Effects of Solid and Liquid Guar Gum on Plasma Cholesterol and Triglyceride Concentrations in Moderate Hypercholesterolemia

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Guar gum is a dietary fiber reported to decrease . plasma cholesterol concentration. This study investigated the effect of guar therapy in 50 men with moderately elevated plasma cholesterol who were randomized to an 8-week study of guar therapy. Three forms of guar gum were used: a medium viscosity solid or liquid form, a high viscosity liquid form or placebo. When the medium viscosity guar therapy groups were combined, 4 weeks of therapy were shown to result in a substantial reduction in total and low density lipoprotein (LDL) cholesterol of 25 mg/dl and 23 mg/dl (p = 0.035 and 0.12), respectively. The high viscosity guar group had a reduction in total cholesterol and LDL cholesterol of 37 and 30 mg/dl, respectively (p <0.003 and p <0.02). Following 8 weeks of therapy, a return toward baseline values was observed. No significant changes were demonstrated in blood chemistries, triglyceride values, total high density lipoprotein (HDL) cholesterol or the HDL₂ fraction of HDL cholesterol. The effect of the solid and liquid forms of guar on plasma cholesterol reduction was similar. This study shows that a nonpharmacologic dietary additive reduces plasma total and LDL cholesterol.

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any individuals can change their plasma lipid profiles by nonpharmacologic therapies that include dietary change, weight loss and exercise. Before initiating pharmacologic therapy, a dietary supplement of a water soluble nonabsorbant fiber such as guar gum may be warranted. Previous clinical investigations have demonstrated total plasma cholesterol reductions of 3 to 16% with guar gum therapy. These studies are listed in Table I and have recently been reviewed.¹ They vary in guar delivery mode, guar dosage, duration of therapy and the subject's initial lipid profile. This study investigated 3 issues: (1) the preference for guar when ingested in a solid (cracker) form versus a liquid form; (2) the lipoprotein and high density lipoprotein (HDL) cholesterol subspecies changes resulting from ingestion of 15 g of guar powder daily; and (3) the differential effect of high viscosity versus medium viscosity liquid guar on plasma lipoprotein concentrations.

METHODS

Subjects: Fifty clinically healthy men (mean age 51 \pm 12 years) were randomly assigned to 1 of 5 groups. Subjects had no history of recent gastrointestinal disorders, or any medical condition that required periodic medications that would alter lipid metabolism. Subjects taking antihypertensive medications were allowed to maintain their medications if there was no change in type or dosage during the trial. Subjects were not permitted plasma lipid-lowering medications for 4 weeks before the trial. Six subjects failed to complete the investigation.

Trial design: The single-blind, randomized, crossover design is illustrated in Figure 1. Groups A and B were treated with a medium viscosity guar. Group A was treated with guar in a solid form for 4 weeks and then was crossed over to 4 weeks of liquid guar therapy. Group B was treated with liquid guar for 4 weeks and then crossed over to 4 weeks of solid guar therapy. Group C received 4 weeks of a solid placebo followed by 4 weeks of a liquid placebo. Group D received 4 weeks of a liquid placebo followed by 4 weeks of a solid placebo. Group E received 4 weeks of high viscosity liquid guar with no crossover. Measurements were recorded at weeks 0, 4 and 8.

All guar groups were treated with 15 g daily. The guar cracker was composed of a mixture of rice flour, corn bran and guar gum. Each cracker weighed 6 g and contained 1.25 g of guar. Three servings per day (4 crackers per serving) resulted in a daily guar dose of 15

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Study	Dose (g/d)	Duration (wks)	Mean Initial TC (mg/dl)	Mean Final TC (mg/dl)	Change (%)
Kahn ⁷	9	4	180 ± 10	150 ± 6	-16.6
Jenkins ⁶	13	8	336 ± 56	_	-13.6
Aro ¹²	15	12	319 ± 10	282 ± 9	-11.7
Tuomilehto ²⁰	15	16	343 ± 13	330 ± 22	-3.8
Tuomilehto ²²	15	12	338	323	6.9
Simons ¹³	18	12	302 ± 23	263 ± 35	-12.8
Smith ²¹	20	3	212 ± 15	181 ± 8	-14.3

g. This added 192 kcal to the subjects' daily caloric intake. The major constituents of the liquid guar drink were fructose, corn bran, orange juice powder, maltrin and guar gum. Three daily servings of the liquid resulted in 189 additional daily kcal. The medium viscosity guar gum was the commercial product DYCOL 4500F (National Starches, Food Division), and the high viscosity guar gum was HENKEL 62H.

