

Effect of diets enriched in almonds on insulin action and serum lipids in adults with normal glucose tolerance or type 2 diabetes¹⁻³

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ABSTRACT

Background: Nuts appear to have cardiovascular benefits but their effect in diabetic patients is unclear.

Objective: The objective was to assess effects of almond-enriched diets on insulin sensitivity and lipids in patients with normoglycemia or type 2 diabetes.

Design: Study 1 assessed the effect of almonds on insulin sensitivity in 20 free-living healthy volunteers who received 100 g almonds/d for 4 wk. Study 2 was a randomized crossover study that compared 4 diets in 30 volunteers with type 2 diabetes: 1) high-fat, high-almond (HFA; 37% total fat, 10% from almonds); 2) low-fat, high-almond (LFA; 25% total fat, 10% from almonds); 3) high-fat control (HFC; 37% total fat, 10% from olive or canola oil); and 4) low-fat control (LFC; 25% total fat, 10% from olive or canola oil). After each 4-wk diet, serum lipids and oral glucose tolerance were measured.

Results: In study 1, almond consumption did not change insulin sensitivity significantly, although body weight increased and total and LDL cholesterol decreased by 21% and 29%, respectively ($P < 0.05$). In study 2, total cholesterol was lowest with the HFA diet (4.46 ± 0.14 , 4.52 ± 0.14 , 4.63 ± 0.14 , and 4.63 ± 0.14 mmol/L with the HFA, HFC, LFA, and LFC diets, respectively; $P = 0.0004$ for fat level). HDL cholesterol was significantly lower with the almond diets ($P = 0.002$); however, no significant effect of fat source on LDL:HDL was observed. Glycemia was unaffected.

Conclusions: Almond-enriched diets do not alter insulin sensitivity in healthy adults or glycemia in patients with diabetes. Almonds had beneficial effects on serum lipids in healthy adults and produced changes similar to high monounsaturated fat oils in diabetic patients. *Am J Clin Nutr* 2002;76:1000–6.

KEY WORDS Nuts, almonds, insulin resistance, type 2 diabetes, lipoproteins, glucose tolerance

INTRODUCTION

There is controversy regarding the relative health benefits of high-carbohydrate diets compared with diets high in monounsaturated fat (MUFA). On one hand, many studies have suggested that high-fat, low-carbohydrate diets have adverse metabolic effects. High-fat diets have been associated with the worsening of insulin sensitivity in many clinical studies of nondiabetic persons (1–4) and in several epidemiologic studies (5, 6). In patients with established diabetes, high-fat diets increase fasting and postprandial glucose and insulin (7) concentrations, whereas adherence to a low-fat diet improves glucose tolerance over 5 y in persons with impaired glucose tolerance (8).

On the other hand, many studies have suggested that high-fat, low-carbohydrate diets have beneficial effects on blood lipids and lipoproteins, particularly in the context of stable body weight. Garg et al (9) reported that a high-MUFA diet (50% total fat, 35% carbohydrate,) produced lower concentrations of plasma triacylglycerols and VLDL cholesterol and higher concentrations of HDL cholesterol than did a high-carbohydrate diet (60% carbohydrate, 25% fat) in patients with type 2 diabetes. Additionally, the high-MUFA diet resulted in improvements in glycemia. Beneficial effects of MUFAs on serum lipids were reported in some (10–12) but not all (13) studies. These studies influenced the current dietary recommendations for patients with diabetes to liberalize intakes of MUFAs when high triacylglycerol and VLDL-cholesterol concentrations are an issue (14).

Considerable research has suggested that nuts—which are high in unsaturated fats, fiber, and micronutrients—have beneficial effects on cardiovascular risk (15, 16). Epidemiologic studies have shown that persons with a high nut consumption have a reduced incidence of both fatal and nonfatal ischemic heart disease (reviewed in reference 15) and lower blood cholesterol (16). Experimental studies have shown improvements in the lipoprotein profiles of persons who consume diets high in walnuts (17, 18), almonds (19–21), pecans (22), macadamia nuts (23), or peanuts (24, 25).

Although these studies suggest that nuts can reduce heart disease risk in healthy persons, the effect of nuts on insulin resistance and in patients with type 2 diabetes have not been well studied. Furthermore, no studies to our knowledge have directly compared the effects of controlled diets high in nuts with those of diets matched for the fatty acid contents of other food sources. Two studies were conducted to address the following hypotheses. First, we hypothesized that an increased nut consumption would beneficially affect insulin sensitivity in free-living, healthy persons. Second, we performed a direct comparison of almonds with other dietary sources of MUFAs to test the hypothesis that an increased nut consumption produces greater benefits than do high-MUFA oils on serum lipids and lipoproteins and glycemia in patients with type 2 diabetes.

