for mortality.<sup>3</sup>

# Those who ate a portion of nuts (28 g / 1 oz) more than 7 times per week had a 20 percent lower death rate. Furthermore, consuming nuts was also associated with a lower risk of death due to cancer, heart disease and respiratory disease.<sup>3</sup>

Guasch-Ferré, et al. (2013) presented cross-sectional data from the beginning of the PREDIMED trial. They assessed 7,216 subjects and the association between the frequency and amount of nuts consumed by participants, compared to non-consumers. Those subjects who ate more than three servings of nuts, including pistachios, per week had a 39 percent lower mortality risk. Notably, the researchers also found similar reductions for cancer, with high cardiovascular risk and cardiovascular mortality risk.<sup>4</sup>

In the largest study published to date on nut consumption and mortality, van den Brandt, et al. (2015) investigated the relationship of nut (tree nut, peanut) and peanut butter intake with overall and cause-specific mortality in a Netherlands Cohort Study of 120,852 men and women aged 55–69 years. The authors found evidence of beneficial effects of nut intake on lower overall and cause-specific mortality (cancer, diabetes, cardiovascular, respiratory, neurodegenerative diseases and other causes excluding external injuries). Nut intake was inversely related to mortality, but peanut butter was not.<sup>5</sup>



<sup>1</sup> Bullo M, Juanola-Falgarona M, Hernandez-Alonso P, Salas-Salvado J. Nutrition attributes and health effects of pistachio nuts. Br J Nutr 2015;113 Suppl 2:S79-S93. 2 Mayhew A, de Souza R, Meyre D, Anand S, Mente A. A systematic review and meta-analysis of nut consumption and incident risk of CVD and all-cause mortality. British Journal of

Nutrition 2016; 115: 212–225. 3 Bao Y, Han J, Hu FB, Giovannucci EL, Stampfer MJ, Willett WC, Fuchs CS. Association of nut consumption with total and cause-specific mortality. N Engl J Med 2013;369:2001-2011.

<sup>4</sup> Guasch-Ferre M, Bullo M, Martinez-Gonzalez MA, Ros E, Corella D, Estruch R, Fito M, Aros F, Warnberg J, Fiol M, Lapetra J, Vinyoles E, Lamuela-Raventos RM, Serra-Majem L, Pinto X, Ruiz-Gutierrez V, Basora J, Salas-Salvado J. Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. BMC Med 2013;11:164. 5 Van den Brandt PA, Schouten LJ. Relationship of tree nut, peanut and peanut butter intake with total and cause-specific mortality: a cohort study and meta-analysis. Int J

Epidemiol2015;44:1038-1049.

#### **Pistachios and Antioxidants**

## Pistachios have a high antioxidant and anti-inflammatory potential, contributing to the growing body of evidence that consumption of pistachios improves health.<sup>1</sup>

Pistachios contain key phytochemicals that may provide antioxidant support for cardiovascular health, including carotenoids ( $\beta$ -carotene and lutein),  $\gamma$ -tocopherol and phenolic compounds such as anthocyanins, flavonoids, lignans, phenolic acids, and proanthocyanidins.<sup>2</sup>

Research published in *The Journal of Nutrition* (June 2010) suggests eating pistachios raises the levels of serum antioxidants, such as lutein and  $\gamma$ -tocopherol, which may contribute to lower levels of oxidised low-density lipoprotein cholesterol (LDL-C).<sup>3</sup> Higher amounts of oxidised LDL C and fat-breakdown products are found in atherosclerotic plaques. These substances are thought to play a role in the development and progression of atherosclerosis, the collection of fatty materials along the arteries. Strategies that reduce oxidative stress are believed to confer cardioprotective effects. This study validates the significant antioxidant benefits of consuming pistachios. A second study published in *Nutrition* showed that pistachio polyphenols, xanthophylls and tocopherols are more than 90 percent bioaccessible during digestion.<sup>4</sup>

## These nutrients contribute to the beneficial relationship between pistachio consumption and health-related outcomes.<sup>4</sup>



<sup>1</sup> Bullo M, Juanola-Falgarona M, Hernandez-Alonso P, Salas-Salvado J. Nutrition attributes and health effects of pistachio nuts. Br J Nutr 2015;113 Suppl 2:S79-S93. 2 Bolling BW, Chen CY, McKay DL, Blumberg JB. Tree nut phytochemicals: composition, antioxidant capacity, bioactivity, impact factors. A systematic review of almonds,

Brazils, cashews, hazelnuts, macadamias, pecans, pine nuts, pistachios and walnuts. Nutr Res Rev 2011;24:244-275. 3 Kay CD, Gebauer SK, West SG, Kris-Etherton PM. Pistachios increase serum antioxidants and lower serum oxidized-LDL in hypercholesterolemic adults. J Nutr 2010;140:1093-1098.

<sup>4</sup> Mandalari G, Bisignano C, Filocamo A, Chessa S, Saro M, Torre G, Faulks RM, Dugo P. Bioaccessibility of pistachio polyphenols, xanthophylls, and tocopherols during simulated human digestion. Nutrition 2013;29:338-344.

