Review

Health benefits of nuts in prevention and management of diabetes

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The effects of tree nuts on risk factors for coronary heart disease (CHD), in particular blood lipids, have been investigated in a number of studies and the beneficial effects are now recognized. The beneficial effects of nuts on CHD in cohort studies have also been clearly demonstrated. However, while there is also reason to believe the unique micro- and macronutrient profiles of nuts may help to control blood glucose levels, relatively few studies have investigated their role in diabetes control and prevention. Nuts are low in available carbohydrate, have a healthy fatty acid profile, and are high in vegetable protein, fiber and magnesium. Acute feeding studies indicate that when eaten alone nuts have minimal effects on raising postprandial blood glucose levels. In addition, when nuts are consumed with carbohydrate rich foods, they blunt the postprandial glycemic response of the carbohydrate meal. Despite the success of these acute studies, only a limited number of trials have been conducted with nuts in type 2 diabetes. These studies have either been of insufficient duration to observe changes in HbA1c, as the standard measure of glycemic control, or have been underpowered. Therefore, more long-term clinical trials are required to examine the role of nuts on glycemic control in patients with prediabetes and diabetes. Overall, there are good reasons to justify further exploration of the use of nuts in the prevention of diabetes and its micro- and macrovascular complications.

Key Words: nuts, cardiovascular disease, coronary heart disease, diabetes, glycemia

INTRODUCTION

Diabetes is associated with micro- and macrovascular complications including, blindness, kidney failure, limb amputation and cardiovascular disease (CVD).[1] The prevalence of diabetes has increased dramatically over the past three decades and current estimates predict a further 50% increase worldwide by the year 2030.[2] The outlook is even worse for developing countries, with a forecasted increase in incidence of 69%.[2] The rise in diabetes rates has been linked to the adoption of a sedentary lifestyle, the increased prevalence of obesity and a changing diet, which has moved away from traditional whole foods and become more reliant on processed foods.

Whole grains, fruit, nuts/seeds, green leafy vegetables, which are staple foods in many developing regions of the world, have been linked to a reduced risk of developing diabetes.[3] Of the aforementioned dietary components, tree nuts are of great interest, because of their unique macro- and micronutrient profile. Frequent consumption of nuts has been linked to lower risk of all-cause mortality[4] and more specifically, in many observational and clinical studies to a lower risk of heart disease[5,6] and to a lower risk of diabetes in the Nurses Health Study.[7] However, despite plausible mechanisms of action for CHD risk reduction, the role of nuts in prevention and management of diabetes has not been studied extensively. The aim of this review is to provide an overview of the current evidence in the area of nuts and diabetes.

NUTS & HEALTH

In western societies, nuts were quite recently considered to be high fat and therefore unhealthy foods. However, this perception has changed over the past decade, as it has been recognized that nuts have a healthy fatty acid profile and nut consumption has been associated with reduced BMI and advocated in weight maintaining diets.[8] The metabolic benefits of nuts stem from their macro- and micronutrient profile. Nuts are low in saturated fat and recognized as a rich source of 'healthy' fats, mono- and polyunsaturated fatty acids (MUFAs and PUFAs, respectively), as well as vegetable protein, fiber, phytosterols, polyphenols, vitamins and minerals (Table 1). Evidence suggests that the macronutrient profile and bioactive

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Table 1. Nutritional profile of commonly consumed, whole, natural nuts (per ounce/28 grams)[†]

	Almonds	Cashews	Pecans	Pistachios	Walnuts
Total Energy, *kcal*	163	157	196	159	185
Protein, *g*	6	5.2	2.6	5.8	4.3
Carbohydrates, by difference, *g*	6.1	8.6	3.9	7.8	3.9
Fiber, total dietary, *g*	3.5	0.9	2.7	2.9	1.9
Sugars, total, *g*	1.1	1.7	1.1	2.2	0.7
Total Lipids, *g*	14	12.4	20.4	12.9	18.5
Saturated fatty acids, *g*	1.1	2.2	1.8	1.6	1.7
Monounsaturated fatty acids, *g*	8.8	6.7	11.6	6.8	2.5
Polyunsaturated fatty acids, *g*	3.4	2.2	6.1	3.9	13.4
Phytosterols,[‡] *mg*	34	44.8	28.9	60.7	20.4
Minerals, *mg*					
Calcium	75	10	20	30	28
Iron	1.1	1.9	0.72	1.1	0.8
Sodium	0	3	0	0	1
Potassium	200	187	116	291	125
Magnesium	76	83	34	34	45
Phosphorus	137	168	79	139	98
Zinc	1	1.6	1.3	0.6	0.9
Copper	0.3	0.6	0.3	0.4	0.5
Manganese	0.7	0.5	1.3	0.3	1
Selenium	0.7	5.6	1.1	2	1.4
Vitamins,[§] *mg*					
Vitamin C	0	0.1	0.3	1.6	0.4
Thiamin	0.1	0.1	0.2	0.2	0.1
Riboflavin	0.3	0	0	0	0
Niacin	1	0.3	0.3	0.4	0.3
Pantothenic acid	0.1	0.2	0.2	0.1	0.2
Vitamin B-6, *μg*	0	0.1	0.1	0.5	0.2
Folate, total, *μg*	14	7	6	14	28
Vitamin B-12, *μg*	0	0	0	0	0
Vitamin A, *IU*	0	0	16	118	6
Vitamin E (total tocopherols)	7.7	1.9	7.6	7.3	6.7

