Nuts and their bioactive constituents: effects on serum lipids and other factors that affect disease risk[1,2]

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ABSTRACT Because nuts have favorable fatty acid and nutrient profiles, there is growing interest in evaluating their role in a heart-healthy diet. Nuts are low in saturated fatty acids and high in monounsaturated and polyunsaturated fatty acids. In addition, emerging evidence indicates that there are other bioactive molecules in nuts that elicit cardioprotective effects. These include plant protein, dietary fiber, micronutrients such as copper and magnesium, plant sterols, and phytochemicals. Few feeding studies have been conducted that have incorporated different nuts into the test diets to determine the effects on plasma lipids and lipoproteins. The total- and lipoprotein-cholesterol responses to these diets are summarized in this article. In addition, the actual cholesterol response was compared with the predicted response derived from the most current predictive equations for blood cholesterol. Results from this comparison showed that when subjects consumed test diets including nuts, there was an ≈25% greater cholesterol-lowering response than that predicted by the equations. These results suggest that there are non–fatty acid constituents in nuts that have additional cholesterol-lowering effects. Further studies are needed to identify these constituents and establish their relative cholesterol-lowering potency. *Am J Clin Nutr* 1999(suppl);70:504S–11S.

KEY WORDS Nuts, plant foods, dietary fat, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, predictive equations, coronary heart disease risk reduction, cardiovascular disease prevention, blood cholesterol, LDL cholesterol, phytochemicals, plant sterols, dietary fiber, copper, magnesium

INTRODUCTION

In nutrition, a new era is emerging that is characterized by the search for dietary constituents that have benefits beyond those ascribed to the macro- and micronutrients. Historically, in the area of cardiovascular disease (CVD), efforts have been directed toward identifying the type and, to some extent, amount of dietary fat that can achieve maximal risk reduction. It is now clear that although a fat-modified diet can significantly affect CVD risk, other components in the diet, such as dietary fiber, plant protein, and soy protein appear to confer additional protective effects that extend beyond the lipid-lowering effects of the recommended diets. Identification of additional dietary constituents that elicit favorable effects will facilitate the development of diets that are even more effective for both the prevention and treatment of CVD and other chronic diseases.

In the search for bioactive components in foods that favorably affect CVD risk, nuts have begun to attract attention. Nuts are complex plant foods that are not only rich sources of unsaturated fat but also contain several nonfat constituents such as plant protein, fiber, micronutrients (eg, copper and magnesium), plant sterols, and phytochemicals (1). Because nuts have a favorable fatty acid profile and contain several bioactive compounds that may confer additional protective effects, there is interest in evaluating the role of nuts in cholesterol-lowering diets. Thus, the purpose of this article is to summarize the results of studies that have examined the effects of diets containing nuts on blood lipids and lipoproteins. Interestingly, when these data were compared with results predicted from regression equations using changes in dietary fatty acid profiles, nuts appeared to elicit a more potent lipid-lowering effect than would be expected. This provocative evidence suggests that there are other bioactive components in nuts that have cholesterol-lowering effects. In addition, other putative beneficial effects of constituents in nuts, beyond those associated with lowering blood cholesterol, are discussed briefly in this article.

PREDICTIVE EQUATIONS FOR BLOOD CHOLESTEROL

Data from well-controlled feeding studies conducted during the past 40 y were used for regression analyses that resulted in development of predictive equations for plasma cholesterol. These equations provided important information about the qualitative and quantitative effects of fatty acid classes on blood cholesterol concentrations. The first predictive equations for cholesterol were developed by Keys et al (2) and Hegsted et al (3) (**Table 1**). These equations were subsequently modified by Mensink and Katan (4), Hegsted et al (5), and Yu et al (6) to predict the effects of fatty acid classes on LDL- and HDL-cholesterol responses (Table 1).

