RESEARCH ARTICLE

THERAPEUTIC EFFECTS OF NUTS IN VARIOUS DISEASES

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ABSTRACT

Nuts are recommended as an important constituent of a healthy diet in human populations throughout the world. Various types of nuts such as almonds, Brazil nuts, hazelnuts, macadamia nuts, peanuts, pecans, pine nuts, pistachios, walnuts, and cashews are commonly consumed by human beings, although individual intake varies remarkably. Nut consumption has been associated with several health benefits, such as antioxidative, hypcholesterolemic, cardioprotective, anticancer, anti-inflammatory, and antidiabetic benefits, among other functional properties. However, although nuts possess these many health benefits, their consumption has been hampered by a lack of adequate information regarding those benefits. The present article provides an overview that focus on human trials that have dealt with regular consumption of various nuts and its impact on cardiovascular diseases, weight management, gallbladder diseases, Immunostimulant action, and hypoglycaemia.

INTRODUCTION

Since prehistoric times, as nuts are evident for their favorable fatty acid and nutrient profiles, there is growing interest in evaluating their role in a healthy diet and have also been widely consumed in many different cultures. Nuts contain a wide variety of antioxidants, including vitamin E, selenium, copper, manganese and also other phytochemicals such as flavonoids, resveratrol and ellagic acid and are increasingly associated with an overall healthy lifestyle and reduced risk of disease. Nuts are especially, a rich sources of selenium. These help protect the body from a range of lifestyle related diseases. Just like fruits and vegetables, the specific content of plant compounds varies from nut to nut. The most common types of nuts consumed worldwide include tree nuts and peanuts. Brufau et al., 2006 defined tree nuts as dry fruits with one seed in which the ovary wall becomes hard at maturity. The most popular edible tree nuts are almonds (Prunus amygdalis), hazelnuts (Corylus avellana), walnuts (Juglans regia), and pistachios (Pistachia vera). Other common edible nuts are pine nuts (Pinus pinea), cashews (Anacardium occidentale), pecans (Carya illinoiensis), macadamias (Macadamia integrifolia), and Brazil nuts (Bertholletia excelsa). Similarly Ros et al., 2006 defined peanuts (Arachis hypogea), as groundnuts or legumes which are widely identified as part of the nuts food group. In addition, peanuts have a similar nutrient profile to tree nuts. When compared with other nuts groundnut is widely used in India.

In almost all countries, nuts are consumed as snacks, desserts or part of a meal, and are eaten whole (fresh or roasted), in spreads (peanut butter, almond paste), as oils or hidden in commercial products, mixed dishes, sauces, pastries, ice creams and baked goods. In the last century, nut consumption in most industrialized nations followed a sliding trend to become only a subsidiary source of energy in the daily diet, except for vegetarians and other health-conscious populations, such as Seventh Day Adventists. However, nut consumption has increased in recent times following both the inclusion of this food group in many guidelines for healthy eating and wide media coverage of recent evidence connecting nut consumption to a wide range of health benefits. Since then, nuts have become an indispensable component of healthy diets. National health and medical research council of Australia released a food guidance system in 2010 suggesting that 2 and 14 serves of nuts a week is required, where a serve is 30 g and is dependent on age, gender, energy needs, and if pregnant or lactating. However, when building total diets from the foundation diet, a 30 g serve daily can be included at all energy levels modelled. Nut consumption also has a favorable effect on various chronic diseases as demonstrated by numerous supplementation studies involving almonds, hazelnuts, Macadamia, peanuts, pistachios, walnuts, and mixed nuts.

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Nutritional Benefits of Nuts

Nuts are a particularly nutrient dense food, comprising of a range of nutrients which can contribute to a reduced risk of coronary heart disease and maintaining heart health. These include healthy fats, dietary fibre, arginine, plant sterols and range of vitamins and minerals known to be important for heart health, including folate, magnesium, potassium, zinc, copper and vitamin E\(^3\) (Nuts for Life, 2011).