#### **Pistachios and Heart Disease**

'Pistachios are nutrient-dense nuts with a healthy nutritional profile including fibre, healthy fats, phytosterols and antioxidant compounds, contributing to a reduced risk of heart disease.'<sup>1</sup>



The World Health Organization recommends nuts as a nutrient-rich food high in unsaturated fats to include in a healthy diet for adults.<sup>2</sup>

A systematic review of 20 prospective cohort studies carried out by Mayhew et al (2016) compared CVD outcomes with the highest with lowest nut consumers. Results showed favourable and significant reduction in risk with nut consumption of CVD mortality (RR 0.73), total CHD (RR 0.66) and CHD mortality (RR 0.70).<sup>3</sup>

In February 2013, the landmark PREDIMED study published in the New England Journal of Medicine showed that a Mediterranean diet supplemented with nuts significantly reduced cardiac events. In this clinical trial of around 7,400 subjects with high risk of cardiovascular disease, those who ate a Mediterranean diet with either 30 g nuts per day or 1 litre of olive oil per week had approximately 30 percent risk reduction in heart disease-related events compared to the low fat control group.<sup>4</sup> Importantly, this risk reduction is the same as for statins, which are cholesterol-lowering drugs.<sup>4</sup>

The mechanism explaining the impact of pistachios on heart disease risk is likely to be more than just reductions in total cholesterol (TC) and LDL-C. Numerous studies have considered the effects of eating pistachios on several risk factors for cardiovascular disease.<sup>5-16</sup> These studies suggest that eating pistachios daily (28 g to 85.0 g or as 10 percent–20 percent of daily calorie intake) may reduce the risk of heart disease in seven ways:

- 1. Lowering TC, LDL-C and non-HDL-C in adults with elevated LDL cholesterol;<sup>5</sup>
- 2. Increasing antioxidants in the blood and decreasing oxidised LDL-C in hypercholesterolemic adults;6
- **3.** Decreasing small dense LDL-C and increasing β-sitosterol levels in the blood when following a moderate fat diet with 20% energy from pistachios compared to the control;<sup>7</sup>
- 4. Providing beneficial anti-inflammatory properties;<sup>8</sup>
- 5. Lowering systolic blood pressure, heart rate and peripheral vascular responses in adults with dyslipidemia;<sup>9</sup>
- 6. Reducing HDL-C particle size in subjects with pre diabetes;<sup>10</sup>
- 7. When coupled with lifestyle counselling, including exercise, improves lipid profile in dyslipidaemia by increasing HDL-C concentrations and reducing LDL-C, total:HDL-C ratio and fasting glucose levels.<sup>11</sup>

A randomised cross over study<sup>10</sup> reviewed the effect of daily consumption of 57g pistachios or a control diet for 4 months on cholesterol in 54 pre-diabetic adults. When on the pistachio diet significant changes to cholesterol occurred: HDL particle size reduced compared to baseline; and compared to the control HDL particle size, non-HDL particle concentration and small LDL concentration decreased, the proportions of small HDL particles increased, and the proportion of medium and large HDL particles decreased. The authors conclude that *'chronic consumption of pistachios shifts the lipoprotein size and particle profile to a less atherogenic pattern'*.

Kasliwal *et al* (2015) randomly assigned 52 adults with dyslipidaemia to one of the following groups<sup>11</sup> - exercise and diet counselling with or without the daily addition of 40g pistachios for 3 months. Daily pistachio consumption showed beneficial reductions in LDL-C, total:HDL-C and fasting blood glucose levels plus and an increase in HDL-C (p<0.05). Improvements were also noted in vascular function. No significant changes were seen in the control group. Additionally Sauder et al (2015) showed improvements in cholesterol, total:HDL-C, triglycerides and fructosamine (p<0.05) following 4 week on a pistachio supplemented diet (20% energy) in 30 adults with well controlled diabetes compared to a control in a randomised cross-over study.<sup>17</sup>

#### **Pistachios and Heart Disease**

In a randomised, controlled, cross-over feeding trial of 28 subjects with dyslipidaemia, West, et al. (2012) found that those consuming 10 percent of calories from pistachios had significant reductions in systolic blood pressure compared to the control diet (mean change in systolic blood pressure, -4.8 mmHg vs -1.8 mmHg, respectively; P<0.05). At the 20 percent calorie level, there were significant reductions in peripheral resistance (-62.1dyne·sxcm5) and heart rate (-3 bpm) versus the control diet (P<0.0001). These reductions in peripheral vascular constriction and the resulting decrease in haemodynamic load may be important factors in lowering the risk of cardiovascular disease in pistachio consumers.<sup>9</sup>

A systematic review and meta-analysis of published randomised controlled trials, Mohammadifard, et al. (2015) estimated the effect of nut consumption (single or mixed nuts) on the blood pressure of adult populations aged 18 years. The authors found that nut consumption significantly lowered systolic blood pressure in participants without type 2 diabetes (mean difference [MD]: -1.29 mm Hg; P=0.02) but not in the total population. Subgroup analyses of different nut types suggested that pistachios, but not other nuts, significantly reduced systolic blood pressure compared to the total population (MD: -1.82 mm Hg; P=0.002). The study also reported that pistachios (MD: -0.80 mm Hg; P=0.01) and mixed nuts (MD: -1.19 mm Hg; P=0.04) appear to have a significant reducing effect on diastolic blood pressure compared to the total population.<sup>6</sup>

#### A diet containing pistachios seems to significantly reduce both systolic and diastolic blood pressure.<sup>6</sup>



The beneficial effect of pistachios on blood lipid levels probably results from its nutritional composition. Per 28g portion, pistachios contain 13 g total fat, of which 3.7 g is polyunsaturated, 6.9 g is monounsaturated and 1.6 g is saturated. The plant sterol content is 59 mg, dietary fibre 2.9 g, protein 5.9 g, thiamine 0.19 mg and potassium 282 mg.<sup>18</sup> Pistachios are high in thiamine, which contributes to normal function of the heart and high in potassium, which contributes to the maintenance of normal blood pressure. Pistachios are high in unsaturated and mono-unsaturated fats, consuming pistachios instead of foods high in saturated fats can help maintain normal blood cholesterol.<sup>19</sup>