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SUBJECTS AND METHODS

Subjects

Two studies were conducted. In study 1, 10 healthy men and 10 premenopausal women were recruited. The subjects were 20–50 y of age with a body mass index (BMI; in kg/m²) of 18–30. To be eligible, subjects were required to have normal blood chemistry values, normal hematocrit, and a fasting glucose concentration <6.67 mmol/L (120 mg/dL).

In study 2, 34 men and women with type 2 diabetes were recruited. The subjects were 30–65 y of age with a BMI of 20–40. Type 2 diabetes had been previously diagnosed by a physician or the subjects had a fasting serum glucose concentration >7.8 mmol/L (140 mg/dL). Subjects taking insulin were excluded. Fourteen of the 17 women were postmenopausal (11 were receiving hormone replacement therapy) and 16 of the subjects were taking oral hypoglycemic agents. Twelve subjects were African American and the remainder were white. All subjects had to have moderately good glucose control (fasting glucose <11.1 mmol/L, or <200 mg/dL) at screening. Those subjects taking medications to lower cholesterol were excluded, as were those with clinically significant nephropathy, neuropathy, or cardiovascular disease. Volunteers were also excluded if their screening LDL-cholesterol concentrations were >5.2 mmol/L (200 mg/dL), fasting triacylglycerol concentrations were >7.8 mmol/L (300 mg/dL), or HDL-cholesterol concentrations were <0.65 mmol/L (25 mg/dL).

In both studies, women who were pregnant or breast-feeding and those with food allergies or sensitivities to nuts were excluded. Informed consent was obtained from all subjects. The study, the protocol, the consent form, and advertisements were approved by Pennington Biomedical Research Center's Institutional Review Board. All subjects received monetary compensation for their participation.

Experimental design

Study 1

On enrollment, whole-body insulin sensitivity was assessed with the use of an insulin-modified frequently sampled intravenous-glucose-tolerance test as previously described (26). Briefly, after fasting blood samples were collected, 300 mg glucose (as 50% dextrose)/kg was injected over 45 s. Time 0 was marked at the end of glucose administration, and blood samples (4 cc) were collected at 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 14, 16, and 19 min. At 20 min, a bolus of insulin (0.03 U/kg, Humulin; Eli Lilly Co, Indianapolis) was injected, and frequent blood sampling resumed at 22, 23, 24, 25, 27, 30, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, and 180 min. Each blood sample was kept chilled on ice and centrifuged at 1800 × g for 10 min at 4 °C; the serum was stored at –20 °C until analyzed for glucose and insulin. The insulin sensitivity index (S_I) and glucose effectiveness (S_G) were calculated by using the Minimal Model method (27). Fasting cholesterol, LDL cholesterol, HDL cholesterol, and triacylglycerols were also measured.

After the baseline assessments, subjects began 4 wk of dietary supplementation with 100 g almonds/d (≈1 cup/d). To aid in compliance, the almonds were provided whole or in a variety of food products such as trail mix, muffins, and cookies. The almonds or almond food products were provided biweekly. During the supplementation period, the subjects were encouraged to maintain their habitual diets; however, they were told how much energy (calories) was provided by 100 g almonds and were advised to

reduce their energy intakes by an equivalent amount in an attempt to keep energy intake constant. Each week, subjects completed a 3-d food diary that was reviewed by a dietitian for compliance. At the end of the 4 wk, the frequently sampled intravenous-glucose-tolerance test and lipid profile were repeated.

Study 2

This study used a randomized, double-blind, crossover design. After enrollment, the subjects were randomly assigned to begin 1 of 4 diet arms. Each diet lasted 4 wk, with a minimum 2-wk break between diet periods. Outcome measures were assessed at the end of each diet period. Each blood sample for lipid and lipoprotein measurements was collected in duplicate on separate days to minimize the influence of biological variability in these measurements. A 2-h, 75-g oral-glucose-tolerance test was conducted to determine glucose tolerance and insulin secretion. Body weight was measured daily, Monday through Friday, during the feeding periods of the study to ensure weight stability.

