Effect of garlic and fish-oil supplementation on serum lipid and lipoprotein concentrations in hypercholesterolemic men[1-3]

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ABSTRACT   This study examined the effects of garlic and fish-oil supplementation (alone and in combination) on fasting serum lipids and lipoproteins in hypercholesterolemic subjects. After an initial run-in phase, 50 male subjects with moderate hypercholesterolemia were randomly assigned for 12 wk to one of four groups: *1*) 900 mg garlic placebo/d + 12 g oil placebo/d; *2*) 900 mg garlic/d + 12 g oil placebo/d; *3*) 900 mg garlic placebo/d + 12 g fish oil/d, providing 3.6 g n−3 fatty acids/d; and *4*) 900 mg garlic/d + 12 g fish oil/d. In the placebo group, mean serum total cholesterol, low-density-lipoprotein cholesterol (LDL-C), and triacylglycerols were not significantly changed in relation to baseline. Mean group total cholesterol concentrations were significantly lower with garlic + fish oil (−12.2%) and with garlic (−11.5%) after 12 wk but not with fish oil alone. Mean LDL-C concentrations were reduced with garlic + fish oil (−9.5%) and with garlic (−14.2%) but were raised with fish oil (+8.5%). Mean triacylglycerol concentrations were reduced with garlic + fish oil (−34.3%) and fish oil alone (−37.3%). The garlic groups (with and without fish oil) had significantly lower ratios of total cholesterol to high-density-lipoprotein cholesterol (HDL-C) and LDL-C to HDL-C. In summary, garlic supplementation significantly decreased both total cholesterol and LDL-C whereas fish-oil supplementation significantly decreased triacylglycerol concentrations and increased LDL-C concentrations in hypercholesterolemic men. The combination of garlic and fish oil reversed the moderate fish-oil–induced rise in LDL-C. Coadministration of garlic with fish oil was well-tolerated and had a beneficial effect on serum lipid and lipoprotein concentrations by providing a combined lowering of total cholesterol, LDL-C, and triacylglycerol concentrations as well as the ratios of total cholesterol to HDL-C and LDL-C to HDL-C.   *Am J Clin Nutr* 1997;65:445–50.

KEY WORDS   Garlic, fish oil, total cholesterol, low-density-lipoprotein cholesterol, high-density-lipoprotein cholesterol, triacylglycerol

INTRODUCTION

The role of elevated serum total cholesterol and low-density-lipoprotein cholesterol (LDL-C) as well as reduced high-density-lipoprotein cholesterol (HDL-C) in the development of coronary artery disease is well-established (1). Patients with accompanying elevated serum triacylglycerol concentrations are at increased risk of developing atherosclerosis and coronary artery disease (2). Both the PROCAM study (3) and the Helsinki Heart Study (4) suggested that hypertriglyceridemia is a powerful additional risk factor of coronary artery disease, particularly when excessive triacylglycerol concentrations coincide with a high ratio (> 5.0) of LDL-C to HDL-C. In addition, recent studies have shown that triacylglycerol is independently related to coronary artery disease risk (5) and to the extent of coronary atherosclerosis (6).

Effective and safe treatment to reduce the simultaneous elevation of total cholesterol and triacylglycerol concentrations is limited (7). The use of nutritional supplements either alone (8) or in combination with a drug (7, 9) has been shown to be effective in lowering total cholesterol and triacylglycerol concentrations in hyperlipidemic subjects. Recently, Contacos et al (7) showed that pravastatin and fish oil, in combination only, effectively lowered both total cholesterol and triacylglycerol concentrations in subjects with both elevated cholesterol and triacylglycerol.

Fish oils rich in the n−3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been shown to effectively reduce elevated triacylglycerol concentrations (10). Fish oils may also raise HDL-C to a modest extent (10). However, supplementation with fish oil has been found to increase serum LDL-C concentrations (10, 11). To provide a more complete management of hyperlipidemia with fish oil, it may be beneficial to use an additional nutritional supplement to simultaneously lower LDL-C concentrations. Supplementation with garlic alone has been found to significantly reduce total cholesterol concentrations (8, 12). The purpose of the present study was to determine whether garlic powder, when given in combination with fish oil, could provide an effective and well-tolerated nutritional regimen for simultaneously reducing

elevated total cholesterol, LDL-C, and triacylglycerol concentrations in hypercholesterolemic men.