Published in 2010 in the Archives of Internal Medicine, a pooled analysis of 25 studies suggests eating nuts, such as pistachios, was significantly associated with lower TC and LDL-C, compared to control diets, further confirming the evidence that regular nut consumption can lower the risk of coronary heart disease. The analysis included 583 normo-lipidemic and hypercholesterolaemic men and women who were not on lipid-lowering medication. Those who consumed an average of 67 g of nuts per day had a mean estimated reduction in TC, LDL-C, LDL-C:HDL-C ratio and TC:HDL-C ratio of 5.1 percent, 7.4 percent, 8.3 percent and 5.6 percent, respectively. The effect of nuts was dose-related, and different types of nuts had similar effects on blood lipids.<sup>20</sup>

Two other PREDIMED study papers, published in 2013 in the Public Library of Science Online Journal and BioMed Central, presented cross-sectional data from the beginning of the trial. Both assessed over 7,200 subjects with high cardiovascular risk and the associations between the frequency and amount of nuts consumed. Those subjects who ate more than three servings of nuts per week, including pistachios, had a 39 percent lower mortality risk. Notably, the researchers also found similar reductions for cancer and cardiovascular mortality risk. A second cross-sectional analysis showed a lower incidence of obesity, including abdominal obesity, metabolic syndrome and diabetes in those subjects who ate more than three servings of nuts, including pistachios, per week.<sup>21,22</sup>

A Life Sciences Research Organization report (2013) that examined the effects of nuts, including pistachios, on heart disease concluded that 'Combining the results of the observational study analyses with the interventional study analyses meeting the FDA criteria, there is strong evidence that consumption of tree nuts has a beneficial effect on cardiovascular health and a real and practical effect in reducing the risk of CVD.<sup>23</sup>

#### **Pistachios and Heart Disease**

#### 'A moderate-fat diet containing pistachios modestly improves some cardiovascular risk factors in adults with well-controlled type 2 diabetes.'6

In a randomised, cross-over, controlled feeding study, Sauder, et al (2014) assessed the effect of pistachio consumption on blood pressure, systemic haemodynamics and heart rate variability in 30 adults with well-controlled type 2 diabetes. The 20% energy pistachio diet significantly reduced total peripheral resistance (-3.7 percent  $\pm 2.9$  percent; P=0.004), increased cardiac output  $(3.1 \text{ percent} \pm 2.3 \text{ percent};$ P=0.002) and improved some measures of heart rate variability compared to the low fat control diet (all P<0.05). Systolic blood pressure was significantly reduced by 3.0 mmHg  $\pm$  1.8 mmHg (P=0.046) following the pistachio diet compared to the low fat control diet.24



1 Bullo M, Juanola-Falgarona M, Hernandez-Alonso P, Salas-Salvado J. Nutrition attributes and health effects of pistachio nuts. Br J Nutr 2015;113 Suppl 2:S79-S93.

2 World Health Organization, Healthy diet factsheet, Available from: Http://www.who.int/mediacentre/factsheets/fs394/en/ [Accessed September 2015], 2015

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- 13 Kay CD, Gebauer SK, West SG, Kris-Etherton PM. Pistachios increase serum antioxidants and lower serum oxidized-LDL in hypercholesterolemic adults. J Nutr 2010:140:1093-1098.
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- 15 Sheridan MJ, Cooper JN, Erario M, Cheifetz CE. Pistachio nut consumption and serum lipid levels. J Am Coll Nutr 2007;26:141-148
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- 17 Sauder K, McCrea C, Ulbrecht J, Kris-Etherton P, West S. Effects of pistachios on the lipid/lipoprotein profile, glycemic control, inflammation, and endothelial function in type 2 diabetes: A randomized trial. Metabolism clinical and experimental. 2015; 64: 1521-1529.
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- 19 EU Register of nutrition and health claims made on foods http://ec.europa.eu/nuhclaims/
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- 24 Sauder KA, McCrea CE, Ulbrecht JS, Kris-Etherton PM, West SG. Pistachio nut consumption modifies systemic hemodynamics, increases heart rate variability, and reduces ambulatory blood pressure in well-controlled type 2 diabetes: a randomized trial. J Am Heart Assoc 2014;3.

#### **Pistachios and Cancer**

In a large prospective study published online in the *British Journal of Cancer*, researchers looked at the association between nut consumption, such as pistachios, and risk of pancreatic cancer among 75,680 women in the Nurses' Health Study. These women had no previous history of cancer.<sup>1</sup>

The researchers found that women who consumed a 28 g serving of nuts, such as pistachios, two or more times per week had a significantly reduced risk of pancreatic cancer compared with those who rarely ate nuts. Importantly, those who ate the most nuts tended to weigh less.<sup>1</sup>

1 Bao Y, Hu FB, Giovannucci EL, Wolpin BM, Stampfer MJ, Willett WC, Fuchs CS. Nut consumption and risk of pancreatic cancer in women. Br J Cancer 2013;109:2911-2916.