All of these equations show that saturated fatty acids (SFA) raise blood cholesterol concentrations approximately twice as

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TABLE 1
Predictive equations for estimating the changes in plasma cholesterol and lipoprotein concentrations in response to changes in dietary fatty acids and cholesterol[1]

Source	Equations
Keys et al (2)	$\Delta TC = 1.35(2\Delta S - \Delta P) + 1.52\Delta Z$
Hegsted et al (3)	$\Delta TC = 2.16\Delta S - 1.65\Delta P + 0.067\Delta C - 0.53$
Mensink and Katan (4)	$\Delta TC = 1.51\Delta S - 0.12\Delta M - 0.60\Delta P$ $\Delta LDL\text{-}C = 1.28\Delta S - 0.24\Delta M - 0.55\Delta P$ $\Delta HDL\text{-}C = 0.47\Delta S + 0.34\Delta M + 0.28\Delta P$
Hegsted et al (5)	$\Delta TC = 2.10\Delta S - 1.16\Delta P + 0.067\Delta C$ $\Delta LDL\text{-}C = 1.74\Delta S - 0.77\Delta P + 0.44\Delta C$ $\Delta HDL\text{-}C = 0.43\Delta S + 0.10\Delta M + 0.22\Delta P + 0.18\Delta C$
Yu et al (6)	$\Delta TC = 2.02\Delta 12{:}0 - 16{:}0 - 0.03\Delta 18{:}0 - 0.48\Delta MUFA - 0.96\Delta PUFA$ $\Delta LDL\text{-}C = 1.46\Delta 12{:}0 - 16{:}0 + 0.07\Delta 18{:}0 - 0.69\Delta MUFA - 0.96\ \Delta PUFA$ $\Delta HDL\text{-}C = 0.62\Delta C12{:}0 - 16{:}0 - 0.06\Delta 18{:}0 + 0.39\Delta MUFA + 0.24\ \Delta PUFA$

[1] TC, plasma total cholesterol (in mg/dL); LDL-C, plasma LDL cholesterol (in mg/dL); HDL-C, plasma HDL cholesterol (in mg/dL); MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid. S, percentage energy from saturated fatty acids/d; M, percentage energy from monounsaturated fatty acids/d; P, percentage energy from polyunsaturated fatty acids/d; Z, square root of daily dietary cholesterol in μg/cal; C, dietary cholesterol in mg/d (3) or in μg/cal (5). To convert to SI units, the equations as presented should be calculated using non-SI units and the resulting value can then be converted to SI units as follows: multiply ΔTC, ΔLDL-C, and ΔHDL-C each by 0.02586.

much as polyunsaturated fatty acids (PUFA) lower them. Monounsaturated fatty acids (MUFA) either have a neutral effect on blood cholesterol concentrations or are mildly hypocholesterolemic. Consumption of dietary cholesterol also increases blood cholesterol concentrations, but its effect is less than that of SFA. The LDL-cholesterol response parallels the total-cholesterol response. Interestingly, all fatty acid classes raise HDL-cholesterol concentrations compared with carbohydrates, but SFAs are the most potent in this respect.

A recent meta-analysis of 395 metabolic-ward studies (7) confirmed the results of the regression analyses conducted to date and extended these findings to show that the results are not affected by experimental design, age, sex, body weight, energy intake, baseline cholesterol intake, or study duration. Thus, the predictive equations are useful for estimating the effects of dietary change on lipids and lipoproteins in any population group. Moreover, these equations can provide important clues about the presence of additional dietary components that exert a cholesterol-lowering effect that is greater than predicted. Any physiologically important deviation from what would be predicted based on the fatty acid profile of the diet provides evidence suggesting the presence of additional bioactive substances that regulate blood cholesterol concentrations.

FAT, FATTY ACID, AND NUTRIENT COMPOSITION OF NUTS

The energy content of nuts ranges from 23.7 to 29.3 kJ/g (161 to 199 kcal/oz) and the fat content is ≈0.51 to 0.73 g/g. Nuts that are higher in energy are higher in fat. Thus, ≈79% of the energy in nuts comes from fat. Nuts are low in SFA and high in unsaturated fatty acids. The predominant type of unsaturated fatty acid in most nuts is MUFA, contributing on average ≈62% of the energy from fat. MUFA and PUFA together contribute ≈91% of the energy from fat. Of the tree nuts, walnuts are unique because they are a rich source of α-linolenic acid. Compared with vegetable oils that are commonly used in the United States, nuts have less SFA than olive oil and slightly more SFA than canola and high-oleic-acid safflower oils, on average. The oleic-acid content of nuts is similar to that of canola oil, but less than that of olive oil and high-oleic-acid safflower oil. Canola oil and nuts contain similar amounts of linoleic acid, and these amounts are appreciably greater than those present in olive oil and high–oleic acid safflower oil. The fatty acid profiles of selected nuts and vegetable oils are shown in **Table 2**.