SUBJECTS AND METHODS

Subjects

Of 100 men screened for their total serum cholesterol concentration with a compact total cholesterol analyzer (Chemtrak 228; Accumeter, Sunnyvale, CA), 50 took part in the study, with each giving written informed consent. The principal criterion for entry was a total cholesterol concentration > 5.2 mmol/L (200 mg/dL). Subjects taking lipid-altering or blood pressure–altering medications or supplements within 4 wk of the beginning of the study were excluded. Other medications were allowed if they were not initiated within 4 wk of the beginning of the study. Subjects taking part in the study did not have diagnosed diabetes mellitus or cardiovascular disease.

The study conformed with the ethical guidelines of the University of Guelph.

Materials and supplements

Garlic pills (Kwai; Lichtwer Pharma, Berlin) were given as one 300-mg sugar-coated pill three times daily with meals. Garlic placebo pills (also from Lichtwer Pharma) were identical in appearance but contained no garlic powder. Fish oil containing n−3 fatty acids (Nupulse; Nu-Life, Markham, Canada) was given as four 1-g capsules (each containing 180 mg EPA and 120 mg DHA) three times daily with meals. Evening primrose oil (Bioriginal; PGE Canada, Saskatoon, Canada) containing n−6 fatty acids was used as a control oil supplement; it was given as three 1.3-g capsules three times daily with meals. Garlic pills were administered in a double-blind fashion. Fish oil and oil placebo were given in a single-blind fashion.

Study design

This randomized, placebo-controlled trial began with a 3-wk run-in phase in which baseline total cholesterol concentrations were confirmed by standard enzymatic techniques (procedure no. 352; Sigma Diagnostics, St Louis). At baseline (week 0), subjects with serum total cholesterol concentrations > 5.2 mmol/L (200 mg/dL) were randomly assigned to one of four treatment groups for 12 wk (week 0 to week 12). The four study regimens were as follows: 1) 900 mg garlic placebo/d + 12 g oil placebo/d; 2) 900 mg garlic/d + 12 g oil placebo/d; 3) 900 mg garlic placebo/d + 12 g fish oil/d, providing 3.6 g n−3 fatty acids/d; and 4) 900 mg garlic/d + 12 g fish oil/d.

Subjects provided overnight (12–14 h) fasting blood samples at weeks 0, 3, 6, 9, and 12. Sitting blood pressure and resting heart rate were taken at each visit by a digital blood pressure monitor. Compliance was assessed by capsule or pill count and serum phospholipid analyses (see below). Blinding to the supplements and their respective placebos was checked at the end of the study by a simple questionnaire. Side effects were monitored throughout the study period. Two 3-d estimated dietary records (two weekdays, one weekend day) were obtained from each subject; one during the 3-wk period before baseline (week 0), the other between week 9 and week 12 of the study. Dietary analysis was performed on the CanWest Diet Analysis Plus program (West Publishing Co, St Paul). Fasting

blood samples were analyzed for total cholesterol, LDL-C, HDL-C, and triacylglycerol concentrations at all time points between week 0 and week 12. Additionally, fatty acid compositions of total serum phospholipid were analyzed at week 0 and week 12.

Laboratory analyses

Blood was drawn by venipuncture into evacuated tubes (Vacutainer; Becton Dickinson, Rutherford, NJ), allowed to sit for 1 h, and then centrifuged (2500 rpm, 1000 × g) for 15 min at 30 °C to recover serum. Serum fractions were divided into aliquots and stored at −20 °C until assayed in one batch. Total cholesterol and triacylglycerol were determined by standard enzymatic techniques (procedure nos. 352 and 339; Sigma Diagnostics). HDL-C was determined in serum after precipitation of apolipoprotein B–containing lipoproteins (procedure no. 352-3; Sigma Diagnostics). LDL-C was calculated with the Friedewald equation (13) except if triacylglycerols were > 4.6 mmol/L (400 mg/dL) at one or more time point in the study, in which case LDL-C was determined directly (procedure no. 353-A; Sigma Diagnostics) at all time points for that subject. Fatty acid analyses were performed by capillary gas-liquid chromatography of the isolated phospholipid (by thin-layer chromatography) after transmethylation using procedures similar to those cited elsewhere (14).