[†]US Department of Agriculture Agricultural Research Service. Nutrient Data Laboratory. http://www.nal.usda.gov/fnic/foodcomp/search. Accessed November 15, 2009.
[‡]Adapted from Segura et al.[15]
[§]Mg unless otherwise stated

components of nuts are responsible for their "heart healthy" effect. It has been proposed that the bioactive compounds may help lower the risk factors of CVD by improving endothelial function,[9] blood pressure[10] and the serum lipid profile,[6,11] in addition to lowering oxidative stress[12,13] and inflammation.[9,14] Although not studied extensively, the folate content of nuts may contribute to lower serum homocysteine concentrations, which may potentially reduce the risk of heart disease.[15,16]

Nuts have also been linked to the risk of developing type 2 diabetes. According to the American Diabetes Association,[17] glycemic control is of crucial importance for prevention and management of diabetes.[17] Evidence suggests that when eaten alone or in combination with mixed meals, the low available carbohydrate content of nuts can help lower the postprandial glucose and insulin responses and, as such, play a beneficial role in glycemic control.[12,18] As previously mentioned, nuts are high in MUFAs and PUFAs. It has been suggested that high MUFA diets can also improve glycemic control[19] possibly by displacing the carbohydrate in the diet and thereby effectively decreasing its glycemic load. However, the potential benefit of nuts may involve other mechanisms as well. Nuts are excellent sources of magnesium. A recent meta-analysis of the prospective studies showed that the intake of magnesium is inversely related to the risk of developing type 2 diabetes.[20]

While nuts are nutrient dense foods and there is a fear of increased energy intake with nut consumption, nut consumption has been associated with lower BMI.[8] The addition of nuts to the diet, in moderation, may therefore, enhance palatability and nutrient quality of the diet without posing a threat for weight gain.[21]

NUTS & CARDIOVASCULAR DISEASE

The protective effect of nuts against the risk of CHD has been demonstrated in a number of cohort studies. A pooled-analysis of results from four major cohorts (Nurses' Health Study (NHS), The Iowa Women's Health Study (IWHS), Adventist Health Study and Physician' Health

Study),[22-25] showed that, in comparison to little or no nut intake, nut consumption of greater than 4 times per week may reduce the risk of death from CHD by 37%.[26] Data from intervention studies, primarily of hyperlipidemic subjects, have added important mechanistic support for these findings by linking nut consumption to reduced serum cholesterol levels. Two recent systematic reviews showed that the intake of 40-100 grams of nuts, 5 or more times per week, can reduce LDL-cholesterol (LDL-C) 3-19% in comparison to Western or lower fat diets.[6,27] These finding were supported by a 2009 meta-analysis that showed the intake of 25-168 grams per day of almonds leads to significant reductions in total cholesterol (TC) and LDL-C (p = 0.03 and p = 0.05, respectively).[28] Other nuts also improve the blood lipid profile in terms of CHD risk. For instance, three recent clinical trials demonstrated that 50-100 grams per day of pistachio nuts significantly improved HDL-cholesterol (HDL-C).[29-31] Overall, the majority of cohort studies indicate that nut consumption decreases risk of developing CHD and clinical studies demonstrate that nuts improve the blood lipid profile. Walnuts and almonds in the Indo-Mediterranean diet study of men after myocardial infarction showed a protective effect in preventing reinfarction.[32] The strength of the data has prompted the United States Food and Drug Agency (USFDA) to approve a qualified health claim for nuts and serum cholesterol reduction.[33]