In addition to the distinctive fatty acid profiles of nuts, they are good sources of several other important nutrients including manganese, copper, magnesium, phosphorus, and zinc. Most nuts, particularly almonds, are good sources of vitamin E. Other nutrients present in notable quantities in most nuts include thiamine, niacin, riboflavin, selenium, potassium, and iron. Brazil nuts are particularly rich in selenium; a 28.4 g (1-oz) serving provides 920% of the recommended dietary allowance (8). Peanuts are a good source of folate and nuts are also high in fiber, providing 5–10% of the recommended daily fiber intake (9) in a 28.4-g serving (1).

FEEDING STUDIES THAT USED DIETS CONTAINING NUTS

To date, 9 studies have evaluated the effects of diets containing nuts on blood lipids and lipoproteins (10–18). The experimental designs of these studies were variable and subject characteristics differed, as did the degree of dietary control (**Table 3**). Six studies (10–15) were designed to specifically evaluate the effects of nuts on plasma lipids and lipoproteins; the nuts studied were almonds, walnuts, and macadamia nuts. Three studies (16–18) used nuts and other fat sources to achieve the fatty acid profile of the experimental diets tested (ie, high-MUFA and high-PUFA test diets). The total-fat and fatty acid profiles of the experimental diets varied, as shown in **Table 4**. In general, the experimental diets containing nuts were low in cholesterol (≈300 mg/d) and saturated fat, although the macadamia nut diet in the study conducted by Colquhoun et al (13) provided 11% of

TABLE 2
Fatty acid composition of nuts and selected oils as percentage of total fat by weight

	Total fat	Fatty acid							
		10:0	12:0	14:0	16:0	18:0	18:1	18:2	18:3n−3
		% of total fat by wt							
Nuts									
Almonds	52.2	0.0	0.0	0.6	6.6	1.9	63.7	20.1	0.7
Hazelnuts	62.6	0.0	0.0	0.2	5.0	2.0	77.7	9.3	0.2
Macadamia nuts[1]	73.2	0.0	0.0	0.6	8.5	3.7	55.8	1.7	0.0
Peanuts	49.2	0.0	0.0	0.1	10.5	2.2	48.1	31.6	0.0
Peanut butter	51.0	0.0	0.0	0.4	11.1	5.3	46.7	26.9	0.2
Pecans	67.6	0.0	0.0	0.0	6.1	1.5	60.9	23.6	1.0
Walnuts	56.6	0.0	0.0	0.0	3.7	2.5	21.0	59.2	5.8
Mean	58.9	—	—	0.3	7.4	2.7	53.4	24.6	1.1
Oils									
Olive oil	100	0.0	0.0	0.0	11.0	2.2	72.5	7.9	0.6
Canola oil	100	0.0	0.0	0.0	4.0	1.8	56.1	20.3	9.3
High-oleic-acid safflower oil	100	0.0	0.0	0.0	4.8	1.3	75.3	14.2	0.0

[1] Contain ≈23% palmitoleic acid (16:1) (as a percentage of total nut fat by weight).

energy from SFA. Total fat content varied, ranging from 26% (14) to 42% (13) of energy. The studies compared the effects of high-MUFA diets on plasma lipids, lipoproteins, or both with those of baseline, reference, or high-SFA diets; high-PUFA diets; or low-fat, high-carbohydrate diets. Spiller et al (10) and Abbey et al (18) also compared high-PUFA diets with high-SFA or reference diets. The study conducted by Sabaté et al (12) was unique because it compared two Step I diets, one of which was high in walnuts and, as a result, was high in PUFAs.