Statistical analyses

Statistical tests were performed with the SAS computer program (SAS Institute Inc, Cary, NC). After logarithmic transformation of the data, efficacy parameters were analyzed by analysis of covariance. Pair-wise comparisons between treatment groups were performed with protected least-significant-difference techniques. Paired t tests were used for within-group effects on difference scores from baseline. All statistical analyses were two-tailed, with $\alpha = 0.05$.

RESULTS

Of the 50 people originally randomly assigned to treatment, 4 withdrew (2 from the garlic placebo + fish oil group, 1 from the garlic + oil placebo group, and 1 from the garlic placebo + oil placebo group) for personal reasons or because of unrelated medical conditions. The baseline characteristics of the 46 remaining subjects are listed in Table 1. There were no significant differences between the baseline characteristics of the original 50 subjects and the remaining 46 subjects (data not shown).

Dietary intakes and body weights at entry and after nutritional supplementation for all subjects are shown in Table 2. No significant differences ($P > 0.05$) were found in dietary composition or body weight between treatment groups either at baseline or after 12 wk of treatment (data not shown).

In the placebo group, mean serum total cholesterol, LDL-C, triacylglycerol, and HDL-C were not significantly changed in relation to baseline. Mean group total cholesterol concentrations were significantly lower with garlic + fish oil (−12.2%) and with garlic alone (−11.5%) by week 12 (Table 3). Significant reductions in total cholesterol with garlic and garlic + fish oil were seen starting at week 9. In the group taking fish oil

TABLE 1
Baseline demographic characteristics by supplementation group[1]

Characteristic	Placebo (n = 11)	Garlic (n = 12)	Fish oil (n = 10)	Garlic + fish oil (n = 13)	Total (n = 46)
Age (y)	45.4 ± 9.8	45.9 ± 12.6	45.4 ± 9.3	46.7 ± 13.1	45.9 ± 11.1
Weight (kg)	85.0 ± 11.3	85.1 ± 8.6	84.2 ± 21.7	84.6 ± 11.9	84.8 ± 13.4
BMI (kg/m²)	26.4 ± 3.5	27.2 ± 3.0	26.8 ± 6.4	26.9 ± 3.5	26.8 ± 4.1
Total cholesterol (mmol/L)	6.46 ± 0.85	6.54 ± 0.88	6.54 ± 1.06	6.51 ± 1.06	6.51 ± 0.93
LDL cholesterol (mmol/L)	4.32 ± 0.83	4.39 ± 0.62	4.42 ± 0.88	4.47 ± 0.96	4.39 ± 0.80
HDL cholesterol (mmol/L)	1.20 ± 0.34	1.26 ± 0.22²	1.12 ± 0.34	1.13 ± 0.19	1.18 ± 0.27
Triacylglycerol (mmol/L)	1.95 ± 1.63	1.98 ± 1.10	2.34 ± 1.76	2.17 ± 1.54	2.10 ± 1.47
Total cholesterol/HDL cholesterol	5.80 ± 1.82³	5.38 ± 1.29²	6.38 ± 2.18	5.94 ± 1.56	5.85 ± 1.69
LDL cholesterol/HDL cholesterol	3.83 ± 1.18³	3.64 ± 0.90²	4.34 ± 1.60	4.08 ± 1.12	3.96 ± 1.19

[1] $\bar{x}$ ± SD.
[2] Significantly different from fish oil and garlic + fish oil, P < 0.05.
[3] Significantly different from fish oil, P < 0.05.

alone, mean group total cholesterol concentrations were not significantly changed.

Mean group LDL-C concentrations were significantly reduced with garlic + fish oil (−9.5%) and with garlic (−14.2%) by week 12 (**Table 4**). In the fish-oil group, mean LDL-C concentrations were significantly raised (+8.5%) by week 3 and persisted until week 12. Significant LDL-C reductions in both groups taking garlic (garlic and garlic + fish oil) were achieved by week 9. There was no significant difference in reductions of LDL-C between the garlic + fish oil and garlic alone groups although the garlic alone group did show a consistent trend toward larger reductions in LDL-C throughout the study.

Mean group fasting serum triacylglycerol concentrations were significantly decreased with garlic + fish oil (−34.3%) and with fish oil alone (−37.3%) (**Table 5**). Reductions in triacylglycerol with fish oil (garlic + fish oil and fish oil alone) were noted by week 3. There was no significant difference in the triacylglycerol reduction seen between fish oil and garlic +

fish oil. In the garlic group, mean triacylglycerol concentrations were not significantly changed.