- Nuts are high in fat but are rich in the healthy fats\(^32\) – monounsaturated and polyunsaturated fats which are important for cholesterol lowering\(^33\). Walnuts are also a rich source of alphalinolenic acid (ALA a plant-based omega-3 fat)\(^32\). Research has shown that ALA from walnuts can reduce inflammation\(^34\), similar to omega-3 fats from fish and also inflammatory disease mortality\(^35\).
- Nuts are high in fibre\(^32\), including soluble fibre which can assist with reducing blood cholesterol levels by lowering cholesterol reabsorption from the gut\(^36\).
- Nuts are a good source of protein, and in particular a rich source of arginine\(^37\) – a building block of protein. This amino acid is converted to nitric oxide in the body which causes blood vessels to dilate and remain elastic and is involved in preventing blood clotting. Hardening of the arteries and blood clotting can lead to heart disease\(^38,39\).
- Nuts are rich in vitamin E, an important antioxidant vitamin which may protect LDL (bad) cholesterol from attaching to, and blocking blood vessel walls\(^38,39\).
- Nuts are a good source of folate, which can reduce blood homocysteine levels. High levels of homocysteine are associated with an increased CVD risk\(^40,41\). Nuts contain plant sterols including beta-sitosterol, campesterol and stigmasterol\(^42\). Plant sterols can reduce total and LDL cholesterol levels by lowering cholesterol reabsorption from the gut\(^42\). This suggests that the plant sterol content of nuts may contribute to their cholesterol lowering effect.
- Nuts are a rich source of minerals including magnesium, copper, zinc, potassium and selenium\(^43\), all of which may play a role in heart health. Magnesium intake is associated with a reduced risk diabetes, metabolic syndrome, high blood pressure and CVD\(^43\) (Bo S.), potassium can assist with blood pressure control\(^44\) and copper, zinc and selenium are antioxidants\(^45\).
- Nuts also contain momentous amounts of squalene and tocopherols. Squalene has important beneficial effects on health and tocopherols are powerful antioxidants, which in high doses may reduce the risk of CHD\(^46\). One of the most developed theories for its cardioprotective effect appears to be pertaining to tocopherol induced inhibition of LDL oxidation, which is proposed to be a key role in the atherogenic process\(^47\). Kornsteiner et al.,\(^48\) states that the Low quantities of tocopherol which can be obtained from average nut consumption are beneficial to CHD patients\(^49\).

Nutrient Content of Nuts

Nutrient content of nuts are exemplary. With the exception of chestnuts, which contain little fat, nuts have a high total fat content, ranging from 46% in cashews and pistachios to 76% in macadamia nuts, and they provide 20 to 30 kJ/g (Table 1). Thus, nuts are one of the natural plant foods richest in fat after vegetable oils. However, the fatty acid composition of nuts is beneficial because the saturated fatty acid (SFA) content is low (4-16%) and nearly half of the total fat content in most nuts is made up of unsaturated fat, monounsaturated fatty acids MUFA (oleic acid), mostly linoleic acid in Brazil nuts, a large number of PUFA over MUFA in pine nuts, and mostly PUFA, both linoleic acid and α-linolenic acid (ALA), the plant omega-3 fatty acid, in walnuts\(^50\). With regard to walnuts, it is the only whole food with the highest content in ALA of all edible plants\(^51\).

Pharmacological Actions of Nuts

Walnuts and CVD

From the study of Sabate, et al.,\(^52\); Abbey, et al.,\(^53\); Chisholm, et al.,\(^54\); Zambon, et al.,\(^55\); Almario, et al.,\(^56\); Iwamoto, et al.,\(^57\); Ros, et al.,\(^58\) the effects of walnut intake on biomarkers of atherosclerotic CVD or on disease outcomes were evaluated in several controlled intervention studies with normo- or hyperlipidemic human subjects. Measurements were made on serum/plasma lipids and lipoproteins, plasma total fatty acid and lipid classes, and RBC fatty acids\(^59-66\). The results from these intervention trials were consistent in showing decreases in total cholesterol and LDL with intakes equivalent to 2 to 3 oz of walnuts daily with no significant adverse effects as reported by Ros, et al.,\(^57\). Cortes et al.,\(^58\) suggested that walnuts may protect the body’s arteries from the harm associated with eating a meal in saturated fat. The researchers hypothesized that walnuts would reverse post prandial endothelial dysfunction associated with consumption of fatty meal and from the study results they concluded that adding walnuts to a high fat meal improved flow mediated dilation independently of changes in oxidation, inflammation, or plasma asymmetric dimethylarginine\(^59\).

In another study of hypercholesterolemic men and women emphasising walnuts in a Mediterranean diet (over other monounsaturated fat rich foods) resulted in greater improvement in endothelium dependent vasodilation and greater reductions in levels of vascular cell adhesion molecule –1 compared to the standard Mediterranean diet. However, reductions in cholesterol were correlated with increased dietary ALA and LDL E tocopherol levels, both reflecting walnut composition\(^56\). Scientifically Omega-3 PUFAs, L-arginine, tocopherol, phenolic antioxidants, folic acid, and magnesium have been associated with healthy endothelial function. As reported by Ros 2009 walnuts are rich in all of these components, and have been shown to improve endothelial function in intervention studies\(^58\). Similarly in this line, European Food Safety Authority (EFSA) has approved a health claim in 2011, which states that a daily consumption of 30 g of walnuts contributes to an improved EDV (endothelium dependent vasodilation)\(^59\).