The 4 diets were as follows: 1) high-fat, high-almond (HFA; 37% total fat, 10% from almonds); 2) low-fat, high-almond (LFA; 25% total fat, 10% from almonds); 3) high-fat control (HFC; 37% total fat, 10% from the MUFAs olive or canola oil); and 4) low-fat control (LFC; 25% total fat, 10% from olive or canola oil). The almond-containing diets provided 57–113 g almonds/d depending on the total energy level. For example, 85 g (3 oz, or 3/4 cup) almonds were provided daily with a 2600-kcal (10.9 MJ) diet. Almonds were provided in entrées (eg, trout almondine) and snack foods (eg, muffins, cookies, and trail mix). A 5-d menu rotation was used to maintain variety throughout the study. The macronutrient composition of each diet (an average of 3 of the 5 menu plans, each at 2 different energy levels), determined by the Pennington Biomedical Research Center's Food Analysis Laboratory is shown in **Table 1**. The targets for fat, carbohydrate, and protein for the high-fat diets were 37%, 48%, and 15% and for the low-fat diets were 25%, 60%, and 15%, respectively.

The subjects were provided with all foods needed for the duration of the study. On weekdays, the subjects were required to consume breakfast and dinner under supervision at the Pennington Biomedical Research Center's dining facility; weekday lunches and snacks and all weekend meals were packaged for take-out. The subjects were initially assigned a total energy intake to maintain body weight, and energy adjustments were made as needed to attempt to maintain weight within 2 kg of each person's initial value. The subjects were not allowed to take vitamin or mineral supplements during the study. To assist with compliance assessment, each participant completed a daily food diary in which they recorded the study foods not eaten, nonstudy foods eaten, beverages consumed, and number of food units eaten.

Laboratory analyses

Total cholesterol, HDL cholesterol, and triacylglycerols were measured on a Synchron CX5 (Beckman, Brea, CA). LDL cholesterol was calculated by using the Friedewald equation (28), assuming that triacylglycerol concentrations were within normal limits. Insulin was analyzed with an automated IMx instrument (Abbott Laboratories, Abbott Park, IL), and blood glucose (glucose oxidase method; 29) and hemoglobin A_{1c} (Hb A_{1c}) were analyzed with a Beckman Coulter Synchron CX7. The normal reference range for Hb A_{1c} in our laboratory is 4.6–6.2%.

HDL particle size was determined by nondenaturing gradient gel electrophoresis as described by Berglund et al (30). Briefly, concave acrylamide gradient gels (4–30%) were cast 4–8 at a time

TABLE 1Chemical composition of the diets provided to subjects participating in study 2¹

	Diet			
	HFA ²	LFA ²	HFC	LFC
Total fat (% of energy)	39.0 ± 1.2	27.2 ± 0.4	36.8 ± 0.9	26.0 ± 0.5
Saturated (% of energy)	6.8 ± 0.5	4.8 ± 0.1	7.4 ± 0.5	5.3 ± 0.3
Polyunsaturated (% of energy)	10.6 ± 0.8	7.7 ± 0.2	8.7 ± 0.9	6.5 ± 0.6
Monounsaturated (% of energy)	22.5 ± 0.6	15.5 ± 0.4	20.7 ± 0.7	14.6 ± 0.1
Carbohydrate (% of energy)	45.8 ± 0.7	58.1 ± 0.4	48.5 ± 0.8	59.8 ± 0.4
Protein (% of energy)	14.9 ± 0.2	14.7 ± 0.2	14.4 ± 0.3	14.3 ± 0.2
Fiber (g) ³	30.9 ± 4.0	31.1 ± 4.0	16.7 ± 1.5	16.6 ± 1.6
Cholesterol (mg) ³	226 ± 17	167 ± 19	270 ± 9	257 ± 13

¹ $\bar{x} \pm \text{SEM}$, reflecting the average values of 3 of the 5 menu plans at 2 energy intakes: 1800 kcal (7.5 MJ) and 2600 kcal (10.9 MJ). HFA, high fat, high almond; LFA, low fat, high almond; HFC, high fat control; LFC, low fat control.

²The estimated total fat intake from almonds at the 2600-kcal intake was 10.1% of energy (0.8% saturated fat, 2.5% polyunsaturated fat, and 6.5% monounsaturated fat).

³The calculated values were derived from Moore's Extended Nutrient Database (MEnu), copyright Pennington Biomedical Research Foundation, 1998.

by using a GSC-8 gel-casting apparatus (Pharmacia, Uppsala, Sweden). The cast gels were allowed to polymerize overnight and were used immediately or stored for < 1 wk wrapped in moist towels in plastic bags. Plasma samples (8 μL) were electrophoresed in a Pharmacia GE-2/4 electrophoresis apparatus in 90 mmol tris/L, 80 mmol boric acid/L, and 3 mmol EDTA buffer/L (pH 8.3). The gels were prerun for 15 min at 125 V before sample application. The samples were electrophoresed at 70 V for 15 min and then at 125 V for 24 h. After electrophoresis, the gels were stained with Oil Red O (Sigma Chemical Co, St Louis) and scanned in a model GS-700 imaging densitometer (Bio-Rad Laboratories, Hercules, CA). The gels were then counterstained with Coomassie R-250 (Sigma Chemical Co) and rescanned. The lipid distribution across 5 subpopulations was determined (31).