Irrespective of the amounts of fat and nuts in the diet, cholesterol-lowering diets that contained nuts reduced total- and LDL-cholesterol concentrations by ≈4–16% and 9–20%, respectively (**Table 5**). The reported reduction of total cholesterol in response to a Step I diet is 3–14% compared with an average American diet in normocholesterolemic men and women (19). In general, the diets that contained higher-fat nuts did not reduce HDL-cholesterol concentrations and increase triacylglycerol concentrations as did the low-fat, high-carbohydrate diets. In contrast, Sabaté et al (12)

TABLE 3
Study designs used to evaluate the effects of nut consumption on plasma lipids and lipoproteins[1]

Study and subjects	TC at baseline	Study duration	Study design	Diet characteristics
	mmol/L			
Spiller et al, 1990 (10) (*n* = 45 M and 45 F with hypercholesterolemia)	6.49[2]	4 wk	Parallel arm	*1*) High-PUFA (and high-MUFA) diet from almonds (100 g/d), *2*) high-MUFA diet from olive oil, 36 g/d, and *3*) high-SFA diet from cheese and butter.
Berry et al, 1991 (16) (*n* = 24 M)	3.81	12 wk	Randomized, controlled, crossover	*1*) High-MUFA diet from almonds, olive oil, and avocado and *2*) high-PUFA diet from walnuts, safflower oil, and soybean oil.
Berry et al, 1992 (17) (*n* = 17 M)	4.06	12 wk	Randomized, controlled, crossover	*1*) High-MUFA diet from almonds, olive oil, and avocados and *2*) low-fat, high-carbohydrate diet.
Spiller et al, 1992 (11) (*n* = 13 M and 13 F with hypercholesterolemia)	6.08	9 wk	Dietary advice, consecutive supplemental field study	*1*) High-MUFA diet from almonds (100 g/d) and *2*) baseline diet.
Sabaté et al, 1993 (12) (*n* = 18 M)	5.12	8 wk	Randomized, controlled, crossover	*1*) NCEP Step I, high-PUFA diet from walnuts (84 g/d) and *2*) NCEP Step I diet.
Abbey et al, 1994 (18) (*n* = 16 M)	5.15	3 wk	Consecutive supplemental field study	*1*) High-MUFA diet from almonds (84 g/d), *2*) high-PUFA diet from walnuts (68 g/d), and *3*) reference diet.
Colquhoun et al, 1996 (13) (*n* = 7 M and 7 F with hypercholesterolemia)	5.69	4 wk	Dietary advice, randomized, crossover	*1*) High-MUFA diet from macadamia nuts and *2*) low-fat, high-carbohydrate diet.
O'Byrne et al, 1997 (14) (*n* = 25 post-menopausal F with hypercholesterolemia)	6.60	6 mo	Dietary advice, parallel arm	*1*) Low-fat, high-MUFA diet from peanuts and *2*) low-fat diet.
Chisholm et al, 1998 (15) (*n* = 21 M with hypercholesterolemia)	6.58	4 wk	Dietary advice, randomized, crossover	*1*) High-PUFA diet from walnuts and *2*) low-fat diet.

[1] TC, total cholesterol; PUFA, polyunsaturated fatty acids; MUFA, monounsaturated fatty acids; SFA, saturated fatty acids; NCEP, National Cholesterol Education Program.
[2] $\bar{x}$.

TABLE 4
Fat and fatty acid profiles of experimental diets used in studies on the effects of nuts on plasma lipids and lipoproteins[1]

Study and diet characteristics	Total fat[2]	SFA[2]	MUFA[2]	PUFA[2]	Cholesterol
					mg
Spiller et al, 1990 (10)					
High-PUFA	NR	4 g	30 g	14 g	NR
High-MUFA	NR	9 g	36 g	4 g	NR
High-SFA	NR	NR	NR	NR	NR
Berry et al, 1991 (16)					
High-MUFA	33	8	16	7	300
High-PUFA	31	7	6	16	300
Berry et al, 1992 (17)					
High-MUFA	33	7	17	8	308
Low-fat, high-carbohydrate	18	5	7	6	328
Spiller et al, 1992 (11)					
High-MUFA	37	5	25	7	134
Baseline	29	6	1	6	184
Sabaté et al, 1993 (12)					
NCEP Step I, high-PUFA	31	6	7	17	125
NCEP Step I	29	9	9	10	237
Abbey et al, 1994 (18)					
High-MUFA	36	8	17	8	199
High-PUFA	37	9	10	16	235
Reference	36	16	12	7	205
Colquhoun et al, 1996 (13)					
High-MUFA	42	11	27	4	190
Low-fat, high-carbohydrate	21	9	8	5	218
O'Byrne et al, 1997 (14)					
High-MUFA, low-fat	26	5	14	2	130
Low-fat, high-carbohydrate	17	5	6	2	129
Chisholm et al, 1998 (15)					
High-PUFA	38	10	10	16	230
Low-fat, high-carbohydrate	30	12	10	5	320