Although the fish-oil and garlic + fish oil groups showed significant increases in HDL-C in relation to baseline, there were no significant differences between the four groups at week 12 (**Table 6**). However, there was a consistent trend of higher HDL-C increases in both fish-oil groups (fish oil alone and garlic + fish oil) compared with both non-fish-oil groups (placebo and garlic alone).

Compared with placebo, for which no significant change was found (by week 12) in the ratios of total cholesterol to HDL-C and LDL-C to HDL-C, the ratio of total cholesterol to HDL-C was significantly reduced in the garlic group (−12.5%) and in the garlic + fish-oil group (−16.2%) but not in the fish-oil (alone) group. The reduction in the ratio of total cholesterol to HDL-C in the garlic + fish-oil group was significantly greater than in the garlic only group (P < 0.05). The ratio of LDL-C to HDL-C was significantly decreased in the garlic group (−15.3%) and in the garlic + fish oil group (−19.0%) with no change (P > 0.05) in the other two groups.

Mean systolic, diastolic, and arterial blood pressures for all subjects at entry were 120.1, 80.9, and 94.0 mm Hg, respectively. By week 12, reductions of 2.4–4.2% (P < 0.05 or P <

TABLE 2
Daily dietary intakes and body weight at entry and after supplementation[1]

Variable	Entry (week 0)	Supplementation (week 12)
Protein		
(% of energy)	17.3 ± 0.6	16.9 ± 0.5
(g)	103 ± 4	104 ± 4
Carbohydrate		
(% of energy)	50.0 ± 1.5	50.2 ± 1.3
(g)	298 ± 14	307 ± 13
Fat		
(% of energy)	30.4 ± 1.2	30.9 ± 1.3
(g)	86.9 ± 5.3	89.5 ± 5.7
Saturated fat (g)	29.9 ± 2.4	31.2 ± 2.3
Monounsaturated fat (g)	32.4 ± 2.0	33.2 ± 2.2
Polyunsaturated fat (g)	16.5 ± 1.1	17.3 ± 1.1
Dietary fiber (g)	23.6 ± 1.5	24.7 ± 1.5
Cholesterol (mg)	337 ± 25	348 ± 24
Body weight (kg)	84.8 ± 2.0	84.9 ± 2.0
Alcohol (% of energy)	2.46 ± 0.65	2.00 ± 0.52
Total intake (kJ)	9905 ± 383	10196 ± 358

[1] $\bar{x}$ ± SEM; n = 39 for dietary variables, n = 46 for body weight.

TABLE 3
Effect of nutritional supplementation on total serum cholesterol concentrations[1]

	Supplementation group			
Time	Placebo	Garlic	Fish oil	Garlic + fish oil
	mmol/L			
Week 0	6.46 ± 0.26	6.54 ± 0.25	6.54 ± 0.34	6.51 ± 0.29
Week 3	6.41 ± 0.31	6.62 ± 0.29	6.59 ± 0.32	6.46 ± 0.26
Week 6	6.33 ± 0.28ᵃᵇ	6.33 ± 0.27ᵃᵇ	6.49 ± 0.29ᵃ	6.15 ± 0.25ᵇ²
Week 9	6.43 ± 0.33ᵃ	6.23 ± 0.30ᵇ³	6.67 ± 0.37ᵃ	5.81 ± 0.22ᶜ⁴
Week 12	6.49 ± 0.31ᵃ	5.79 ± 0.23ᵇ⁴	6.51 ± 0.38ᵃ	5.71 ± 0.20ᵇ⁴
	(0.5 ± 1.8)⁵	(−11.5 ± 2.1)⁵,⁶	(−0.5 ± 2.1)	(−12.2 ± 1.3)⁵,⁶

[1] $\bar{x}$ ± SE. Values with different superscript letters are significantly different from other groups at the corresponding time, P < 0.05.
[2–4] Significantly different from baseline: [2] P < 0.01, [3] P < 0.05, [4] P < 0.001.
[5] Percentage change from week 0 in parentheses.
[6] Significantly different from placebo and fish oil, P < 0.01.

