

## Original Article

## A LOW-DOSE ALMOND-BASED DIET DECREASES LDL-C WHILE PRESERVING HDL-C

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**Background:** The aim of this study was to compare lipid-altering effects of an almond-based diet with a reference diet. In a randomized single blind, cross-over clinical trial study, the effect of almond (25 g/day) on serum lipoproteins of mild hypercholesterolemic patients were studied.

**Methods:** This eight-week dietary trial was divided into two consecutive four-week intervention periods. Both diets conformed to National Cholesterol Educational Program (NECP) step 1 diet and contained identical foods and macronutrients, except for almond. After a washout period, each patient consumed the opposite dietary regimen for 4 weeks. In the almond group, subjects used 25 g/ day of almond powder. Thirty hyperlipidemic adult men and women were considered eligible, after a preliminary medical history review and laboratory screening for lipid profile.

**Results:** Combined average for both of the cross-over phases showed that almond induced a reduction in total cholesterol (TC) of  $8 \pm 27$  mg/dL and in low-density lipoprotein-cholesterol (LDL-C) of  $9 \pm 29$  mg/dL. The reference diet did not induce a significant reduction in TC and LDL-C (for TC  $P < 0.01$ , and LDL-C,  $P < 0.05$ ). Neither treatments induced significant changes in high-density lipoprotein-cholesterol (HDL-C) and triglyceride (TG).

**Conclusion:** Our findings suggest a favorable lipid-altering effect induced by the almond, even in lower dose than previous studies (25 g vs. 100 g). These may be due to the interactive or additive effects of the numerous bioactive constituents found in almond.

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**Keywords:** Almond • cholesterol • clinical trials • cross-over study • low-density lipoproteins

### Introduction

Since ancient times, nuts and oil seeds have been considered as healthy foods worldwide. Native Americans, Mediterranean countries, Incas, Romans, Greeks, Indian, and Persians used to eat different kinds of nuts such as sunflower seed, peanut, walnut, pistachio, and almond. Notwithstanding the fact that nuts are an intrinsic part of the diets of some eastern and Mediterranean regions, where both serum cholesterol levels and incidence of heart disease are low.<sup>1</sup>

### Nuts and healthy diets

Almond, as a whole food, contains numerous beneficial nutritive and bioactive compounds like fatty acids, dietary fibers, micronutrients, and photochemical.<sup>2-6</sup> Almond is a rich source of monounsaturated free fatty acids (MECP) (mainly  $\omega$ -9, about 10 g/ounce) and a relatively good source of polyunsaturated free fatty acids (PUFA) (3.5 g/ounce). Proteins found in nuts have an arginin-rich amino acid profile, which is thought to be protective.<sup>2</sup> Additionally, almond, in particular, is especially rich in many tocopherols, including  $\alpha$ -tocopherol, the most active form of vitamin E, which has shown potent antiatherogenic and antilipidemic effects.<sup>2,5,7</sup> A number of biochemical activities of phytochemicals have been shown or hypothesized to influence a wide array of metabolic functions and risk of diseases. Current evidence suggests that many of these compounds

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are protective and play important roles in preventing or delaying the onset of chronic disease, such as coronary heart disease, cancer, noninsulin-dependent diabetes mellitus, and colon dysfunction.<sup>8, 9</sup> Tocopherol is found in high amounts in some nuts and seed oils, quenching free radicals and helping to prevent oxidative damage to cellular constitution.<sup>8</sup>

### **LDL reduction benefits**

Epidemiologic studies have shown that diets with a high monounsaturated fat to saturated fat ratio and polyunsaturated fat to saturated fat ratio seem to bring about lower serum cholesterol levels and reduce the incidence of coronary artery disease.<sup>1, 2, 4, 6 – 10</sup> Current research suggests that diets high in polyunsaturated fat are potentially carcinogenic, especially for female breast carcinoma.