#### Pistachios, Weight Management and a Healthy Diet

Results from several studies suggest that adults who consume nuts, such as pistachios, versus those who do not, may have lower body weight, obesity and a lower prevalence of health risks such as heart disease and metabolic syndrome. They also have healthier diets.<sup>1-6</sup>

Furthermore, pistachios were used as a portion-controlled snack in a weight loss study. The participants in the study who ate 53 g pistachios daily improved their body mass index (BMI) and triglycerides compared with those who ate a refined carbohydrate snack. Both groups lost weight during the 12-week study.<sup>7</sup> Pistachios likely control weight through satiety signals, increased satiety and lower metabolisable energy.<sup>7-10</sup> Wilson et al (2014) noted no changes in body weight or BMI in 22 obese adults when a small dose (35g/1.25 ounces) of pistachios were consumed daily before bedtime for 6 weeks.<sup>11</sup>

In an observational survey, O'Neil, et al. (2013) found tree nut consumers had higher daily intakes of calories (2,468 calories vs 2,127 calories) and nutrients of concern: fibre (21 g vs 16 g), potassium (3,028 mg vs 2,691 mg), magnesium (408 vs 292 mg), monounsaturated fatty acids (MUFA) (36 g vs 29 g) and PUFA (21 g vs 17 g), but lower intakes of added sugars (15 teaspoons vs 18 teaspoons), SFA (25 g vs 27 g) and sodium (3,197 mg vs 3570 mg) than non-consumers. Tree nut consumers also had lower weight (80 kg vs 82 kg; P=0.0049), BMI (28 kg/m2 vs 29 kg/m2; P<0.0001) and waist circumference (96 cm vs 98 cm; P=0.0006) compared with non-consumers. In addition, those who consumed tree nuts had lower systolic blood pressure (120 mmHg vs 122mmHg; P=0.0120) and higher HDL-C (good cholesterol) (55 mg/dL vs 53 mg/dL; P=0.0020).<sup>2</sup>

In another study by O'Neil, et al (2015), National Health and Nutrition Examination Survey (NHANES) 2005–2010 data were used to examine the associations of tree nut consumption with health risks in 14,386 adults aged  $\geq$ 19 years. Tree nuts included almonds, Brazil nuts, cashews, hazelnuts, macadamias, pecans, pine nuts, pistachios and walnuts. Group definitions were non-consumers <7 g/day and consumers of  $\geq$ 7 g/day tree nuts. Tree nut consumption, including pistachios, was associated with lower BMI (P=0.004), waist circumference (P=0.008), systolic blood pressure (p=0.001), Homeostatic Model Assessment-Insulin Resistance (P=0.043) and higher HDL-C (P=0.022), compared with no consumption, and a lower likelihood of obesity (–25 percent), overweight/obesity (–23 percent) and elevated waist circumference (–21 percent).<sup>6</sup>

In a mixed nut study, a PREDIMED cross-sectional analysis of 7,210 subjects from the beginning of the trial showed those subjects who ate more than three servings of nuts, including pistachios, per week had a lower incidence of obesity, including abdominal obesity, metabolic syndrome and diabetes.<sup>12</sup>

In June 2013, Flores-Mateo, et al. reported in the American Journal of Clinical Nutrition the results of a meta-analysis of 33 clinical nut-feeding studies that compared a control diet with a diet containing nuts and weight outcomes. The researchers found that compared with control diets, nuts, including pistachios, did not significantly increase body weight, waist circumference or BMI. Differences between the groups were: weight: –0.47 kg, 95% Cl: –1.17, 0.22 kg; BMI:–0.40 kg/m2, 95% Cl: –0.97, 0.17 kg/m2; and waist circumference: –1.25 cm, 95% Cl: –2.82, 0.31 cm.<sup>13</sup>

In a review of published nut research, Vadivel, et al. (2012) reported evidence that points to the prevention of obesity and other health benefits with consumption of nuts, including pistachios. This review reaffirms that whereas nuts are nutrient and energy dense, the research does not support that increased consumption may lead to unwanted body weight gain. In fact, the opposite was found: that eating nuts in moderate amounts

does not increase body weight. Also, because of their energy density, protein and high-fibre content, tree nuts are satisfying, which the authors suggested may reduce overeating. The authors conclude from the studies to date that 'frequent nut consumption may lower the risk of obesity in healthy subjects and those with the metabolic syndrome'. The authors also concluded that the inclusion of nuts, such as pistachios, in amounts of around 30–50 g per day 'is advisable to ensure various health benefits without the risk of body weight gain.<sup>14</sup>



#### **Pistachios, Weight Management** and a Healthy Diet

#### Four research studies on pistachios suggest that pistachios likely control weight through increased satiety and satiety signals to reduce calorie consumption.7-10

Li, et al. (2010), in a randomised, parallel, isocaloric, reduced-calorie, weight loss study in overweight and obese subjects (N=59), used pistachios or pretzels as a portion-controlled snack (approximately 230 calories). Unsurprisingly, both groups lost weight during the 12-week study. The participants in the study who ate pistachios significantly improved their BMI (-4.3 percent vs -2 percent, P<0.05) and triglycerides (P<0.01) compared with those who ate a refined carbohydrate snack.<sup>8</sup>

Kennedy-Hagen, et al. (2011) and Honselman, et al. (2011) found that in-shell pistachios have a unique effect on reducing caloric intake.<sup>9,10</sup> The first study, used a randomised crossover design and subjects – a convenience sample of faculty and staff at a Midwestern university (N=118) – were given two bowls, one with pistachios to consume through the working day and another in which to place the empty shells. When the bowl with empty shells was left unemptied for the day, the subjects were more mindful of the amount they consumed, resulting in the consumption of significantly fewer calories (P<0.05).<sup>10</sup>