NUTS & DIABETES

Since patients with type 2 diabetes are at a higher risk of developing heart disease, it is important to determine if the intake of nuts can produce similar cardio-protective effects in this high-risk population. A number of studies have addressed this issue. A 2009 analysis of women with type 2 diabetes from the NHS cohort showed that those consuming 5 or more servings of nuts and peanuts per week had significantly lower serum LDL-C levels and overall, a 44% lower risk of developing CVD in comparison to those who almost never consumed nuts.[34] A number of clinical trials have examined this effect as well. Tapsell et al. have looked at the effect of walnuts on lipid parameters of patients with type 2 diabetes in two separate clinical interventions.[35,36] In the first trial, a 6-month parallel study, 58 diabetics were assigned to three diets: 1) a conventional low fat control diet, 2) a low but modified fat diet higher in the long-chain omega-3 fatty acids, and 3) a low fat plus 30 g/d walnut diet high in the short chain omega-3 fatty acid. The diet supplemented with 30g of walnuts significantly reduced LDL-C and increased HDL-C in patients with type 2 diabetes.[36] However, the second study, a 12-month parallel trial, consisting of two arms: 1) low fat diet without walnuts and 2) low fat diet with 30g/d of walnuts showed only a significant reduction in LDL-C and a significant increase in HDL-C from baseline in both groups and no significant between treatment effects.[35] One limitation of these studies is that the baseline LDL-C levels of the patients were relatively low (less than 2.9 mmol/L) and in the second study[35] the baseline HDL-C were somewhat high (approximately 1.5 mmol/L). This would make it difficult to attain statistically significant reductions in LDL-C or further increases in HDL-C. A 4-week cross-over study by Lovejoy et al.[37] looked at the effect of 4 diets (high fat, high almond; low fat, high almond; high fat control (olive oil); low fat control) on lipid parameters of diabetic patients. The high fat, high almond group resulted in the greatest reduction in TC, however, this reduction was mostly due to reductions in HDL-C.[37] Overall, the study failed to show that almonds were more effective than other MUFA sources in reducing blood lipid parameters in patients with type 2 diabetes. The patients in this study, similar to those by Tapsell et al.[35,36] had serum LDL-C levels below 3 mmol/L. Furthermore, this study compared the effect of various sources of MUFA on lipid parameters. It may be that the beneficial effect of nuts on serum lipids depends on the level of MUFAs and not on their specific source. Lastly, Scott et al.,[38] in a 42-week intervention in 35 patients with metabolic syndrome or diabetes, showed that a standard therapeutic American Heart Association[22] diet (15% MUFA – no almonds) and a high protein, high MUFA (22% with almonds) diet lead to similar reductions in lipid parameters in a 42-week intervention. However the authors cited the small sample size, high dropout (12 out of 35 patients dropped out within the first 6 weeks) and weight loss as possible confounders.[38] It is also important to consider that the control diet was a “heart healthy” diet, which would expectedly result in significant reductions in blood lipids. Thus the addition of almonds to this heart healthy diet provided no additional benefits on blood lipids in patients with type 2 diabetes.

Overall, there is strong evidence from cohort studies that nuts decrease cardiovascular disease risk and in clinical studies that nut consumption improves the blood lipid profile in hyperlipidemic subjects. However, there is limited evidence for a link between nuts and an improved blood lipid profile for patients with type 2 diabetes. This points to the need for more, long-term clinical interventions of nuts in type 2 diabetes. However, it is possible that nuts may improve markers other than serum lipids in patients with type 2 diabetes. The changes in these risk factors may in part account for the strong inverse association between nut intake and the risk of CVD observed in the cohort study of women with type 2 diabetes.[34]

NUTS & GLYCEMIC CONTROL

While current evidence indicates that the frequent intake of nuts is protective against CHD, the effect of nuts on the risk of developing type 2 diabetes is not as conclusive. Two cohort studies (NHS, IWHS), which only included women, have evaluated the effect of nut consumption on the risk of developing type 2 diabetes.[7,39] However, these two studies have reported conflicting results. The results from the NHS cohort show a 27% reduction in the risk of developing diabetes in individuals who consumed nuts five or more times per week compared with those who rarely or never ate nuts (RR of 0.73 (95% CI: 0.60-0.89).[7] However data from the IWHS cohort did not show a link between nut/peanut intake and the risk of developing type 2 diabetes.[39]

Despite the inconsistencies in the cohort findings, there are reasons to believe that nuts may reduce the risk of developing diabetes. Adequate glycemic control is crucial for prevention and management of type 2 diabetes.[17] Foods that elicit low post-meal glucose and insulin