TABLE 4
Effect of nutritional supplementation on serum LDL-cholesterol concentrations[1]

| | Supplement group | | | |
Time	Placebo	Garlic	Fish oil	Garlic + fish oil
	mmol/L			
Week 0	4.32 ± 0.25	4.39 ± 0.18	4.42 ± 0.27	4.47 ± 0.27
Week 3	4.19 ± 0.25[a]	4.26 ± 0.23[a]	4.75 ± 0.32[b2]	4.68 ± 0.29[b]
Week 6	4.16 ± 0.27[a]	4.26 ± 0.27[a]	4.78 ± 0.41[b2]	4.47 ± 0.28[a]
Week 9	4.19 ± 0.28[a]	3.90 ± 0.28[b3]	4.94 ± 0.43[c3]	4.19 ± 0.28[a2]
Week 12	4.26 ± 0.31[a]	3.77 ± 0.24[b3]	4.81 ± 0.40[c2]	4.06 ± 0.24[b5]
	(−1.1 ± 2.8)[4]	(−14.2 ± 2.6)[2,6]	(8.5 ± 5.6)[2,7]	(−9.5 ± 3.2)[2,6]

[1] $\bar{x}$ ± SE. Values with different superscript letters are significantly different from other groups at the corresponding time, $P < 0.05$.
[2,3,5] Significantly different from baseline: [2] $P < 0.05$, [3] $P < 0.001$, [5] $P < 0.01$.
[4] Percentage change from week 0 in parentheses.
[6] Significantly different from placebo and fish oil, $P < 0.01$.
[7] Significantly different from placebo, garlic, and fish oil, $P < 0.05$.

TABLE 6
Effect of nutritional supplementation on serum HDL-cholesterol concentrations[1]

| | Supplement group | | | |
Time	Placebo	Garlic	Fish oil	Garlic + fish oil
	mmol/L			
Week 0	1.20 ± 0.10	1.26 ± 0.06	1.12 ± 0.27	1.13 ± 0.05
Week 3	1.19 ± 0.10[a]	1.36 ± 0.11[b2]	1.22 ± 0.09[b3]	1.22 ± 0.08[b3]
Week 6	1.24 ± 0.10[a]	1.34 ± 0.10[ab2]	1.20 ± 0.14[ab2]	1.27 ± 0.07[b4]
Week 9	1.28 ± 0.11[a]	1.38 ± 0.09[a3]	1.26 ± 0.12[a4]	1.26 ± 0.08[a4]
Week 12	1.26 ± 0.11[ab]	1.29 ± 0.08[a]	1.21 ± 0.11[ab2]	1.24 ± 0.06[b3]
	(4.9 ± 1.7)[5]	(2.6 ± 3.2)	(8.5 ± 4.4)[2]	(9.1 ± 3.0)[2]

[1] $\bar{x}$ ± SE. Values with different superscript letters are significantly different from other groups at the corresponding time, $P < 0.05$.
[2-4] Significantly different from baseline: [2] $P < 0.05$, [3] $P < 0.01$, [4] $P < 0.001$.
[5] Percentage change from week 0 in parentheses.

the subjects taking garlic pills, and in none of the garlic placebo group. One subject reported a slight feeling of nausea with fish oil that did not persist throughout the study. No other serious side effects (other than occasional belching) were reported with either the fish oil or the oil placebo.

DISCUSSION

We evaluated the efficacy of single and combined therapy with garlic and fish oil in subjects with moderate hypercholesterolemia. In our study, treatment with garlic or fish oil significantly decreased serum total cholesterol and triacylglycerol, respectively; the combination of garlic and fish oil significantly reduced both serum lipids.

Garlic supplementation alone has been reported to reduce total cholesterol by 9–12% without a significant effect on HDL-C concentrations (8, 12), and in one study may have moderately lowered triacylglycerol concentrations (8). Although the reduction in total cholesterol (12% by week 12) and LDL-C (14% by week 12) observed with garlic alone in this study is typical for this preparation and dose, the expected decrease in fasting serum triacylglycerol was not seen. The lowering of total cholesterol observed with garlic is believed to be largely due to a reduction in LDL-C (15), which may be due to an inhibition of hepatic cholesterol biosynthesis (possibly via inhibition of hydroxymethylglutaryl-CoA reductase) by allicin and/or other components (16). It should also be noted that certain garlic preparations (eg, garlic oils) do not show the degree of cholesterol lowering seen with specific powdered formulations (17).