[1] NR, not reported; PUFA, polyunsaturated fatty acids; MUFA, monounsaturated fatty acids; SFA, saturated fatty acids; NCEP, National Cholesterol Education Program.
[2] As percentage of energy unless otherwise indicated.

reported reductions in both HDL-cholesterol and triacylglycerol concentrations in subjects who consumed the Step I, high-PUFA diet that contained walnuts. Interestingly, studies that used 3 other high-PUFA diets (15, 16, 18) that provided similar amounts of PUFA did not report an HDL-cholesterol–lowering effect, which may have been due to higher contents of SFA (15, 18) or dietary cholesterol (15, 16, 18) provided by the high-PUFA test diets.

Collectively, the few studies reported to date showed that cholesterol-lowering diets containing nuts had favorable effects on total- and LDL-cholesterol concentrations. It is important to note, however, that the studies conducted have not truly evaluated the specific effects of nuts on plasma lipids and lipoproteins. Rather, in the studies reviewed herein, nuts were used along with other foods simply as a food source to manipulate the nutrient profiles of the test diets (ie, mainly the total fat contents and fatty acid profiles). Thus, a question that remains to be resolved is, what are the effects of the various nuts on plasma lipids and lipoproteins? This question could be evaluated by using well-controlled experimental diets (eg, Step I, Step II, and average American) to which various nuts could be added and compared with a control fat source. This approach would control the total-fat and fatty acid profiles of the diets, so that any differences observed would be the result of other nut constituents. Studies such as these will clarify the putative health benefits of nuts beyond those attributable to their favorable fatty acid profiles.

Although these proposed studies should provide useful information about any health effects associated with the nonfat components of nuts, it is evident from the existing data that nuts can be included in, and even used to design, cholesterol-lowering diets that have desirable fat contents and fatty acid profiles. Because of their distinguishing macronutrient and fatty acid characteristics, nuts can be used to reduce the SFA content of the diet by replacing SFA energy with energy from unsaturated fatty acids while maintaining the amount of dietary fat. This is an effective strategy for not only achieving reductions in total- and LDL-cholesterol concentrations but also preventing the HDL-cholesterol–lowering and triacylglycerol-raising effects of low-fat, high-carbohydrate diets.

EVIDENCE OF NONFAT HYPOCHOLESTEROLEMIC FACTORS IN NUTS

There is convincing evidence that the fatty acid profiles of nuts have favorable effects on blood lipids, but a related and as of yet unanswered question is, Are there other constituents in nuts that also affect blood cholesterol concentrations? This is a most intriguing question because there are several potentially bioactive components in nuts. Studies conducted with soy products have shown beneficial effects of both soy protein and phytoestrogens (20, 21). Given that nuts contain plant protein and many different

TABLE 5
Effects of experimental diets containing nuts on plasma lipids and lipoproteins[1]

Study and diet characteristics	Total cholesterol	LDL cholesterol	HDL cholesterol	Triacylglycerol
		% change		
Spiller et al, 1990 (10)				
High-PUFA compared with baseline	−12	NR	NR	NS
High-MUFA compared with baseline	−5	NR	NR	NS
High-SFA compared with baseline	+4	NR	NR	NS
Berry et al, 1991 (16)				
High-MUFA compared with baseline	−10	−14	0 (NS)	–10 (NS)
High-PUFA compared with baseline	−16	−20	−4 (NS)	−9 (NS)
Berry et al, 1992 (17)				
High-MUFA compared with baseline	−8	−14	+1 (NS)	−4 (NS)
Spiller et al, 1992 (11)				
High-MUFA compared with baseline	−9	−12	0 (NS)	−4 (NS)
Sabaté et al, 1993 (12)				
NCEP Step I, high-PUFA compared with NCEP Step I	−12	−16	−5	−8
Abbey et al, 1994 (18)				
High-MUFA compared with reference	−7	−10	0 (NS)	+1 (NS)
High-PUFA compared with reference	−5	−9	+3 (NS)	+4 (NS)
Colquhoun et al, 1996 (13)				
Low-fat, high-carbohydrate compared with baseline	−8	−11	−13	−9 (NS)
High-MUFA compared with baseline	−8	−11	+1 (NS)	−21
O'Byrne et al, 1997 (14)				
High-MUFA, low-fat compared with baseline	−10	−12	0 (NS)	−1 (NS)
Low-fat, high-carbohydrate compared with baseline	−2 (NS)	0 (NS)	0 (NS)	+12 (NS)
Chisholm et al, 1998 (15)				
High-PUFA compared with low-fat, high-carbohydrate	−2 (NS)	−4 (NS)	+3 (NS)	+8 (NS)