Elevated plasma level of total and low-density lipoproteins (LDL) are major risk factors for coronary heart disease (HD) and their reduction in high-risk men could lead to a lower incidence of fatal and nonfatal cardiac events.<sup>10</sup> More than half of the coronary heart disease in the United States is attributable to abnormalities in the levels and metabolism of plasma lipids and lipoproteins. Elevated lipoprotein levels in most patients with CHD reflects the adverse impact of a sedentary lifestyle, excess body weight, and diets high in total and saturated fats. More than 70 clinical trials examining the effect of cholesterol reduction have been reported. These studies unequivocally demonstrated that lowering LDL reduces fatal and nonfatal heart attacks.<sup>10 – 13</sup>

### **Aim of study**

Direct experimental evidence supporting beneficial effects of nuts, especially almond, walnut, and macadamia was investigated, especially on almond by Spiller et al in the late 1980s.<sup>7</sup> Previous studies have used a relatively medium to high dose of nuts (e.g. 100 – 500 g raw almond) for observing a significant decrease in serum LDL level. Nuts, have a distinctive amino acid profile with high arginine content, a precursor of nitric oxide (a potent vasodilator). Furthermore, because low-dose protective phytochemicals including phytosterols, saponins, and carotenoids are needed to maintain these favorable effects on plasma cholesterol and all these materials have been found in large amounts in nuts, hence, we conducted a dietary intervention study,

incorporating equal amounts of almond and placebo to determine whether the consumption of whole almonds would have differential effects on plasma lipids. We hypothesized that the effects of almond in a lower amount would differ from those of higher doses as stated in previous studies.

## **Patients and Methods**

### **Study design**

In a randomized single blind, cross-over clinical trial, 30 hyperlipidemic subjects were studied. The structure of study was similar to previous studies designed by Spiller and his colleagues.<sup>2, 7, 14</sup>

This eight-week dietary trial was divided into two consecutive four-week intervention periods. Baseline blood lipid levels were measured on days 1 and 3 of the baseline diet study. Then, subjects were ranked by their total cholesterol (TC) values to either almond or reference diet during the first phase of the study. They consumed either almond or a reference diet for a period of 4 weeks. Blood lipid measurement was again taken on the 28<sup>th</sup> day of the first treatment phase.

After a washout period of 5 – 7 days on the 35<sup>th</sup> day of the first treatment phase, the almond group was crossed over by the reference diet and the reference diet was crossed over by the almond group for another 4 weeks. Blood lipid measurement was again taken on the 28<sup>th</sup> day of the second treatment phase, as show in Figure 1.

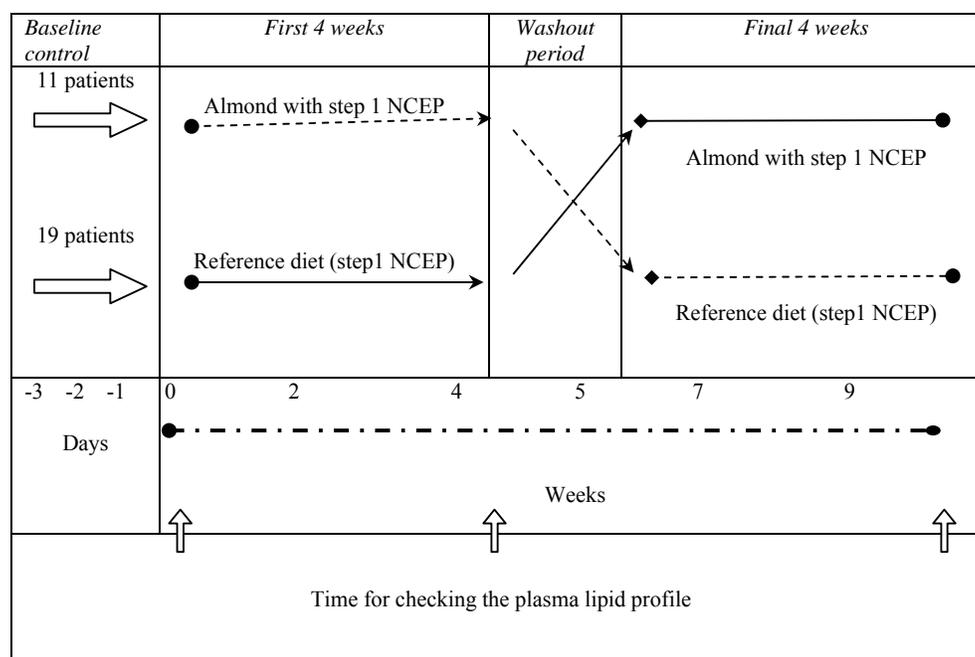
Subjects were weighed at the beginning of the study, at the cross-over point, and at the end of the study. They were asked not to attempt to gain or lose weight while on the study.