In the second study, a convenience sample (N=140) were asked to evaluate brands of pistachios as kernels and in-shell as well as feelings of fullness and satisfaction after self-selection of a portion of pistachios. Subjects offered the in-shell pistachios consumed an average of 125 calories, whereas subjects offered pistachio kernels consumed an average of 211 calories, a difference of 86 calories. Interestingly, fullness and satisfaction ratings were not significantly different. The authors suggested that consumption was lower when consuming in-shell pistachios possibly due to the time taken to shell the pistachios; the additional volume noted when consuming in shell pistachios; and the empty shells acting as a visual cue.<sup>9</sup>

Growing evidence suggests that nut consumption, including pistachios, improves diet quality and provides a number of bioactive compounds that help with weight management, glycaemic control and vascular health.<sup>15</sup>

'Evidence points to tree nuts, including pistachios playing a useful role in the prevention of obesity and other health benefits.'14

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<sup>8</sup> Li Z, Song R, Nguyen C, Zerlin A, Karp H, Naowamondhol K, Thames G, Gao K, Li L, Tseng CH, Henning SM, Heber D. Pistachio nuts reduce triglycerides and body weight by comparison to refined carbohydrate snack in obese subjects on a 12-week weight loss program. J Am Coll Nutr 2010;29:198-203.

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<sup>15</sup> Bullo M, Juanola-Falgarona M, Hernandez-Alonso P, Salas-Salvado J. Nutrition attributes and health effects of pistachio nuts. Br J Nutr 2015;113 Suppl 2:S79-S93.

#### Pistachios, Blood Glucose, Diabetes and Insulin Sensitivity

## Pistachios and Other Cardiometabolic Effects Including Blood Glucose, Diabetes and Insulin Sensitivity.

Since the 2003 U.S. Food and Drug Administration approved health claim for nuts and heart disease, there has been an increase in the number of studies showing the potential benefits of tree nut consumption, including pistachios, on blood glucose, diabetes, metabolic syndrome and insulin sensitivity.

As part of the EPIRDEM (Effect of Pistachio Intake on insulin Resistance and Type 2 Diabetes Mellitus) study 54 subjects (25-65yo) with pre-diabetes took part in a randomised, controlled, cross over trial. Subjects consumed a pistachio supplemented diet (57g/d) or control (containing olive oil) for 4 months each with a 2 week wash out period. Diets were matched for energy, protein, fibre and saturated fat. The results of this study population indicated some beneficial effects in those with pre-diabetes whilst on the pistachio diet:

- 1) Significant (p<0.05) reductions in fasting blood sugar and insulin levels, and a beneficial effect on insulin resistance HOMA-IR, a marker of pre-diabetes<sup>1</sup>
- 2) Some signs of inflammation, specifically GLP-1 & IL-18, decreased significantly from baseline (p<0.05)<sup>1</sup>
- 3) Positively altered the expression of some microRNAs which are related to insulin metabolism and type 2 diabetes<sup>2</sup>

Two acute studies suggest that pistachios attenuate the rise in blood glucose after a meal when combined with high carbohydrate foods, both in healthy persons and in those with metabolic syndrome.<sup>3,4</sup>

Kendall, et al. (2011) conducted two acute feeding studies that examined the effects of pistachio consumption on postprandial glucose levels.<sup>3,4</sup> Pistachios, when fed alone to 10 healthy subjects, at portion sizes of 28 g, 56 g or 84 g, have little effect on blood sugar levels. Pistachios, when fed with a carbohydrate-rich meal, lowered the blood glucose response in a dose-dependent manner, e.g. the higher the dose of pistachios, the more the blood glucose level was lowered or attenuated. Pistachios, (56.7 g) added to different common carbohydrate foods, such as rice and pasta, significantly reduced the relative blood glucose response of the carbohydrate meals with which they were eaten.<sup>3</sup>

In a second study in persons (N=20) with metabolic syndrome, Kendall, et al. (2014) found similar results.<sup>4</sup> The researchers examined the effect of pistachios on postprandial glucose and insulin levels compared with five study meals that varied in the amount and type of fat, but were matched according to available carbohydrates. Within each group of available carbohydrate meals, postprandial glucose levels were the highest following the white bread-only meal and attenuated when pistachios were consumed (P<0.05). Compared with white bread, pistachio consumption reduced postprandial glycaemia, increased glucagon-like peptide 1 levels and may have insulin-sparing properties, which could be beneficial for individuals with diabetes and metabolic syndrome.<sup>4</sup>

Gulati, et al. (2014), in a 24-week, randomised, controlled trial of 60 Asian Indians with metabolic syndrome, examined the effects of 20 percent of calories from pistachios, as part of a diet that met the Asian Indian dietary guidelines, on their cardiometabolic profile. The pistachio intervention group compared with the control group had significantly improved fasting blood glucose (P<0.04), TC (P<0.02), LDL-C (P<0.006), waist circumference (P<0.02), and high-sensitivity C-reactive protein (hs-CRP; P<0.05). A diet containing pistachios may improve the cardiometabolic profile of those with metabolic syndrome.<sup>5</sup>

#### Pistachios, Blood Glucose, Diabetes and Insulin Sensitivity

#### Compared with a low-fat diet, a Mediterranean diet enriched with nuts could be beneficial for the management of metabolic syndrome.<sup>6</sup>