[1] NR, not reported; PUFA, polyunsaturated fatty acids; MUFA, monounsaturated fatty acids; SFA, saturated fatty acids; NCEP, National Cholesterol Education Program.

phytochemicals, it is not unreasonable to speculate that the nonfat fraction of nuts could exert beneficial biological effects.

We reasoned that to determine whether there is any basis for this theory, any discrepancies between changes in total- and LDL-cholesterol concentrations estimated from the predictive equations and the actual values observed as a result of changes in dietary fatty acid consumption would be revealing. Specifically, if the observed change exceeded the predicted change in plasma lipids, this might indicate the presence of bioactive, nonfat, cholesterol-lowering compounds.

We conducted an analysis to compare the observed changes to the predicted changes in total-, LDL-, and HDL-cholesterol concentrations. To accomplish this, we first calculated the change in dietary fatty acid composition when subjects were switched from an experimental diet not containing nuts, or a baseline diet, to an experimental diet containing nuts. These values were used to calculate the predicted total-, LDL-, and HDL-cholesterol responses to the change in dietary fatty acids using the Hegsted et al (5) and Mensink and Katan (4) regression equations. One of the original equations developed for total cholesterol (3) was also used. The observed changes were simply determined by calculating the mean changes in total-, LDL-, and HDL-cholesterol concentrations (12–15, 18). The Student's *t* test was then used to compare the predicted with the observed lipid and lipoprotein changes.

The evidence shown in **Figure 1** suggests that components in nuts further reduce total- and LDL-cholesterol concentrations beyond the effects predicted by equations based on the fatty acid profiles of nuts ($P < 0.05$) (3, 4, 5). The magnitude of the cholesterol-lowering effect is ≥25% greater than would be predicted based on the fatty acid profiles of the test diets studied. Similarly, a recent study (22) that investigated the effect of a diet high in vegetables, fruit, and nuts found that total serum cholesterol was reduced 34% and 49% more than was predicted by the Keys et al (2) and Hegsted et al (3) equations, respectively. The interpretation we favor is that there seem to be other constituents in nuts that account for this response. We hasten to add, however, that this conclusion is based on limited data and there is no direct experimental evidence to support this conclusion. Thus, it will be important to conduct the necessary studies to clarify this potentially important nutrition question. This question could be readily addressed by conducting controlled feeding studies in which one experimental diet includes nuts and is compared with another test diet that has the same fat content and fatty acid profile but does not contain nuts.

BEYOND LIPIDS: OTHER NUTRIENTS IN NUTS THAT ARE THOUGHT TO CONFER HEALTH BENEFITS

Nuts are complex plant foods. In addition to being a rich source of fat (which accounts for ≈60% of the weight and 80% of the energy) and unsaturated fatty acids, they are a unique source of plant protein that is high in arginine, fiber, and various micronutrients. Nuts are also sources of phytosterols and other phytochemical compounds with potential serum cholesterol-modulating effects. The phytochemicals in nuts include ellagic acid, flavonoids, phenolic compounds, luteolin (a major antioxidant), and tocotrienols. Several other bioactive compounds have been identified in plant products (**Table 6**) (23). Little is known about the presence or quantities of these compounds in different nuts. It will be important to characterize these compounds in nuts and