### **Subjects**

Thirty-five hypercholesterolemic adults, recruited from a central clinic (Vali-e-Asr Day Clinic) in Isfahan city, were included in this study after a preliminary medical history review and laboratory screening for TC greater than 220 mg/dL. Patients were excluded if they had coronary heart disease, diabetes mellitus, taking lipid-lowering agents, or had total cholesterol levels  $\geq$  350 mg /dL and triglyceride (TG) < 400 mg/dL.

All subjects were ranked by the first baseline TC, from lowest to highest, and then separated into 2 groups. The patients were then randomly placed in each group.

During the study, three patients from the first group (almond diet first) and one patient from the



**Figure 1.** Schematic view of this study.

second (reference diet initially) group were lost because of their preexisting gastrointestinal problems, which made it difficult for them to continue with the diet.

Thirty patients completed both phases of the study. The mean age of these subjects was  $56 \pm 6.1$  years (mean  $\pm$  SD, range 48 to 82 years); their body weight was  $63 \pm 8.9$  kg (ranged between 50 – 79 kg); and their body mass index (BMI defined as the weight in kg divided by the square of height in meters) was  $24.1 \pm 4.5$  (ranged between 17.5 – 36.1). Seventeen patients were males and 13 females. They had a mean baseline TC level of  $264 \pm 27$  mg/dL, an LDL-C of  $170 \pm 30.6$  mg/dL, an HDL-C of  $40 \pm 9.7$  mg/dL, TG of  $264 \pm 71$  mg/dL, and a TC/HDL ratio of  $6.9 \pm 1.6$ .

Subjects were told to take only medications approved by the investigators and to inform them immediately, should medications become necessary. They were also asked to maintain their normal daily activities and other routine lifestyle habits and record in diaries any signs of side effects due to the medications used or any deviation from their experimental diets. Checking the patient diaries showed that none deviated from their primary recommendations. No subject reported side effects during the almond diet.

The study design and protocol were approved by the investigational center review committee on the use of human subjects in research, at Isfahan

University of Medical Sciences, Isfahan, Iran. All subjects provided written informed consents.

## Diets

### Baseline period

Following the first baseline blood sampling, subjects were individually instructed to keep 3-day weighed food records, just a week before the start of study. Subjects were also told not to change their typical food pattern during this baseline period and received no specific information about the experimental diet until the end of the period. These instructions were intended to discourage subjects from initiating dietary changes before the commencement of the dietary section of the study.

### Study period

Information from 3-day records was used to compare the fat content of each subject's diet before and during the intervention.

A cholesterol-lowering diet was selected as the reference diet. It was designed according to the dietary guidelines for healthy American adults.<sup>11</sup> Macronutrient and dietary fiber content of nuts and reference diets are listed in Table 1.

The reference diet included foods from most of the major food groups, but did not contain nuts, nut butter and margarines, and nut oils of any kind. Alternatively, in the current study, all foods were classified into one of the four categories based on

**Table 1.** Macronutrient and dietary fiber content of nuts and reference diets.

	Almond diet	Reference diet	Difference
Total energy (Kcal/d)	1900	1920	20
Protein (%)	17	15	2
Carbohydrates (%)	47	45	2
Total fat (%)	37	29	8*
Sat (g/d)	23	19	
MUFA (g/d)	19	29	
PUFA (g/d)	10	13	
Dietary fiber (g)	12	20	8*

Sat = saturated fat; PUFA = polyunsaturated fatty acids; MUFA = monounsaturated fatty acids; \* = significant; Kcal = kilocalorie; d = day.

their total cholesterol, amount of saturated fats and calories. Therefore, subjects learned how often they could consume unlimited (like fruits, vegetables, grain products, and < 2.5% fat dairy products), limited (such as medium fat cheese, meat, and egg), not allowed (mayonnaise and butter, and whole fat dairy products), and unchanged (such as tea and coffee) foods. Thus, a detailed list of foods describing the basic dietary pattern was given to each subject and explained to them by the investigators.

The almond diet was identical to the reference diet, with preservation of NCEP step 1 diet. The almond diet substituted two serving of almond powder per day (25 g/day) for each phase. Each 25 g almond consisted of 150 Kcal, 11 g total fat, 5 g proteins, and 3.3 g dietary fiber.

In the reference diet, approximately 145 to 155 Kcal per day were added to the background diet, for the equivalence of caloric intake. Additionally, the total fat of each diet was matched.

Eleven subjects followed the almond diet first, and nineteen the reference diet. During each visit for blood sampling, every subject individually met the study nutritionist, and details of diet compliance were discussed.