Three additional mixed nut studies that included pistachios have been conducted on individuals with diabetes 2 or metabolic syndrome.<sup>7,8,9</sup> The results from the largest randomised clinical trial to date on nuts and diabetes showed a significant reduction in HbA1c, a long-term marker of blood sugar control, and a significant reduction in LDL-C.8 This 3-month parallel design study was conducted on 117 non-insulin-dependent adults with diabetes (mean age of 62 years) who were treated with oral hypoglycaemic medications. The subjects were randomised to one of three diets for 12 weeks. All diets included a supplement of 475 kcal per 2,000-kcal diet and met American Diabetes Association and National Cholesterol Education Program Step II recommendations. The first diet included 75 g of mixed nuts (including pistachios); the second diet included 37.5 g of mixed nuts and a half portion of muffins; and the third diet contained a full portion of muffins. Those subjects receiving 75 g of mixed nuts had significantly reduced LDL and TC levels (P<0.001) compared with the full dose muffin group, and a significant reduction in HbA1c (P<0.001) compared with the other two diets.

The results of a large epidemiological cohort study at Harvard suggested that frequent tree nut and peanut butter consumption (five 28 g servings per week) is associated with a significantly lower cardiovascular disease risk in women with type 2 diabetes. Tree nut and peanut butter consumption is also associated with a better lipid profile, including lower concentrations of LDL C and TC.<sup>9</sup>

Jaceldo-Siegel, et al. (2014), as part of the Adventist II trial, examined tree nut consumption and risk of metabolic syndrome in 803 adults. The researchers found that high tree nut consumption (mean of 16 g/day) was associated with a lower occurrence of metabolic syndrome and obesity. The risk for metabolic syndrome was significantly less, by 7 percent, if 28 g of tree nuts per week was consumed. Those who were high tree nut consumers also had a significantly lower prevalence of obesity (P=0.0007) compared with the low tree nut consumers.7

A systematic review and meta-analysis of the effect of tree nuts on criteria of metabolic syndrome was conducted by Blanco Mejia, et al (2014). Eligibility criteria were met by 49 randomised controlled trials including 2,226 participants who were otherwise healthy or had dyslipidaemia, metabolic syndrome or type 2 diabetes. Pooled analyses demonstrated a metabolic syndrome benefit of tree nuts through modest decreases in triglycerides and fasting blood glucose with no adverse effects on other criteria across nut types.<sup>10</sup>

In a double-blind, randomised, placebo-controlled, crossover trial, Parham, et al (2014) evaluated the effectiveness of pistachio nut supplementation on glycaemic measures in 48 patients with type 2 diabetes. Patients received a snack of 25 g pistachio nuts twice a day for 12 weeks or a control meal without nuts. An 8-week washout was followed by a crossover. The authors found a marked decrease in HbA1c (-0.4 percent) and fasting blood glucose concentrations (-16 mg/dL) in the pistachio group compared with the control group (P≤0.001 for both).<sup>11</sup>

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<sup>10</sup> Blanco Mejia S, Kendall CW, Viguiliouk E, Augustin LS, Ha V, Cozma AI, Mirrahimi A, Maroleanu A, Chiavaroli L, Leiter LA, de Souza RJ, Jenkins DJ, Sievenpiper JL. Effect of tree

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#### **Pistachios and Men's Health**

#### Diet plays an important role in men's health.

## Adding nutrient-rich foods like pistachios to the diet can give men a nutritional boost.

Pistachios have a wealth of nutrients that are important for overall health, including phytosterols, antioxidants, healthy fats, fibre, protein and potassium. Nutrition experts recommend pistachios as a satisfying snack that can benefit men, and women, of all ages.

#### **ANTIOXIDANTS**

Pistachios contain antioxidant nutrients such as vitamin E, copper, manganese, selenium, zinc, riboflavin, polyphenols and the carotenoids lutein and zeaxanthin that may play a beneficial role in heart health. Studies suggest that adding pistachios to a healthy diet may help to lower levels of oxidised LDL-C and other measures of oxidative damage. These factors are thought to be involved in the hardening of the arteries, one of the main causes of heart attacks and stroke, and the leading cause of death among men. One study found that eating one serving (32-63g) of pistachios daily may help to raise antioxidant levels in the blood.1 Scientists believe that boosting blood antioxidant levels is one mechanism of how pistachios may protect from heart disease.<sup>1</sup>

While further studies are needed to confirm the results, emerging evidence also suggests that antioxidants may help with muscle recovery. Pistachios are a natural source of the antioxidants lutein,  $\alpha$ -carotene and  $\gamma$ -tocopherol, and laboratory studies suggest that pistachios have a strong antioxidant capacity.<sup>1</sup>

Each year, an estimated 17 million people die of cardiovascular diseases, particularly heart attacks and strokes. A substantial number of these deaths can be attributed to physical inactivity and unhealthy diet, which increase individual risks to cardiovascular diseases.<sup>4</sup>



#### **Pistachios and Men's Health**

#### **ERECTILE DYSFUNCTION**

Pistachios are high in unsaturated and mono-unsaturated fats, consuming pistachios instead of foods high in saturated fats can help maintain normal blood cholesterol. Pistachios are also high in thiamin which contributes to a normal heart function, and are a high source of fibre.<sup>5</sup> They also contain the amino acid arginine, which appears to enhance blood flow by boosting nitric oxide, a compound that relaxes blood vessels. These heart-protective properties of pistachios prompted scientists to investigate the effect of a pistachio diet on erectile function.<sup>6</sup>