Statistical analysis

Study 1

An analysis of variance (ANOVA) with repeated measures was used to compare outcome variables before and after the almond supplementation period. All analyses were adjusted for sex, and analyses of dietary variables were also adjusted for total energy intake. Tukey's adjustment was used for multiple comparisons. A *P* value < 0.05 was considered statistically significant.

Study 2

A two-factor ANOVA with repeated measures was used to compare cholesterol, lipoproteins, glucose, and insulin concentrations at the end of each of the 4 diet periods. The factors were fat source (almonds compared with oil) and fat level (high fat compared with low fat), and all analyses were adjusted for total energy intake. Diet order was not a significant covariate for any analysis; therefore, it was not included in the final analysis. For all analyses of laboratory values, the average value of blood samples on 2 separate days was used. Tukey's adjustment was used for multiple comparisons. A *P* value < 0.05 was considered statistically significant.

RESULTS

Study 1

The mean ($\pm \text{SEM}$) age of the subjects was 25.1 ± 1.0 y and the mean BMI was 23.0 ± 0.3 . All subjects enrolled completed the

study. Changes in body weight and metabolic and cardiovascular risk factors from baseline to week 4 of almond supplementation are shown in **Table 2**. Body weight increased slightly but significantly in the subjects by the end of the study (*P* = 0.006). There was no significant main effect of time or sex on S_1 or S_G . For both S_1 and S_G , however, there was a significant time-by-sex interaction because these indexes increased in women but decreased in men. The increase in S_1 in women ($0.90 \pm 0.09 \times 10^{-4} \text{ min}^{-1} \cdot \mu\text{U}^{-1} \cdot \text{mL}^{-1}$) was nearly significant (*P* = 0.09) as was the increase in S_G ($0.39 \pm 0.03 \text{ min}^{-1} \times 10^2$; *P* = 0.06). The decreases in S_1 and S_G in men (by $0.42 \pm 0.09 \times 10^{-4} \text{ min}^{-1} \cdot \mu\text{U}^{-1} \cdot \text{mL}^{-1}$ and $0.23 \pm 0.03 \text{ min}^{-1} \times 10^2$, respectively) were not significant. Despite the increase in body weight, significant decreases were observed in both total and LDL cholesterol by the end of 4 wk of almond supplementation in both sexes. In addition, main effects of both time and sex were observed on HDL cholesterol, which also decreased significantly from baseline and was significantly lower in men than in women. Both the ratio of total to HDL cholesterol and of LDL to HDL cholesterol decreased after almond supplementation, and there was a main effect of sex on both ratios. There were no significant effects of diet or sex on triacylglycerols. Adjustment for changes in body weight did not alter these results.

Self-reported changes in dietary intake on 3-d food records during the period of almond supplementation are shown in **Figure 1**. Total energy intake increased slightly, but not significantly, from 9.8 ± 0.5 MJ (2341 ± 119 kcal) to 10.7 ± 0.5 MJ (2556 ± 119 kcal) during supplementation. However, fat intake (adjusted for total energy) increased significantly, whereas carbohydrate intake decreased significantly. Protein intake was unchanged. The changes in fat intake were due, as expected, from significant increases in intakes of both MUFAs and polyunsaturated fats, whereas saturated fat intakes remained unchanged.

Study 2

Of the 34 subjects enrolled, 30 (17 women and 13 men) completed the entire 4-arm crossover study. Dropout was due to time conflicts or personal reasons in 3 subjects and to gall bladder surgery in 1 subject. Data are reported only for those subjects who completed the study. At enrollment, the average age of the subjects was 53.8 ± 1.9 y ($\bar{x} \pm \text{SEM}$) and their BMI was 33.0 ± 1.0 . At enrollment, the subjects' total cholesterol concentration was

TABLE 2

Changes in body weight, insulin action, and serum lipids and lipoproteins in 20 healthy volunteers before and after 4 wk of supplementation with almonds in study 1¹