Table 2. Effect of nuts on markers of glycemic control in long term clinical interventions

Author (Year)	Length	Design	Number of Subjects (m:f)	Study population	Control/Background Diet	Treatment Diet(s) (Dose)	Outcome Measures[†]	Between-Treatment Results
Lovejoy (2002)a[37]	4 weeks	Not Controlled	20 (10:10)	Healthy	Habitual diet	Almonds (100g/d) + Habitual diet	1) Fasting glucose 2) Fasting Insulin 3) Glucose Effectiveness 4) Insulin sensitivity index	No significant changes in any of the parameters in comparison to baseline
Lovejoy (2002)b[37]	4 weeks	Cross-over	30 (13:17)	Type 2 diabetes	1) high-fat control (HFC; 37% total fat, 10% from the MUFAs olive or canola oil) 2) low-fat control (LFC; 25% total fat, 10% from olive or canola oil)	1) Almonds (10% total energy: 57-113g/d) + HFA 2) Almonds (10% total energy: 57-113g/d) + LFA	1) Fasting glucose 2) Fasting Insulin 3) 2-hr glucose 4) 2-hr Insulin 5) HbA1c	No main effect of fat source or fat level on any glucose or insulin parameters
Scott (2003) [38]	42 weeks	Parallel	35 (N/A)	Metabolic syndrome & Type 2 Diabetes	American Heart Association diet (15% protein, 30% fat, and 15% MUFAs)	Almonds + High Protein, High Fat (25% protein, 40% fat, and 22% MUFAs)§	Fasting glucose	1) No difference between treatments 2) glycemic control was normalized in all 10 patients with impaired fasting glucose; it was also normalized in 2 and reduced to impaired fasting glucose in 3 of 7 patients with diabetes[‡]
Tapsell (2004) [36]	6 months	Parallel	58 (34:24)	Type 2 Diabetes	Low fat diet (<30% fat) Modified low fat (using exchange lists inclusive of fatty acids considerations	Walnuts (30 g/d) + modified low fat diet	HbA1c	No between treatments differences in HbA1c
Estruch (2006) [10]	3 months	Parallel	772 (339:433)	High CVD Risk[¶]	Low Fat diet	1) Mixed nuts (30 g/d of almonds, hazelnuts & walnuts) + Mediterranean diet 2) Olive oil (1 L/wk) + Mediterranean diet	1) Fasting glucose 2) Fasting insulin[††] 3) HOMA[††]	1) All three parameters were significantly lower in the two Mediterranean diets in comparison to the control 2) No significant differences between the two Mediterranean diets
Mukuddem-Petersen (2007) [43]	8 weeks	Parallel	64 (29:35)	Metabolic syndrome	20% protein, 33% fat	1) Cashew nuts (20% of total energy: 63 - 108 g/d) 2) Walnuts (20% of total energy: 63 - 108 g/d)	1) Fasting glucose 2) 2-hr glucose 3) Fructosamine	1) Fasting glucose increased significantly in the cashew nut group in comparison to the control (p = 0.04) 2) No between treatments differences in 2-hr glucose and fructosamine
Tapsell (2009) [35]	12 months	Parallel	50 (N/A)[€]	Type 2 Diabetes	20% protein, 30% fat, 15% MUFA, 5% PUFA	Walnuts (30 g/d) + control (10% MUFA, 10% PUFA)	1) Fasting glucose 2) Fasting insulin 3) HbA1c	1) No between treatments differences in glucose and HbA1c 2) Greater reduction in fasting insulin in walnut group (p = 0.046)

[†]Only those relating to glycemic control were selected, [‡] no other details with respect to this finding were provided, [§] Almonds were added to the diet during the last 24 weeks of the intervention; no dose provided, [¶] Included 421 patients with type 2 diabetes (55% of subject), [††] Calculated for subjects without diabetes, [€] Only 35 subjects were analyzed