Laboratory methods: Fasting blood samples were obtained by venipuncture. Plasma lipids and lipoproteins were measured in the Stanford University Lipid Research Laboratory. Laboratory methods were those of the Lipid Research Clinics and standardized through the National Heart, Lung and Blood Institute-Centers for Disease Control lipoprotein standardization program.² Total cholesterol and triglycerides were measured with enzymatic techniques and HDL cholesterol was determined on the remaining plasma after precipitation of very low density lipoprotein (VLDL) cholesterol and LDL cholesterol with dextran sulfate. LDL cholesterol was determined by the calculation method of Friedewald et al.³ HDL₂ cholesterol and HDL₃ cholesterol were separated by the precipitation method of Gidez et al.⁴ Blood chemistries were performed on a Vicker autoanalyzer.

Four-day diet records were obtained at baseline, at the end of the first guar phase (4 weeks) and at the end of the second guar phase (8 weeks). Components of the diet were determined using a modified version of the nutrient composition database provided by the Nutrition Coding Center, Minneapolis, Minnesota.⁵ Questionnaires to determine side effects and guar form preference were obtained at 8 weeks.

Statistical analysis: A t test procedure between group absolute values and percent change values was

GROUP (n)	4 wk	8 wk
A (10)		ID){
B (10)	(LIQUID)	
C (6)		10) (ali
D (6)		
E (12)		•

FIGURE 1. Stanford guar gum study design.

52 THE AMERICAN JOURNAL OF CARDIOLOGY VOLUME 62

used. Paired guar and placebo solid or liquid delivery mode results were compared as well as combined solidliquid medium viscosity guar, with solid-liquid placebo results.

RESULTS

Six subjects, all in the medium viscosity guar group, failed to complete the trial. Three of them withdrew because of personal reasons. One subject discontinued due to gastrointestinal side effects, the fifth subject dropped out due to a strong distaste for the solid guar form and a sixth subject's data were excluded due to significant alcohol consumption. Statistical analyses were performed on the remaining 44 subjects. No significant changes in body weight or resting blood pressure were noted.

Preference: Analysis of the preference questionnaire revealed that the liquid form was preferred over the solid form by 80% of group A, 80% of group B, 50% of group C and 83% of group D. No preference was recorded by 10% of group A, 10% of group B, 17% of group C and 0% of group D. The high viscosity guar was not available in a solid form.

Plasma lipids: Baseline plasma lipid measurements were similar for all groups with the exception of significantly lower triglycerides (p = 0.02) and significantly high HDL cholesterol (p = 0.09) in the combined placebo group when compared with the combined guar group (Table II).

Following 4 weeks of guar therapy, significant reductions in total and LDL cholesterol were observed, while triglycerides, HDL cholesterol, and HDL₂ choles-

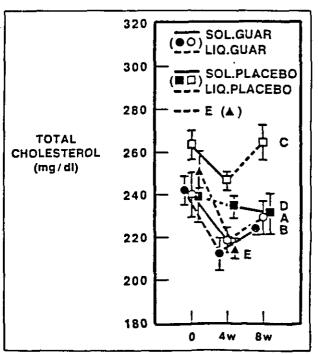


FIGURE 2. Changes in plasma total cholesterol for the 3 guar (A, B and E) and 2 placebo (C, D) groups after 4 and 8 weeks of guar or placebo administration. The solid line represents the solid cracker form and the *dotted line* represents the liquid form.

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Group	No.	``TG (mg∕di)	TC (mg/dl)	LDL C (mg/dl)	HDL C (mg/di)	HDL ₂ C (mg/dl)
Α.	10	143 ± 52	240 ± 34	168 ± 30	43.4 ± 11	7.6 ± 5.2
B	10	171 ± 99	242 ± 25	158 ± 25	46.8 ± 12	12.6 ± 10.6
С	6 -	96 ± 21*	263 ± 19	184 ± 21	$59.8 \pm 10^{\circ}$	20.0 ± 7.4
D	6	109 ± 55*	239 ± 29	173 ± 29	44.7 ± 61	9.0 ± 1.8
E	12	135 ± 73	252 ± 32	171 ± 33	50.5 ± 13	13.4 ± 8.6

mean ± standard deviatio

* p = 0.016 (A + B vs C + D); * p = 0.092 (A + B + TG = trigiycende; TC = total cholesterol; LDL C cholesterol; HDL, C = high density lipoprotein cholesterol; HDL₂C = high density lipoprotein₂ cholesteroi