Erectile dysfunction can accompany heart disease or vascular problems because relaxation of blood vessels (the processes required to sustain an erection) can become impaired. To find out if pistachios could help men suffering from chronic erectile dysfunction, researchers added 100 g of pistachios each day to the diet of 17 married male patients. After 3 weeks, the men showed marked improvements in a number of measures of erectile function including sexual intercourse satisfaction, orgasmic function, sexual arousal and overall satisfaction. In addition, peak systolic velocity in the penis increased 22 percent.<sup>6</sup>

While more research is needed to confirm the results, emerging research suggests that eating pistachios may improve circulation to penile tissues and so improve sexual performance in men suffering from erectile dysfunction.<sup>1</sup>

Pistachios are a source of selenium, which contributes to normal spermatogenesis, and a source of zinc, which contributes to normal fertility and reproduction; and the maintenance of normal testosterone levels in the blood.<sup>5</sup>

#### **PHYTOSTEROLS**

Phytosterols are plant-derived substances that have been shown to lower blood cholesterol levels by interfering with the absorption of cholesterol from other foods.<sup>7</sup> Early human diets were rich in phytosterols, but today's typical diet is quite low by comparison.<sup>8</sup> Pistachios have the highest levels of  $\beta$ -sitosterol – a type of phytosterol – among nuts.<sup>3</sup> Some clinical trials also suggest that phytosterols may help maintain normal prostate health.<sup>9</sup>



#### **Pistachios and Men's Health**

#### **PROTEIN & EXERCISE**

Another primary concern for men is maintaining lean body tissue and muscle tone over the years. This requires a workout routine that includes both strength training and cardiovascular exercise. Additionally, a healthy diet can support the processes that happen within muscle tissue after exercise to promote muscle growth and prevent fatigue.

Research has shown that eating protein is beneficial for muscle recovery when consumed after intense exercise, <sup>10</sup> pistachios are a source of protein which contribute to the maintenance of muscles.<sup>5</sup> With 6 g of protein per 28 g serving, pistachios make an ideal post exercise snack. The Academy of Nutrition and Dietetics suggests refuelling with a mix of protein and carbohydrates 15–20 minutes post exercise for optimal muscle repair and recovery and to replenish muscle glycogen stores.<sup>11</sup> A 28 g serving of pistachios, along with a serving of fruit and adequate water, makes a great snack after a particularly strenuous workout.

#### **B VITAMINS**

100g pistachio provide over 15 percent of the daily Reference Intake of thiamin (B1), riboflavin (B2) and pyridoxine (B6) and as such pistachios are a source of these three vitamins that contribute to normal energy-yielding metabolism.

#### POTASSIUM

Finally, pistachios are a high source of potassium, which is a major electrolyte that plays an important role in normal body functions, contributing to nerve and muscle function. A 28 g serving of pistachios actually has as much potassium as half of a large banana.

Potassium also benefits muscle in another way: while further studies are needed to confirm the results, initial research suggests that eating foods rich in potassium may help preserve muscle in older adults.<sup>12</sup> This is important because muscle mass gradually declines after age 50, and muscle loss leads to muscle weakness. which can affect quality of life.12

Additionally, it is now recognised that including sources of potassium, such as pistachios, in the diet contributes to maintaining normal blood pressure.<sup>5</sup>

Food is more than just fuel. Eating right can help men to feel good while improving their health. Small gradual changes towards healthy eating can make a big difference. So rather than reaching for a bag of crisps/chips, biscuits or other processed snack foods, choose pistachios instead!

<sup>1</sup> Kay CD, Gebauer SK, West SG, Kris-Etherton PM. Pistachios increase serum antioxidants and lower serum oxidized-LDL in hypercholesterolemic adults. J Nutr 2010-140-1093-1098

<sup>2</sup> Sousa M, Teixeira VH, Soares J. Dietary strategies to recover from exercise-induced muscle damage. Int J Food Sci Nutr 2014;65:151-163

<sup>3</sup> Bullo M, Juanola-Falgarona M, Hernandez-Alonso P, Salas-Salvado J. Nutrition attributes and health effects of pistachio nuts. Br J Nutr 2015;113 Suppl 2:S79-S93. 4 World Health Organization, World atlas, Available from: http://www.who.int/cardiovascular\_diseases/resources/atlas/en/ [Accessed September 2015] 2015.

<sup>5</sup> EU Register of nutrition and health claims made on foods http://ec.europa.eu/nuhclaims/

<sup>6</sup> Aldemir M, Okulu E, Neselioglu S, Erel O, Kayigil O. Pistachio diet improves erectile function parameters and serum lipid profiles in patients with erectile dysfunction. Int J ImpotRes 2011;23:32-38

<sup>7</sup> Scientific Opinion on the substantiation of health claims related to plant sterols and plant stanols and maintenance of normal blood cholesterol concentrations (pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010; 8(10):1813.

<sup>8</sup> Jew, S, AbuMweis, S & Jones, P. Evolution of the human diet: Linking our ancestral diet to modern functional foods as a means of chronic disease prevention. J Med Food 2009; 12(5).

<sup>9</sup> Wilt TJ, MacDonald R, Ishani A. beta-sitosterol for the treatment of benign prostatic hyperplasia: a systematic review. BJU Int 1999;83:976-983.