Similar trends were seen in a meta-analysis of walnut feeding studies measuring effects on serum lipid levels and other risk factors for CVD\(^60\). Compared to other tree nuts which contain abundant MUFA, walnuts contain mostly PUFAs, namely the omega-3 FA, α-linolenic acid and the omega-6 linoleic acid. The meta-analysis covered 13 studies including 365 subjects total. Subjects had normal cholesterol levels in 4 studies, modest hypercholesterolemia in 6 studies, and either diabetes, obesity, or metabolic syndrome in each of the 3 remaining studies. The meta-analysis revealed a decrease in total cholesterol of 10.29 mg/dL and 9.23 mg/mL in LDL cholesterol after a walnut diet compared to controlled diets (weighted mean difference; \(P < 0.001\) for both values).
HDL cholesterol levels did not change significantly, and although the change in triglycerides was not significantly different, there was a larger decrease after the walnut diet versus baseline than after the control diet.

Walnut and Weight Management

Sabate et al., conducted a randomized, crossover trial and found a minimal weight gain in the subjects who ate 28 to 56 g of walnuts daily for 6 months40. Jenkins et al., reported that the weight gain associated with walnut consumption was considerably lower than the predicted level41, whereas Almario et al., observed no significant change in body weight and the percentage of body fat from walnut consumption42. Similarly Banel and Hu reviewed 13 studies involving 365 participants who were administered with walnut-containing diets for 4 to 24 wk. Walnut diets ranged from 10-24% of total calories. The results showed that the walnut containing diets produced significantly greater decreases in TC and LDL-C concentrations compared with the control diets. At the same time, HDL-C and triacylglycerols were not significantly affected by the walnut diets compared with the control diets. Thus, they concluded that walnut consumption had no adverse effect on body weight43.

Walnut and Antioxidants

Reiter et al., (2005) showed that walnuts are a source of melatonin, a hormone that protects cell against oxidative damage in experiment rats44. Canales et al.,2007 conducted a non blinded, cross-over, placebo-controlled trial randomly assigned 22 volunteers (60% overweight and 40% obese) to a walnut meal (WM) or control meal (CM) during two different 5 week periods. The volunteers given the WM had significantly increased serum catalase (CAT) activity, total glutathione and oxidized glutathione (GSSG) in comparison with CM45. Studies of walnuts rich in polyunsaturated fatty acids (PUFAs) have shown a resistance of LDL to in vitro oxidative stress46,47. Thus, the tocopherols and other antioxidants present in walnuts likely prevent the potential adverse effects of increasing the LDL content of PUFAs. Polyphenolic phytochemicals isolated from walnuts have shown to be effective inhibitors of plasma and LDL oxidation in ex vivo experiments conducted by Ansterson et al.,200148, which are claimed to be beneficial to health. Mandalari et al., demonstrated the prebiotic activity of almond seeds by investigating the potential prebiotic effect of almond seeds in vitro by using mixed fecal bacterial cultures. Two almond products, finely ground almonds (FG) and defatted finely ground almonds (DG), were subjected to a combined model of the gastrointestinal tract which included in vitro gastric and duodenal digestion, and the resulting fractions were subsequently used as substrates for the colonic model to assess their influence on the composition and metabolic activity of gut bacteria populations. FG significantly increased the populations of bifidobacteria and Eubacterium rectale, resulting in a higher prebiotic index (4.43) than was found for the commercial prebiotic fructooligosaccharides (4.08) at 24 h of incubation49. In the same way, from the study of Gibson et al.,(1995), it is understood that almonds altered the composition of gut bacteria by stimulating the growth of bifido bacteria and Eubacterium rectale49.

Almonds and Immunostimulant Action

Adriana Arena, et al., evaluated in their study, that with almonds, high levels of cytokine production were observed i.e., interferon-α (INF-α), interleukins (IL-12), INF-gamma and tumour necrosis factor (TNF-α). Their data suggested that almonds improved the immune surveillance of the peripheral blood mono nuclear cells towards viral infections. Almonds also were found to induce a

<table>
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<th>Nuts</th>
<th>Energy (kJ)</th>
<th>Fat (g)</th>
<th>SFA (g)</th>
<th>MUFA (g)</th>
<th>PUFA (g)</th>
<th>PUF (g)</th>
<th>LA (g)</th>
<th>ALA (g)</th>
<th>Protein (g)</th>
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SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; LA, linoleic acid; ALA, α-linolenic acid.

significant decrease in the Herpes simplex virus (HSV-2) replication93.