Treatment with fish oil in this study showed a reduction in serum fasting triacylglycerol (30–40%) consistent with that in previous reports from hyperlipidemic humans (10). An inhibition of hepatic fatty acid synthesis by EPA and DHA and impaired triacylglycerol synthesis (including very-low-density lipoprotein assembly and secretion) are among some of the mechanisms proposed for the plasma triacylglycerol-lowering effect of dietary fish oil (10, 18). Addition of garlic to fish oil did not significantly change the reduction in triacylglycerol observed with the fish-oil concentrate alone. Although our subjects did not generally have overt hypertriglyceridemia at entry, their mean fasting triacylglycerol values (2.1 mmol/L, or

0.005) in mean systolic, diastolic, and arterial pressures were found for all three treatment groups (fish oil alone, garlic alone, and garlic + fish oil) relative to the placebo group.

According to capsule or pill counts at the end of the study, 100% of subjects who completed the study took > 80% of the supplements given. Blinding to the supplements was checked by the use of a questionnaire at the end of the study. Garlic pills and garlic placebo pills were identified correctly by 76% and 67% of the subjects, respectively. Fish oil and oil placebo were identified correctly by 100% and 61% of the subjects, respectively. As a measure of compliance with the fish-oil supplementation, serum phospholipid fatty acid profiles were measured at entry and after 12 wk of supplementation (**Table 7**). The results are characteristic of other studies in which fish-oil supplementation was at similar levels (14). The ratio of EPA to arachidonic acid increased significantly ($P < 0.001$) in the fish-oil groups (fish oil alone and garlic + fish oil) but did not change significantly ($P > 0.05$) in the groups taking no fish oil (placebo and garlic only groups) (Table 7).

All supplements used in this study had relatively few reported side effects. Odor due to garlic was reported in 20% of

TABLE 5
Effect of nutritional supplementation on serum triacylglycerol concentrations[1]

| | Supplement group | | | |
Time	Placebo	Garlic	Fish oil	Garlic + fish oil
	mmol/L			
Week 0	1.95 ± 0.49	1.98 ± 0.32	2.34 ± 0.56	2.17 ± 0.43
Week 3	2.15 ± 0.79[a]	2.07 ± 0.51[a]	1.64 ± 0.43[b2]	1.53 ± 0.21[b2]
Week 6	1.95 ± 0.51[a]	1.86 ± 0.31[a]	1.62 ± 0.26[b2]	1.49 ± 0.19[b2]
Week 9	2.11 ± 0.80[a]	2.16 ± 0.54[a]	1.40 ± 0.20[b2]	1.30 ± 0.18[b2]
Week 12	1.94 ± 0.51[a]	1.85 ± 0.37[a]	1.46 ± 0.23[b2]	1.36 ± 0.17[b2]
	(−0.6 ± 4.3)[3]	(−6.1 ± 7.6)	(−37.7 ± 4.8)[4,5]	(−34.3 ± 4.8)[4,5]

[1] $\bar{x}$ ± SE. Values with different superscript letters are significantly different from other groups at the corresponding time, $P < 0.05$.
[2,4] Significantly different from baseline: [2] $P < 0.001$, [4] $P < 0.05$.
[3] Percentage change from week 0 in parentheses.
[5] Significantly different from placebo and garlic, $P < 0.001$.

TABLE 7
Effect of nutritional supplementation on fatty acid composition of serum phospholipid[1]