<sup>10</sup> The Nutrition Society Textbook Series. Sport and Exercise Nutrition. Ed: Lanham-New, Stear, Shirreffs, Collins, Wiley-Blackwell, published 2011. 11 Mohr CR. Timing your nutrition. Academy of Nutrition and Dietetics (2012). Available from:

http://www.eatright.org/resource/fitness/exercise/exercise-nutrition/timing-your-nutrition.[Accessed September 2015].
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#### **Pistachios as a Post Exercise Snack**

### American pistachios are a powerhouse of important vitamins, minerals and nutrients that help support active lifestyles.

The ideal post exercise snack is portable, satisfying and supplies the body with the energy and important nutrients it needs to refuel after exercise. Pistachios can help to meet the post exercise needs of casual fitness enthusiasts and athletes.

Physical activity is an essential component of a healthy lifestyle but can sometimes lead to exercise-induced muscle damage and sore muscles from oxidative stress and inflammation. This can lead to a decline in muscle activity and delayed recovery. While further studies are needed to confirm the results, emerging evidence suggests that antioxidants may help with muscle recovery.1 Pistachios are a natural source of the antioxidants lutein,  $\beta$ -carotene and  $\gamma$ -tocopherol,<sup>2</sup> and laboratory studies suggest that pistachios have a strong antioxidant capacity.<sup>3</sup>

# Among nuts, pistachios have a lower fat and energy content and the highest levels of potassium, γ-tocopherol, vitamin K, phytosterols, xanthophyll carotenoids, certain minerals (Cu, Fe and Mg), vitamin B6 and thiamin.<sup>2</sup>

Pistachios offer far more than just calories and protein for active people. They also have hard to-get nutrients, they are a source of magnesium and phytochemicals. Pistachios are also a good source of copper and manganese. In fact, research shows that nut eaters tend to have a diet with overall higher nutrient quality.<sup>2</sup> Additionally, in a randomised cross over controlled feeding study, Kay, et al. (2010) found that people eating one or two servings of pistachios had greater levels of plasma lutein,  $\beta$ -carotene and  $\gamma$ -tocopherol compared to the low fat control diet.<sup>3</sup>

The body loses potassium with sweat during intense exercise. Potassium is a major electrolyte that plays an important role in normal body functions, such as nerve function and muscle control. Include potassium-containing foods along with water to help replenish this important mineral after exercise.<sup>4</sup>

The typical serving size of pistachios is 28g, or about 49 kernels – more nuts per serving than any other nut! While these green kernels are a calorie-dense food, research suggests that nut eaters do not weigh more than people who avoid nuts.<sup>5</sup> Not only do pistachios take longer to crack open; their high nutrient density (protein, unsaturated fat and fibre) contributes to satiety,<sup>6</sup> which in turn may help keep you feeling fuller longer.

<sup>1</sup> Sousa M, Teixeira VH, Soares J. Dietary strategies to recover from exercise-induced muscle damage. Int J Food Sci Nutr 2014;65:151-163.

Bullo M, Juanola-Falgarona M, Hernandez-Alonso P, Salas-Salvado J. Nutrition attributes and health effects of pistachio nuts. Br J Nutr 2015;113 Suppl 2:S79-S93.
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<sup>3</sup> Kay CD, Gebauer SK, West SG, Kris-Etherton PM. Pistachios increase serum antioxidants and lower serum oxidized-LDL in hypercholesterolemic adults. J Nutr 2010;140:1093-1098.

<sup>4</sup> Mohr CR. Timing your nutrition. Academy of Nutrition and Dietetics (2012). Available from: [Accessed September 2015].

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<sup>5</sup> Flores-Mateo G, Rojas-Rueda D, Basora J, Ros E, Salas-Salvado J. Nut intake and adiposity: meta-analysis of clinical trials. Am J Clin Nutr 2013;97:1346-1355. 6 Li Z, Song R, Nguyen C, Zerlin A, Karp H, Naowamondhol K, Thames G, Gao K, Li L, Tseng CH, Henning SM, Heber D. Pistachio nuts reduce triglycerides and body weight by

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	Nutrient content per 100 g <sup>1</sup>	per 28 g (approx. 49 pistachios)
Energy	2429kJ / 586 kcal	680kJ / 164 kcal
Fat	46 g	13 g
of which		
- saturates	5.6 g	1.6 g
- mono-unsaturates	25 g	6.9 g
- polyunsaturates	13 g	3.7 g
Carbohydrate	17 g	4.8 g
of which		
- sugars	7.7 g	2.2 g
Fibre	10 g	2.9 g
Protein	21 g	5.9 g
Salt	1.1 g	0.3 g

VITAMINS & MINERALS	per 100 g	% Reference intake per 100 g
Vitamin E	2.2 mg	18
Vitamin K	13 µg	18
Thiamin	0.7 mg	63
Riboflavin	0.23 mg	17
Vitamin B6	1.1 mg	80
Folic acid	51 µg	26
Potassium	1010 mg	50
Phosphorus	469 mg	67
Magnesium	109 mg	29
Iron	4 mg	29
Zinc	2.3 mg	23
Copper	1.3 mg	129
Manganese	1.2 mg	62
Selenium	10 µg	18
Chromium	39 µg	98

Reference intake of an average adult (8,400 kJ/ 2,000 kcal)

1 United States National Nutrient Database for Standard Reference. Release 28 Software v.2.3.2. The National Agricultural Library. Nuts, pistachio nuts, dry roasted, with salt added. http://ndb.nal.usda/gov/ndb/search





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