Almonds and Hypoglycaemic Action

The ethanolic extract (250 and 500mg/kg) of the leaves, flowers and seeds of almonds were taken up by Shah et al.,(2011) to evaluate its anti diabetic activity against normal and streptozotocin induced diabetic mice. The oral administration of the extract for 21 days resulted in a significant reduction in the blood glucose levels. At the end of the experiment (15th day), the blood glucose levels were 80.6 ± 1.8 and 77.6 ± 1.4 mg/dl in the diabetic mice which were treated with 250 and 500 mg/kg b. w. of the leaf extract respectively. The flower and seed extracts, at a dose of 500mg/kg b. w., also showed significant reduction (P< 0.001) in the blood glucose levels of the diabetic mice on the 15th day of the study81.

Jenkins et al.,(2006) conducted a study in fifteen healthy individuals, 7 men and 8 women, with an age of 26.3 ± 8.6 years were studied. All the subjects completed 5 study sessions, each lasting 4hours, with a minimum 1 week washout between the tests. The subjects consumed the control meal on 2 occasions, and the almond, parboiled rice, and mashed potato meals only once. The blood glucose concentration over the 4 hour testing for each meal revealed that the almond (55±7) and rice meals (38±6) showed lower values than that of the instant mashed potato meal (94± 11) (P<0.003). The almond and rice meal glycaemic index values did not differ (P = 0.25). Similarly, the post-prandial glucose peak heights for the almond (5.9 ± 0.2 m mol/L) and rice (5.8 ± 0.1 m mol/L) meals were lower than the peak heights for the potato meal (6.6 ± 0.2 m mol/L) and the control white bread (6.9 ± 0.2 mmol/L) (P< 0.001). Finally from the study it was concluded that Almonds decrease post-prandial glycaemia and oxidative damage in healthy individuals82.

Almonds and Hypertension

There are promising results that regular nut consumption can attenuate an already existing hypertension, like that of Jenkins et al.,(2008) who were able to show with almonds17. In this one-year trial the participants lowered their blood pressure significantly (systolic: -4.2 ± 1.3 mmHg, diastolic: -2.3 ± 0.7 mmHg) through a vegetarian diet with almonds, whereby people with higher blood pressure responded more strongly to this dietary treatment83.

Hazelnuts and Cardiovascular Diseases

Among tree nuts, hazelnut plays a major role in human nutrition and health because of its unique fatty acid composition (predominantly MUFA), fat soluble bioactives (tocopherols and phytosterols), vitamins (vitamin E), essential minerals (selenium), essential amino acids, antioxidant phenolics (caffeic acid), dietary fiber (soluble), bioactives and phytochemicals84,85. In addition to MUFA, some other components found in hazelnut have been reported to reduce plasma total and LDL cholesterol concentrations, including PUFA86,87, phytosterols88,89 and soluble dietary fiber90,91. Moreover, hazelnut is an excellent source of vitamin E82, which has been shown to reduce the risk of CHD93. This cardioprotective effect appears to be due to vitamin E-induced inhibition of LDL oxidation84. Finally, whole nuts including hazelnut may provide a variety of non-fat cardioprotective constituents including arginine86 and copper94. Besides its nutritional value, the presence of distinctive taste- and aroma-active components of hazelnut may have positive influence in increasing its consumption84,85.

Mercangil et al.,(2006) found that eating 1 serving/ day of hazelnuts favourably altered multiple plasma lipid variables and reduced the risk of coronary heart disease. The consumption of 40g/day (approximately 1-1/3oz) of hazelnuts by hypercholesterolemic adult men resulted in significance increase in monounsaturated fatty acid(MUFA)intake. Both dietary cholesterol concentration and body weights of subjects remained stable throughout the study. The study showed that a high- fat and high- MUFA-rich hazelnuts diet was superior to low fat control diet because of favourable changes in plasma lipid profiles, thereby positively affecting the coronary heart disease risk profile97.