### Treatments

All the almond powder bags were prepared and preweighed in the Pharmaceutical Department of Shahrekord University of Medical Sciences. A 4-week supply of almonds was packaged in a small bag and distributed between the subjects at the beginning of the study phase.

### Plasma cholesterol and lipoprotein measurements

At each blood sampling, two 10 mL blood samples were drawn into vacuoliner tubes containing NaEDTA, after a 12-hour fast. Each vacuoliner tube was then centrifuged for 15 minutes at 800 g. The specimens were analyzed on the evening of the study day, following blood

sampling. High-density lipoprotein cholesterol (HDL-C) was separated from plasma by a precipitation procedure, using heparin and manganese chloride. TC present in the remaining portion of plasma and in the separated HDL-C fraction was measured by an enzymatic procedure on a bichromatic spectrum analyzer (Vali-e-Asr Clinical Laboratory, Isfahan). TG was analyzed by a similar enzymatic procedure on the spectrum analyzer. These analytical procedures were standardized and met the performance requirement of lipoprotein standardization program of the Iranian Central Laboratory.

LDL-C was estimated according to the Friedewald et al algorithm.<sup>15</sup>

### Statistical methods

The two cross-over sequence groups were compared for any baseline differences by the one-way analysis of variance (ANOVA) statistical test. The baseline level for each subject was the average of two measurements obtained during the baseline period (day 1 and 3). The average baseline plasma lipid levels were subtracted from the average lipid levels obtained for each subject. A cross-over ANOVA on these differences was used to test the treatment phases, the two sequence groups, and the two diet treatments. Only if the ranked data were found to be significant, the results were considered as significant ( $P < 0.05$ ). Significant  $P$  value for testing the null hypotheses of no difference among the two dietary regimen was computed on the basis of approximate  $F$  statistics. All the results are expressed as mean  $\pm$  SD.

## Results

### Plasma lipids

Thirty subjects completed the study. Results from a one-way ANOVA indicated that there were no significant difference between the two sequences of subjects for any of the plasma lipid measurements at baseline. Changes in plasma lipid

**Table 2.** Effect of diets containing almond or reference diet on plasma cholesterol and lipoproteins.

Treatment	TC	TG	LDL-C	HDL-C	TC/HDL
Baseline*	259 ± 19.3	295 ± 71	160 ± 32.3	39.6 ± 10.8	7.02 ± 2.14
Almond	252 ± 35	252 ± 71	157 ± 30*	43 ± 7	6 ± 1.5
Reference diet	268 ± 25	235 ± 75	179 ± 31	48 ± 9	6.6 ± 1.7

Values are mean ± SD and are in mg/dL. TC = total cholesterol; TG = triglyceride; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; TC/HDL = total cholesterol to high-density lipoprotein cholesterol ratio; \* = baseline values are means of days 1 and 3 (before treatment). \* = significant difference ( $P < 0.05$ ).

parameters are shown in Table 2.

When the changes indicated in Table 3 were tested against zero (where the null hypothesis shows no difference from the baseline), the almond caused a statistically significant reduction in LDL-C ( $P < 0.01$  and  $F = 6.4$ ) and TC ( $P < 0.05$  and  $F = 3.1$ ). ANOVA analysis did not show any significant change in HDL-C and TG levels during the diet period.

### Body weights

Body weights were not changed during the study. Mean subject weights were  $62.8 \pm 9$  kg at baseline and  $63 \pm 8.8$  kg at the end of the survey ( $P = 0.8$ ). It seems that subjects did not change their total caloric intake during the study.

## Discussion

This study was performed in order to test the hypothesis that a diet containing lower doses of almond, compared to other studies, could induce beneficial changes in serum lipids.

Our results suggest that the objectives of this study were achieved. These findings showed that a diet containing almond in lower doses than that used in other studies (25 g/day vs. 100 g/day), can induce a protective alteration in the lipoprotein profile, compared to the reference diet. This survey also showed a significantly favorable decrease in LDL-C (about 6%) and TC (about 4%) relative to the reference diet. This amount appears to be well tolerated and the total decrease in LDL-C was somewhat similar to the other studies on almond and also walnut or pistachio.<sup>3, 7, 18, 20, 24</sup> Moreover, in the present study, HDL-C level was not changed by almond as a result of reduction in TC, being attributed to changes in LDL-C, as found in the present-based diet. This finding was comparable to the results of other investigators (Table 4).