	Before		After		P		
	Men	Women	Men	Women	Main effect of time	Main effect of sex	Sex-by-time interaction
Body weight (kg)	77.2 ± 2.3	57.5 ± 2.3	78.1 ± 2.33	57.8 ± 2.3	0.006	0.0001	NS
Fasting glucose (mmol/L)	5.16 ± 0.11	4.90 ± 0.11	5.17 ± 0.11	5.05 ± 0.11	NS	NS	NS
Fasting insulin (pmol/L)	33.6 ± 4.2	34.8 ± 4.2	38.4 ± 4.2	34.8 ± 4.2	NS	NS	NS
S _i (×10 ⁻⁴ min ⁻¹ · μU ⁻¹ · mL ⁻¹)	3.31 ± 0.41	4.75 ± 0.41	3.73 ± 0.41	3.85 ± 0.41	NS	NS	0.04
S _G (min ⁻¹ × 10 ²)	2.14 ± 0.17	2.71 ± 0.17	2.38 ± 0.17	2.33 ± 0.17	NS	NS	0.006
Cholesterol (mmol/L)	4.50 ± 0.18	4.75 ± 0.18	3.59 ± 0.18	3.70 ± 0.18	0.0001	NS	NS
LDL cholesterol (mmol/L)	3.01 ± 0.16	3.02 ± 0.16	2.22 ± 0.16	2.10 ± 0.16	0.0001	NS	NS
HDL cholesterol (mmol/L)	1.0 ± 0.05	1.40 ± 0.05	0.88 ± 0.05	1.22 ± 0.05	0.0002	0.0001	NS
Triacylglycerols (mmol/L)	1.02 ± 0.11	0.76 ± 0.11	0.99 ± 0.11	0.79 ± 0.11	NS	NS	NS
LDL:HDL cholesterol	3.02 ± 0.20	2.37 ± 0.20	2.54 ± 0.20	1.76 ± 0.20	0.0005	0.01	NS
Total:HDL cholesterol	4.51 ± 0.24	3.65 ± 0.24	4.11 ± 0.24	3.08 ± 0.24	0.003	0.006	NS

¹ $\bar{x} \pm \text{SEM}$. S_i, insulin sensitivity index; S_G, glucose effectiveness.

5.1 ± 0.15 mmol/L, LDL was 2.91 ± 0.3 mmol/L, HDL was 1.25 ± 0.04 mmol/L, and fasting glucose was 8.85 ± 0.48 mmol/L.

Changes in cholesterol and lipoproteins in response to the 4 different diets are shown in **Table 3**. Significant main effects of fat level (low fat compared with high fat) on total cholesterol and triacylglycerols and a significant main effect of fat source (almonds compared with oil) on HDL cholesterol with a trend toward a main effect of fat source on LDL cholesterol ($P = 0.06$) were observed. Total cholesterol was lowest with the HFA diet. Triacylglycerol concentrations were significantly higher, as expected, with both low-fat diets than with their matched high-fat diets, but no significant effects of almond enrichment on triacylglycerols were observed. Although the ratio of LDL to HDL cholesterol was unchanged by any diet, a significant main effect of fat level and a trend toward a main effect of fat source ($P = 0.06$) on the ratio of total to HDL cholesterol was observed. Lipid and lipoprotein concentrations during all experimental diets were lower than those at the time of enrollment, suggesting that all experimental diets were lower in total and saturated fat or both than were the subjects' habitual diets.

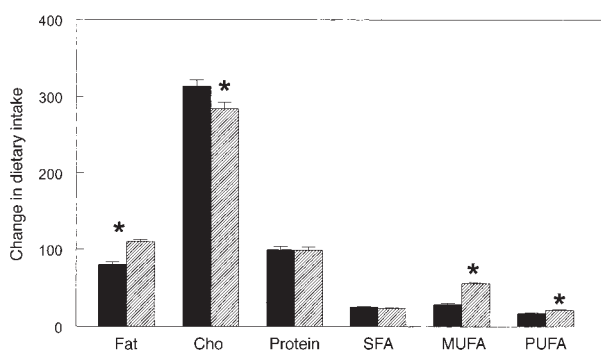


FIGURE 1. Mean (\pm SEM) changes from baseline (■) to 4 wk (▨) in self-selected dietary intakes (adjusted for total energy) during 4 wk of almond supplementation in 20 healthy volunteers in study 1. *Significantly different from baseline, $P < 0.05$. Cho, carbohydrate; SFA, saturated fat; MUFA, monounsaturated fat; PUFA, polyunsaturated fat.

Because the decrease in HDL cholesterol with the almond-enriched diets was somewhat unexpected, we examined changes in HDL subpopulations. This analysis showed no significant main effects of diet (fat source or fat intake) on HDL subpopulation distribution (Table 3). A total of 8 subjects had at least one HDL-cholesterol concentration < 0.91 mmol/L (35 mg/dL) during the study. The response of these subjects to the diets was variable and not significantly different from those with an HDL concentration > 0.91 mmol/L.