responses, such as low glycemic index foods,[40] have been effective in increasing insulin sensitivity, preventing hyperinsulinemia and overall, improving glycemic control in patients with type 2 diabetes.[41] Acute studies have shown that almonds, taken alone or in combination with other carbohydrate-rich foods, can have a similar effect by significantly lowering postprandial glucose and insulin responses.[12,18] Another study has shown that nuts in combination with other foods can improve glycemic control in patients with type 2 diabetes.[42] However, only the aforementioned studies by Tapsell et al.,[35,36] Lovejoy et al.[37] and Scott et al.[38] in addition to two other studies[10, 43] have specifically looked at the effect of nuts on markers of glycemic control in the non-acute clinical trials (Table 2). Three of these studies showed significant improvements in glycemic control in comparison to baseline.[10,35,38] However, none of the studies have shown significant improvements in glycated proteins (HbA1c). The study by Tapsell et al.[35] did find a significant between treatment effect with nuts in serum insulin, while the study by Estruch et al.[10] showed a significant reduction in fasting glucose in comparison to the control but not the olive oil group. The inconsistencies in the findings make it difficult at this stage to reach definite conclusions on the role of nuts on glycemic control over the long term. Some of these inconsistencies may be attributed to the variations in the health status of the study participants, subject number, length of trial, outcome measures and dose of nuts used. Therefore, randomized, long-term clinical interventions that focus on the effect of varying doses of mixed nuts in patients with type 2 diabetes are required.

However, there may be other mechanisms by which nuts can reduce the risk of type 2 diabetes and its complications. Inflammation has been linked to the risk of diabetes and heart disease.[44] Evidence suggests that nuts by themselves or as part of a cholesterol lowering diet may significantly lower markers of inflammation including C-reactive protein (CRP).[9,45] Furthermore, a recent meta-analysis of the prospective studies showed that a 100mg per day increase in dietary magnesium intake reduces the risk of developing diabetes by 14% (RR of 0.86; 95% CI: 0.77-0.95)[20]. The nuts listed in Table 1, contain 34-83 mg of magnesium per 28 grams, which translates to 8.5%-25% of daily requirements in adults. The current findings and the plausibility of the discussed mechanisms of action warrant further research into the role of nuts in prevention and management of type 2 diabetes.

CONCLUSION

Research indicating the beneficial effect of nuts on coronary heart disease risk is strong. There is evidence that suggests that nuts and their bioactive components may also help in the management of diabetes. However, further studies on prevention are required and while acute and observational studies are supportive, evidence of improved glycemic control from long-term randomized controlled trials is lacking. Therefore, in order to understand the role of nuts in prevention and management of this disease, more long-term clinical interventions that examine the role of nuts in pre-diabetic and diabetic patients are justified.

AUTHOR DISCLOSURES

David Jenkins has served on the Scientific Advisory Board of Loblaw Brands Ltd, Sanitarium, Herbalife International, Nutritional Fundamentals for Health, Pacific Health Laboratories, Metagenics/MetaProteomics, Bayer Consumer Care, Almond Board of California, California Strawberry Commission, Orafti, Unilever and Solae. Cyril Kendall has served on the Scientific Advisory Board of Paramount Farms. David Jenkins and Cyril Kendall have received grants from Barilla, Solae, Unilever, Hain Celestial, Loblaw Brands, Sanitarium, Almond Board of California, International Tree Nut Council, California Strawberry Commission, the Western Pistachio Commission, Orafti, and the Canola and Flax Councils of Canada. David Jenkins has been on the speakers' panel for the Almond Board of California. Cyril Kendall has been on the speakers' panel for the Almond Board of California, Paramount Farms and the International Tree Nut Council.

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Review

Health benefits of nuts in prevention and management of diabetes

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核果在糖尿病預防及管理的健康益處

核果對於冠狀動脈心臟病(CHD)危險因子，尤其是血脂的影響，已被廣泛研究且確認它們的有益效用。世代研究中，核果對冠狀動脈心臟病的有益效應也已被清楚的證實。雖然有理由去相信核果的獨特巨量或微量營養素可以幫助血糖的控制，僅有少數研究探究它們在糖尿病控制及管理的角色。核果含有較低的可利用性醣類、健康的脂肪酸組成、高的植物性蛋白、纖維及鎂。急性餵食研究指出，當單獨食用核果，對於餐後血糖值的升高幾乎無影響。此外，當核果與富含醣類的食物一起食用，會減緩醣類食物的餐後血糖反應。儘管有這些成功的急性研究，僅有少數的試驗測試核果在第二型糖尿病的效應。這些研究要不是缺乏足夠的時間去觀察血糖管理基準之糖化血色素的改變，就是統計檢力不夠。因此，需要較長期的臨床研究去評估核果在糖尿病前期或是糖尿病人之血糖管理的角色。整體來說，有很正確的理由去更進一步的探究核果的使用在糖尿病及微血管和大血管的併發症的預防。

關鍵字：核果、心血管疾病、冠狀動脈心臟病、糖尿病、血糖