Fatty acid	Baseline (n = 46)	Placebo (n = 11)	Garlic (n = 12)	Fish oil (n = 10)	Garlic + fish oil (n = 13)
			% by wt of total fatty acids		
16:0	28.3 ± 0.2	27.7 ± 0.4	27.6 ± 0.4[2]	27.6 ± 0.4	27.8 ± 0.5
18:0	12.4 ± 0.2	11.8 ± 0.2	12.1 ± 0.5	12.6 ± 0.4[3]	12.9 ± 0.5[4]
18:1	11.8 ± 0.2	10.2 ± 0.4[2]	9.9 ± 0.4[2]	10.0 ± 0.5[2]	10.0 ± 0.3[2]
18:2n−6	20.0 ± 0.4	21.4 ± 0.6	20.8 ± 0.8	15.7 ± 1.1[2,4]	15.5 ± 1.1[2,4]
18:3n−6	0.08 ± 0.01	0.13 ± 0.02	0.14 ± 0.03[2]	0.06 ± 0.01[4]	0.02 ± 0.01[2,4]
20:3n−6	3.1 ± 0.1	3.6 ± 0.2[2]	4.1 ± 0.3[2,3]	1.7 ± 0.2[2,4]	1.8 ± 0.1[2,4]
20:4n−6 (AA)	10.8 ± 0.3	13.0 ± 0.6[2]	13.1 ± 0.7[2]	7.2 ± 0.4[2,4]	7.9 ± 0.4[2,4]
20:5n−3 (EPA)	1.2 ± 0.1	1.0 ± 0.1	0.8 ± 0.1	7.5 ± 0.6[2,4]	7.5 ± 0.6[2,4]
22:6n−3 (DHA)	3.2 ± 0.1	2.9 ± 0.2	3.1 ± 0.2	7.6 ± 0.4[2,4]	7.3 ± 0.4[2,4]
Σ n−6	34.5 ± 0.4	38.5 ± 0.4[2]	38.6 ± 0.5[2]	24.9 ± 1.2[2,4]	23.7 ± 2.0[2,4]
Σ n−3	5.9 ± 0.2	5.2 ± 0.3	5.2 ± 0.3	16.3 ± 1.8[2,4]	16.8 ± 1.0[2,4]
n−3:n−6	0.17 ± 0.01	0.14 ± 0.01	0.14 ± 0.01	0.74 ± 0.10[2,4]	0.69 ± 0.06[2,4]
EPA:AA	0.11 ± 0.01	0.08 ± 0.01	0.06 ± 0.01	1.08 ± 0.14[2,4]	0.97 ± 0.08[2,4]

[1] $\bar{x}$ ± SEM for baseline values and after 12 wk of supplementation. The four supplement groups (n = 10–13) are compared with the baseline values (n = 46). AA, arachidonic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.
[2] Significantly different from baseline, $P < 0.05$.
[3] Significantly different from placebo, $P < 0.05$.
[4] Significantly different from placebo and garlic, $P < 0.05$.

186 mg/dL) would be considered above desirable based on some recent reports (19).

Fish-oil treatment has often been found to result in an increase in LDL-C concentrations, possibly via an increased conversion of very-low-density lipoprotein to LDL particles (10, 11). A significant rise in LDL-C (+8.5%) was seen in this study in the group taking fish oil alone. The addition of garlic to fish oil not only prevented the moderate LDL-C–raising effect of the fish oil but actually produced a significant lowering (−9.5%).

The rise in serum HDL-C concentrations relative to baseline (by 9%) as observed for the two fish-oil groups (fish oil alone and garlic + fish oil) are of interest as are the apparently favorable shifts (decreases) in the ratios of total cholesterol to HDL-C and LDL-C to HDL-C (including significantly lower ratios at week 12 for the garlic + fish oil combination). The significant reduction in the ratios of total cholesterol to HDL-C and LDL-C to HDL-C with the garlic + fish oil supplement has potential health significance in view of recent emphasis on these ratios as important predictors for coronary artery disease (20).

Blood pressure has been reported to be moderately reduced by both garlic (21) and fish-oil (22) supplements. In this study, there was a small (2–4%) but significant reduction in mean systolic, diastolic, and arterial blood pressures with all treatments (garlic alone, fish oil alone, and garlic + fish oil) when compared with placebo. All treatments produced similar reductions, although this reduction in blood pressure was achieved within 3 wk for the groups taking fish oil (fish oil alone and garlic + fish oil) and by 9 wk for the garlic alone group. The moderate lowering of blood pressure with garlic may be due to increased nitric oxide production and a more vasodilatory state (23), whereas the EPA and DHA in fish oil may operate, at least in part, via altered eicosanoid synthesis (24).

The fatty acid composition of serum phospholipid has been found to reflect intake of dietary n−3 fatty acids well (25).

Along with the capsule or pill count, analysis of serum fatty acids confirmed high compliance with the treatment given.

In conclusion, garlic supplementation significantly decreased both total cholesterol and LDL-C, whereas fish-oil supplementation significantly decreased triacylglycerol concentrations and increased LDL-C concentrations in moderately hypercholesterolemic men. The combination of garlic and fish oil prevented a moderate fish-oil–induced rise in LDL-C. Co-administration of garlic and fish oil was well-tolerated in the short term and had a beneficial effect on serum lipid and lipoprotein concentrations by providing a combined lowering of total cholesterol, LDL-C, and triacylglycerol concentrations along with overall decreases in the ratios of total cholesterol to HDL-C and LDL-C to HDL-C.

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