Finally, we examined the effect of the diets on glucose and insulin concentrations during a 2-h OGTT (Table 3). No main effect of fat source (almond compared with oil) or fat level (high fat compared with low fat) on any glucose or insulin index was observed. A significant interaction of fat source and fat level on both fasting and 2-h glucose concentrations was evident on the basis that glucose concentrations were lower with the LFC than with the HFC or LFA diet (significant for 2-h glucose). Not surprisingly, we observed significant effects of energy intake on both fasting and 2-h glucose and insulin concentrations (data not shown).

Some changes in lipid concentrations would be expected on the basis of changes in the fatty acid composition of the different diets. We therefore examined whether the observed changes in total cholesterol and lipoproteins resulting from the almond-enriched diets corresponded to the changes predicted with the equations developed by Mensink and Katan (32; **Figure 2**). In general, the observed decreases in total cholesterol and LDL cholesterol with the almond diets were greater than would be predicted from changes in fatty acid composition. The prediction equations based on diet composition would predict an increase in HDL cholesterol, whereas a decrease was actually observed.

DISCUSSION

The results of these studies yield several important conclusions. In healthy adults (study 1), it appears that the increase in nut consumption did not substantially influence insulin sensitivity. However, body weight increased significantly after 4 wk of supplementation with almonds, which may have masked or reduced changes in insulin sensitivity. Despite the weight changes, total cholesterol and both LDL and HDL cholesterol decreased significantly after almond supplementation. In patients with diabetes,



TABLE 3

Cholesterol and lipoprotein values after high- and low-fat diets enriched in almonds or refined oils in 30 subjects with type 2 diabetes in study 2¹

	Diet				P		
	HFA	HFC	LFA	LFC	Main effect of fat source	Main effect of fat level	Interaction
							(fat source by fat level)
Total cholesterol (mmol/L)	4.46 ± 0.14	4.52 ± 0.14	4.63 ± 0.14	4.63 ± 0.14	NS	0.0004	NS
LDL cholesterol (mmol/L)	2.51 ± 0.10	2.58 ± 0.10	2.53 ± 0.10	2.53 ± 0.10	0.06	NS	NS
HDL cholesterol (mmol/L)	1.13 ± 0.04	1.17 ± 0.04	1.13 ± 0.04	1.16 ± 0.04	0.002	NS	NS
Triacylglycerols (mmol/L)	1.77 ± 0.18	1.68 ± 0.18	2.10 ± 0.18	2.0 ± 0.18 ^b	NS	0.0001	NS
LDL:HDL cholesterol	2.30 ± 0.1	2.30 ± 0.1	2.30 ± 0.1	2.30 ± 0.1	NS	NS	NS
Total:HDL cholesterol	4.1 ± 0.1	4.0 ± 0.1	4.2 ± 0.1	4.2 ± 0.1	0.06	0.0002	NS
HDL _{2b} (%)	13.3 ± 2.8	14.4 ± 2.8	12.0 ± 2.8	13.3 ± 2.8	NS	NS	NS
HDL _{2a} (%)	10.7 ± 1.1	10.5 ± 1.1	10.7 ± 1.1	10.1 ± 1.1	NS	NS	NS
HDL _{3a} (%)	29.8 ± 1.5	29.5 ± 1.5	31.2 ± 1.5	30.4 ± 1.6	NS	NS	NS
HDL _{3b} (%)	24.7 ± 1.8	24.8 ± 1.8	25.3 ± 1.8	25.2 ± 1.8	NS	NS	NS
HDL _{3c} (%)	21.5 ± 2.1	20.8 ± 2.1	20.7 ± 2.1	21.0 ± 2.1	NS	NS	NS
Fasting glucose (mmol/L)	8.14 ± 0.49	8.73 ± 0.48	8.63 ± 0.48	8.00 ± 0.49	NS	NS	0.006
2-h Glucose (mmol/L)	15.2 ± 0.7 ^{a,b}	15.7 ± 0.7 ^a	15.7 ± 0.7 ^a	14.6 ± 0.7 ^b	NS	NS	0.008
Fasting insulin (pmol/L)	88.2 ± 10.2	88.8 ± 9.6	89.4 ± 9.6	93.6 ± 10.2	NS	NS	NS
2-h Insulin (pmol/L)	331.8 ± 67.2	303.6 ± 66.6	318.0 ± 66.0	335.4 ± 66.6	NS	NS	NS
Hemoglobin A _{1c} (%)	7.0 ± 0.3	7.2 ± 0.3	7.1 ± 0.3	6.8 ± 0.3	NS	NS	NS

¹Least-squares $\bar{x} \pm$ SEM adjusted for total energy intake. HFA, high fat, high almond; HFC, high fat control; LFA, low fat, high almond; LFC, low fat control. Means with different superscript letters are significantly different, $P < 0.01$.

almond-enriched diets significantly decreased HDL cholesterol; however, there was no effect of fat source on the ratios of LDL to HDL or of total cholesterol to HDL, suggesting that almonds have lipid effects similar to high-MUFA oils. Almond diets did not alter glycemia relative to control diets.