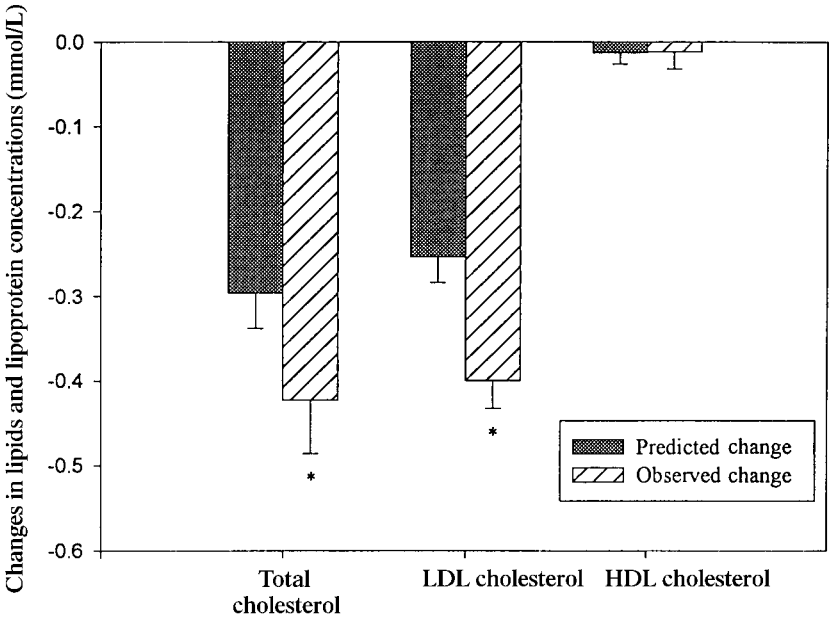

FIGURE 1. Comparison of observed changes (mean ± SE) in total-, LDL-, and HDL-cholesterol concentrations (12–15, 18) with those calculated by using the predictive equations for plasma cholesterol of Hegsted et al (5) and Mensink and Katan (4) (*see* Table 1; data are means of the results from both equations). *Observed change was significantly different from the predicted change, $P < 0.05$ (*t* test).

determine whether they are functional nutrients that confer any health benefits. There is some compelling evidence suggesting that flavonoids have cardioprotective effects. Epidemiologic studies (24, 25) have shown that flavonoid intake is significantly and inversely associated with coronary heart disease mortality.

Nuts contain n−3 fatty acids, which have been shown to elicit cardioprotective effects. The highly unsaturated n−3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are primarily responsible for this effect (26). However, α-linolenic acid also has a role because it is converted to some extent to EPA and DHA (27). Compelling evidence for an effect of α-linolenic acid was reported in the Lyon Diet-Heart Trial (28), in which patients who had suffered a myocardial infarction followed an American Heart Association Step I, Mediterranean-type diet rich in α-linolenic acid. Despite the lack of improvement in plasma lipids, lipoproteins, and body mass index, there was a marked reduction in coronary events and there were no sudden deaths in the treatment group compared with 8 in the control group. It has been suggested that the cardioprotective effects of n−3 fatty acids might be due to their antithrombogenic effects (29). n−3 Fatty acids have been shown to reduce platelet aggregation (both reactivity and adhesion) and vasoconstriction (30, 31). In addition, n−3 fatty acids have been shown to favorably affect hemostasis via effects on fibrinolysis (32) and blood clot formation (33).

Nuts are a source of dietary fiber (≈7 g/100g), of which ≈25% is soluble fiber. Soluble fiber has been shown to reduce total- and LDL-cholesterol concentrations and improve glycemic control (34). Thus, in the context of a high-MUFA diet in which nuts are the primary source of MUFA, nuts (ie, 100 g) can contribute appreciably to the recommended fiber intake (ie, 20–35 g/d) (9).

Vitamin E in high doses (>100 IU/d) has been shown to reduce the risk of coronary heart disease (35). This cardioprotective effect appears to be due to vitamin E-induced inhibition of LDL oxidation [vitamin E is transported in the LDL particle (36)], a key step in the atherogenic process. Nuts are a rich source of vitamin E, although the quantities obtained from typical nut consumption are far less than the amounts shown to have beneficial effects on coronary heart disease. Nonetheless, nut consumption is still an effective means of increasing vitamin E intake.

Folic acid is also found in nuts. Consumption of 100 g nuts provides ≈16% of the daily reference intake (DRI) for folic acid, which is 400 μg/d (9). Adequate consumption of folic acid is important for preventing elevated homocysteine concentrations, which have been shown to correlate with the severity of carotid-artery stenosis (37).

On average, 1 ounce of nuts contains ≈18% of the DRI for copper (2 mg) (9) and therefore nuts can be a significant source of this essential mineral (38). Copper plays a key role in hematopoiesis and diets low in copper have been associated with adverse changes in lipids, glucose tolerance, blood pressure, and electrocardiograms (39).