An explanation of the enhanced lipid-altering activity of the almond-based diet could be the contribution made by an inquired intake of plant foods and a decreased intake of animal foods. It is clear that saturated fatty acid (SFA) increases both TC and LDL-C.<sup>17</sup> Therefore, almond which is a rich source of monounsaturated free fatty acids (MUFA) (mainly  $\omega$ -9, about 10 g/ounce) and a relatively good source of polyunsaturated free fatty acids (PUFA), and has relatively large amounts of linoleic acids (about 11 g per 100 g of edible portion), could induce a protective lipid profile in hypercholesterolemic subjects.<sup>7</sup> However, the increase in MUFA in this study was associated with a higher intake of fiber and vegetable protein from plant foods such as grains and nuts. These factors are known to influence lipid levels.<sup>3,7,16,25</sup> Moreover, almond may be preferred to walnut due to the current research, suggesting that diets high in polyunsaturated fats as in walnut, in large amount, are potentially carcinogenic, especially for breast carcinoma of the women.<sup>24</sup>

Meanwhile, the differences in effectiveness between the almond in this survey and other similar studies (Table 3, for total cholesterol, 4% vs. 10 – 15% and for LDL-C 6% vs. 14 – 20%) may be due to higher doses of almond or other nuts high in MUFA in other studies.<sup>2, 6, 7, 18, 23 – 25</sup> A summary of studies on the cholesterol-lowering effects using almond or other nuts (e.g. walnut) as an adjunct to NCEP step 1 diets are presented in Table 3.<sup>2, 6 – 7, 18 – 22</sup>

Almond is an easy food to consume, with an ideal fatty acid pattern for a high MUFA diet and a good PUFA: SFA ratio.<sup>7</sup> When the consumption of nuts high in MUFA increases, the fat content of the diet is expected to reduce plasma cholesterol rather than elevating it, possibly due to the MUFA content of these nuts.

The enormous variety of these foods which are

**Table 3.** Reduction in plasma cholesterol and lipoprotein by diets containing almond or reference diet.

Treatment	TC*	TG	LDL-C <sup>¶</sup>	HDL-C
Almond diet	-7 ± 4	-43 ± 1	-3 ± 1	4 ± 2
Reference diet	9 ± 4	-54 ± 4	19 ± 2	9 ± 1

Values are mean ± SEM and are in milligram/dL. TC = total cholesterol; TG = triglyceride; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; \* = significant between treatments at  $P < 0.01$ ; ¶ = significant between treatments at  $P < 0.05$ .

**Table 4.** Summary of studies of the cholesterol-lowering effects of almond as an adjunct to NCEP step 1 diets.

	Diet and Design	Dose g/d	No.	% of changes		
				TC	LDL-C	HDL-C
Spiller, et al <sup>7</sup>	9 weeks single group free-living trial. No control	100	27	-10%	-12%	No change
Spiller et al <sup>2</sup>	4 weeks randomized supplemented feeding trial	100	30	-15%	-17%	No change
Berry et al <sup>20</sup>	Compare MUFA (almond) to PUFA (walnut)	200	41	Almond -10% Walnut -16%	Almond-14% Walnut-20%	No change
Abbey et al <sup>19</sup>	9 weeks raw almond and walnut in normolipidemic male.	>200	16	Almond -7% Walnut -5%	Almond-10% Walnut-9%	No change
Berry et al <sup>6</sup>	Cross-over trial High MUFA with baseline	200		-8%	-14%	No change
Spiller et al <sup>21</sup>	4 weeks free living diet high in MUFA of plants	150	15	-8%	-15%	No change
Spiller and Brace <sup>1</sup>	8 weeks cross-over; low fruits and vegetables compared with plant-rich diet (almond and walnut).	150	12 female	-13%	-16%	No change
Sabate et al <sup>18</sup>	Walnut control randomized cross-over	84	18	-12%	-16%	-5%
Curb et al <sup>22</sup> (unpublished)	4 weeks <i>Macadamia</i> ; cross-over			-7%	-9%	+9%
Farquhar <sup>3</sup>	Randomized trial with 3 groups (almond compared with olive oil or control)	100	52	-10%	-16%	No change

TC = total cholesterol; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol.

available, convenient, and well accepted suggest that plant diets, such as the one in this study, could be an effective or a focal point for hypolipidemic diets. However, further research is warranted to identify additional effects of plant-based diets and its required dosage using unrefined, minimally pressed foods on heart disease risk factors and the atherogenic pressed.

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