Many studies have shown that diets enriched in nuts favorably influence serum lipids and lipoproteins (reviewed in reference 33). Typically, this response is greater in hyperlipidemic patients. The results of study 1 showed that total cholesterol still decreased substantially (by 21%) in the normolipidemic subjects during almond supplementation. Other studies also observed a decrease in lipids after nut consumption in normolipidemic patients (22, 25, 34), although the decreases (5–10%) were not as great as those seen in the present study. It is not clear why the decrease in cholesterol in the present study was greater, although possibly the amount of nuts supplemented or subtle variations in phytonutrient content of the almonds used relative to those in earlier studies may have played a role.

Another important finding of study 1 was that body weight increased significantly during almond supplementation, presumably because of increased energy intakes, despite the fact that subjects were counseled to reduce other sources of energy intake. The increased body weight observed when almonds were added to the diet of free-living subjects raises caution concerning dietary changes involving nuts and makes it clear that nuts must replace other concentrated sources of energy and fat in the diet.

The results of the study in the subjects with type 2 diabetes indicate that high-fat diets containing almonds result in the lowest concentrations of total cholesterol; however, this reduction was primarily due to significant decreases in HDL cholesterol. Although previous studies in nondiabetic subjects have shown that the addition of almonds to the diet lowered total cholesterol (19–21), the finding that diets high in almonds lowered HDL cholesterol was unexpected. Previous studies have found that almond-enriched diets have no effect on HDL cholesterol (19, 20, 34). On the other hand, Sabate' et al (17) observed that walnut-enriched diets decreased HDL cholesterol by 4.9% (NS), which is comparable with our 4.7%

decrease in HDL cholesterol with the almond-enriched diets. Because a significant decrease in HDL cholesterol was also found in the healthy subjects in study 1, this effect is not unique to subjects with diabetes. In understanding these changes in HDL cholesterol, it would have been of interest to have apolipoprotein A-I concentrations measured; however, unfortunately, that was not done in the present studies. Thus, the mechanism by which almonds reduce HDL cholesterol requires further research.

In the context of somewhat lower total and LDL cholesterol concentrations, the relative effect of short-term changes on HDL cholesterol is unclear. In the present study, there was no significant effect of almonds relative to those of oil on the ratio of LDL to HDL cholesterol or of total to HDL cholesterol. Thus, our data do not suggest any adverse effects of replacing other fat sources with

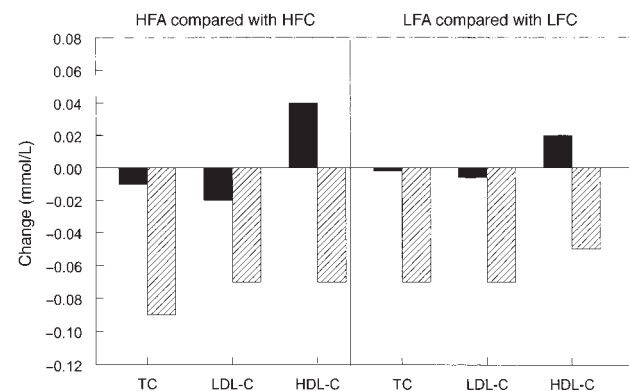


FIGURE 2. Comparison of predicted changes (■) in serum total cholesterol (TC) and lipoproteins based on the fatty acid composition of the diet (from reference 32) and observed changes (▨) in 30 patients with type 2 diabetes in study 2. HFA, high-fat, high-almond diet; HFC, high-fat control diet; LFA, low-fat, high-almond diet; and LFC, low-fat control diet.

almonds in the diet, yet neither do they suggest a unique benefit to almonds relative to those of other MUFA sources.