Hazelnuts and Hypercholesterolemia

Tey et al.,(2011) conducted a randomized crossover study with three phases, in which 48 mildly hypercholesterolemic participants were asked to consume 30g of ground, sliced or whole hazelnuts for 4 weeks. Body weight, plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triacylglycerol (TAG), apolipoprotein (apo) A1, apo B100 and α-tocopherol were measured at baseline and at the end of each dietary phase. However, in the results when compared with baseline, mean values at the end of each hazelnut intervention were significantly higher for HDL-C (P = 0.023) and α-tocopherol (P = 0.005), and significantly lower for TC (P < 0.001), LDL-C (P < 0.001), TC:HDL-C ratio (P < 0.001), apo B100 (P = 0.002) and apo B100:apo A1 ratio (P < 0.001), with no significant difference in body weight (P = 0.813). Moreover from the study results it was underlined that a daily consumption of 30 g hazelnuts led to a significant improvement of the α-tocopherol status in subjects with hypercholesterolemia98.

Pistachio and Cholesterol

Koci et al., (2006) studied the effects of the consumption of pistachio nuts on plasma lipid profile and oxidative status in 24 healthy men and 20 healthy women with normal lipid levels. The subjects consumed their regular diets for the first one week period and after that half of the subjects(12 men and 10 women)were randomised to a group fed with regular diet and the other half were randomized to a group fed pistachios, which involved nuts for 20% of their daily caloric intake for three weeks. After three weeks the mean plasma total cholesterol, malondialdehyde(MDA) levels, and total cholesterol/HDL and LDL/HDL ratios were significantly decreased, while HDL and antioxidant potential (AOP) levels and AOP/MDA ratios were significantly increased in the subjects on the pistachio diet. The results indicate that the consumption of pistachios nuts decreased oxidative stress and improved total cholesterol and LDL levels in healthy volunteers99. Similarly, in an analysis of the phytosterol(cholesterol- lowering properties)content of nuts and seeds, Phillips et al., (2005) found that of the products typically consumed as snack foods in the united states, Pistachios and sunflower kernels were the richest sources of phytosterols(270-289mg/100g)100. Although most feeding trial use high dose of over 2 grams of phytosterols a day, Ostund’s studies showed beneficial effects of reduced cholesterol absorption at lower levels, similar to the levels found in plant-based diets with pistachios101.
Pistachios and Hypertension

In the study of “Diets containing pistachios reduce systolic blood pressure and peripheral vascular responses to stress in adults with dyslipidemia. Hypertension” investigated by West et al.,2006 found reduction in the systolic blood pressure after eating 42 g or 84 g pistachios respectively (−4.8 mmHg resp. −2.4 mmHg) together with a significant decrease in the peripheral resistance of the blood vessels (−62.1 dyne × s/cm²) and the heart rate (−3 bpm) after eating 84 g¹⁰².

Pistachios and Cancer

In the study of Rezaei et al.,2012 “Induction of apoptosis and cell cycle arrest by pericarp polyphenol-rich extract of Baneh in human colon carcinoma HT29 cells” reported a greater impact of a pistachio extract on HT29 cells (cell cycle arrest, inhibition cell growth and increased apoptosis) compared to the common anti-cancer drug Doxorubicin¹⁰⁹.

Pecans and Cholesterol

Morgon and Clayshulte, 2000 conducted a randomized, controlled, parallel study involving 19 healthy adults who followed either a control diet(no nuts) or a pecan diet which included 68 grams of pecans per day (with no addition nuts). After eight weeks of the study it was found that, those following the pecan diet had a 6% decrease in LDL compared to the baseline value. Effects of total cholesterol, HDL and TG were not significant¹⁰⁴. Haddad et al., (2006) conducted found that eating pecans every day may inhibit unwanted oxidation of blood lipids. The aim of the study was to determine whether plasma concentrations of tocopherols and measures of antioxidant capacity and oxidative stress are affected by the consumption of pecans. The results presented evidence of the potential protective effects of pecan consumption in healthy individuals¹⁰⁸.

CONCLUSION

According to current knowledge, the consumption of nuts can be fully recommended as part of a healthy diet, but a regular consumption of a sufficient portion size is necessary for both prophylactic and clinical applications of nuts. Therefore, the U.S. Food and Drug Administration recommend 42.5g of nuts per day.¹⁰⁶ However, bioactive compounds presents in tree nuts play an important role in health promotion and the prevention of chronic diseases. These components beneficially alter serum lipid profiles, protect against oxidative stress and inflammation, and improve insulin sensitivity. The beneficial attributes in nuts are ascribed to a number of bioactive compounds that synergistically or/and additively reduce the risk factors for various chronic diseases.

References


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197