Almost all nuts are good sources of magnesium, providing ≈8–20% of the DRI (400 mg) (9) for this essential mineral in a 28.4-g (1-oz) serving (1, 40). Magnesium is important in maintaining the proper balance of calcium to potassium; low magnesium status can contribute to dysrhythmias, myocardial infarction, and possibly hypertension. Magnesium is also critical to enzyme function, healthy tooth enamel, muscle relaxation, and nerve transmission.

A meta-analysis of 38 controlled clinical studies showed that consumption of soy protein (ie, 47 g/d) reduced total- and LDL-cholesterol concentrations by ≈10% (20). The biological mechanisms responsible for this hypocholesterolemic effect are not clear. There is some evidence suggesting that arginine, the second most abundant amino acid found in nut proteins, may account for the

TABLE 6
Bioactive compounds found in plant products[1]

Indoles
Indole-3-carbinol
Indole-3-acetonitrile
3,3'-Diindomethane
Glucosinolates
Isitguictabates
Sulforaphen
Phenolics
Caffeic acid
Ellagic acid
Curcumin
Flavonoids
Luteolin
Quercetin
Myricetin
Apigenin
Kaempferol
Isoflavones
Genistein
Formononetin
Daidzein
Biochanin A
Terpenes
d-Carvone
d-Limonene
Organosulfuric compounds
Allyl methyl disulfide
Diallyl sulfide
Diallyl disulfide
Diallyl trisulfide

[1] Adapted from Kitts (23).

hypocholesterolemic effect observed (41, 42). In addition, there is evidence that the phytoestrogens in soy protein have cardioprotective effects (43). Little is known about phytoestrogens in nuts.

Plant sterols inhibit cholesterol absorption. Sitosterol, the most abundant plant sterol in vegetable oils, has been shown to elicit a marked hypocholesterolemic effect (44). Little is known about the plant-sterol content of nuts and the effects, if any, on cholesterol absorption and blood-cholesterol concentrations.

It is clear that nuts contain many nutrients and dietary factors that may confer protective health effects. Some of the components in nuts that are thought to be beneficial are listed in **Table 7**. A great deal of research will be needed to clarify the effects of these constituents found in nuts on the risk of coronary heart disease and other chronic diseases.

TABLE 7
Components in nuts that are thought to be beneficial

n–6 and n–3 Monounsaturated and polyunsaturated fatty acids
Fiber
Micronutrients
Vitamin E
Folic acid
Copper
Magnesium
Plant protein (arginine)
Phytochemicals
Plant sterols

PLANNING HEART-HEALTHY DIETS CONTAINING NUTS

Because they are low in SFAs, nuts can be incorporated easily into cholesterol-lowering diets that provide ≤30% of energy from fat and <10% of energy from SFAs. Because the total-fat and SFA allowances for an 8372-kJ (2000-kcal) diet are ≈67 g and 22 g, respectively, it is not difficult to include a serving of nuts [≈28 g (1 oz), which provides ≈16–17 g fat and 1–2 g SFA] in a 1-d menu. In a cholesterol-lowering diet that is higher in total fat (ie, ≈35% of energy from fat) and low in SFA, it is easy to incorporate 2 servings of nuts in a 1-d menu. For example, peanut butter can be used as a major source of protein in a meal (ie, as a peanut butter sandwich or as a spread on a bagel for breakfast). In addition, a serving of mixed nuts could be substituted for a serving of cookies as a snack. It would also be possible to include small quantities of nuts in a low-fat diet that provides 25% of energy from fat simply by substituting nuts isoenergetically for other fat sources in the diet (ie, margarine or mayonnaise).

SUMMARY AND CONCLUSIONS

Nuts have many beneficial attributes. The foremost at this time, simply because of the extensive data available, is the favorable fatty acid profile, which can be exploited in planning blood cholesterol-lowering diets. There may be a number of other bioactive compounds in nuts that potentiate cholesterol-lowering effects and independently affect risk factors for various chronic diseases. However, the data on this topic are limited and much research is needed to define the roles that these compounds may play in reducing the risk of chronic diseases, as well as the biological mechanisms involved. Irrespective of this, there are sufficient data to justify the recommendation to include nuts in the diet. As discussed, nuts can be readily incorporated into the diet. Efforts are needed to educate the public about the health benefits of nuts and ways to use them in planning a healthy diet.

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