In addition, no significant effects of almonds on the relative proportion of different HDL subpopulations were evident. Previous studies (30) showed that decreases in dietary total and saturated fat result in decreases in both HDL₂ and HDL₃, with the greatest changes in the HDL₂ subfractions. These changes were reflected in a shift in HDL subpopulation distribution (determined by gradient gel electrophoresis) from the larger HDL_{2b} population to the smaller HDL_{3c} population. Physiologically, the HDL subpopulation is associated with the metabolism of triacylglycerol-rich lipoproteins, with the less-dense HDL₂ subpopulation most associated with the cardioprotective effects of HDL. In the present study we similarly observed a weak trend for reduction in the less dense HDL_{2b} subpopulation with both fat reduction and almond use; however, the changes were not significant.

It is important to note that adding almonds to either high-fat or low-fat diets in patients with type 2 diabetes had little effect on fasting or postprandial glucose or insulin concentrations. Glucose concentrations 120 min after an oral glucose load were lowest with the LFC diet (significantly lower than with the LFA or HFC diet), but there was no main effect of fat source on glucose. Hb A_{1c} was also not significantly different across the 4 diets. Thus, the data suggest that the addition or replacement of other foods by almonds in the diets of patients with diabetes has no deleterious consequences on glycemic control. This result was not completely unexpected given the lack of effect of almond supplementation on insulin sensitivity or glucose in healthy adults in study 1.

It is also important in the context of the debate on the relative merits of low-fat compared with high-fat diets that the low-fat diets per se did not result in any adverse effects on glucose or insulin. In fact, the LFC diet resulted in the lowest postprandial glucose concentrations. Previous research by Garg et al (9) suggests that low-fat, high-carbohydrate diets may adversely affect glucose or insulin concentrations in patients with diabetes, although more recent data suggest that low-fat diets improve glycemia (6). Our results after 4 wk of feeding low-fat diets enriched in MUFAs do not support a deleterious effect of low-fat diets on glycemia. The differences in the results of our study and those of Garg et al's may have to do with the composition of the carbohydrate (ie, simple compared with complex), the fiber content of the experimental diets, or the relative enrichment of MUFAs in the low-fat diets. We did, however, observe that low-fat diets increased total cholesterol and triacylglycerols, which in the context of a weight-maintaining study was not unexpected and was reported by others (9).

The fiber content of the diet may be important for the difference between the predicted and observed changes in serum lipids (Figure 2). In general, the changes we observed in all lipid fractions with either low-fat or high-fat almond diets were greater than those predicted by standard equations. This result could either indicate a general error in the equations or possibly some unique effect of almonds or one of the other dietary components. Fiber has been shown to lower blood lipids even in the context of diets low in saturated fat and cholesterol (35). The dietary fiber content was higher with the almond diets with the control diets (Table 1) in study 2, primarily because of the amount of fiber in the almonds. The addition of 100 g almonds in study 1 should also have substantially increased fiber intake in the free-living subjects. Thus, fiber may have played an important role in modulating the lipid changes observed in both studies. Of course, it is also possible that other components of almonds, such as vitamin E and phytochemicals, may have played a role in the observed changes.

Several limitations of these studies deserve comment. One example is the use of self-reported dietary data in study 1. It was because of this that we decided to perform the controlled feeding study, ie, study 2. We also recognized that it would have been ideal to have a control group that did not receive almonds in study 1; however, this was not possible because of limited resources. With 20 subjects, we had the statistical power to detect a change in S_1 of $1.0 \times 10^{-4} \text{ min}^{-1} \cdot \mu\text{U}^{-1} \cdot \text{mL}^{-1}$, a clinically meaningful change. The observed change was considerably smaller and thus is probably not biologically relevant. In study 2 our population was somewhat unusual in that, overall, the subjects had fairly low cholesterol and LDL-cholesterol concentrations at enrollment, despite their diabetes. It is possible that different results would have been obtained if we had increased the lower cutoff for either total or LDL cholesterol.

In summary, our results suggest that almonds have no effect on insulin sensitivity in healthy adults nor do they affect glycemia in patients with type 2 diabetes. Low-fat diets, regardless of the fat source, had no adverse effects on glycemia or insulinemia in patients with type 2 diabetes. Our data confirm previous studies showing that almonds reduce serum total cholesterol concentrations in healthy persons. Although there was a significant decrease in HDL cholesterol in patients with type 2 diabetes who consumed almond-enriched diets, no effect dietary fat source on the ratio of LDL to HDL cholesterol or of total to HDL cholesterol was observed, implying that the effects of almonds on lipids are similar to those induced by high-MUFA oils. Nevertheless, the changes in serum lipids induced by adding almonds to the diet were greater than those predicted by the change in fatty acid composition of the diet, suggesting that fiber or some other component of almonds may modulate these effects. 

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