TABLE III Lipid Values for Combined Guar (G), Combined Placebo (P) and the HVG (E) Groups at Baseline (O), and the Mean Change from Baseline Values at Four Weeks (4) and Eight Weeks (8)

Group	TG (mg/dl)	TC (mg/dl)	LDL C (mg/dl)	HDL C (mg/dl)	HDL ₂ C (mg/dl)
60	157 ± 79	241 ± 29	163 ± 28	45 ± 11.4	10.1 ± 8.5
G4	6±74	-25 ± 20 ¹	-23 ± 201	-2 ± 5.1	~1.1 ± 6.8
G8	19 ± 48	$-14 \pm 19^*$	-16 ± 21*	-1 ± 4.3	0.6 ± 7.3
P0	103 ± 40	251 ± 27	179 ± 25	52 ± 11.0	14.5 ± 7.7
P4	10 ± 47	-11 ± 13	-12 ± 18	-2 ± 4.4	-0.3 ± 4.1
P8	5 ± 35	-3 ± 21	-3 ± 21	-1 ± 6.5	1.4 ± 5.0
EO	135 ± 73	252 ± 32	171 ± 33	50.5 ± 13	13.4 ± 8.6
E4	-15 ± 60	-37 ± 20^{5}	-30 ± 18 **	-1.9 ± 7	-0.4 ± 5.3

terol remained stable. A 9.2% and 13.7% reduction from baseline values in total and LDL cholesterol was found in group A while group B demonstrated a 12.0% and 14.6% reduction in total and LDL cholesterol, respectively. Figure 2 illustrates the mean change in the individual groups for total cholesterol measured at 4 and 8 weeks. Group B revealed a significant reduction in total (p = 0.029) and LDL cholesterol (p = 0.073) when compared with the placebo group. Group A demonstrated a mean LDL cholesterol reduction of 23 mg/ dl but this was not statistically significant due to a concomitant reduction of 18 mg/dl in the placebo group. Following crossover to the alternate delivery mode and 4 additional weeks of guar therapy, an increase in plasma cholesterol was observed. After 8 weeks of therapy, the percent total and LDL cholesterol change from baseline values for group A were 4.6% and 10.7% and for group B were 7.4% and 8.2%. The increase in total and LDL cholesterol values between 4 and 8 weeks resulted in a loss of the statistical significance that was observed at 4 weeks.

Because the effects were generally similar for the liquid and solid forms, the groups were further analyzed by combining both medium viscosity guar groups and both placebo groups regardless of the order of solidliquid administration. These values are listed in Table III and the absolute combined values for total cholesterol are illustrated in Figure 3. The medium viscosity guar groups revealed a 10.4% reduction in total cholesterol (p <0.035) and a 14.1% reduction in LDL cholesteroi (p <0.15) from baseline to 4 weeks. At 8 weeks, a 5.8% reduction in total (p < 0.12) and a 9.8% reduction in LDL cholesterol (p <0.12) were observed. When compared with the change in the placebo group, a further reduction of 6.0% (p < 0.01) and 7.4% (p < 0.10) in total and LDL cholesterol was seen with medium viscosity guar therapy at 4 weeks and reductions of 4.6% (p <0.20) and 8.1% (p <0.20) for total and LDL cholesterol, respectively, at 8 weeks. Triglycerides, HDL cholesterol and HDL₂ cholesterol demonstrated no significant change during the course of the trial.

Viscosity: When compared with the liquid placebo group, group E demonstrated a significant reduction in total (p <0.003) and LDL cholesterol (p <0.02) at 4

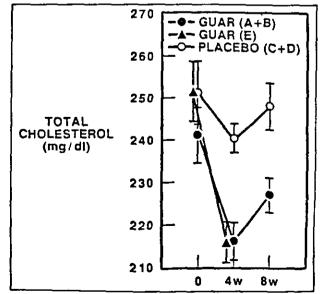


FIGURE 3. Changes in plasma total cholesterol for the combined guar groups, combined placebo groups and the high viscosity guar group after 4 and 8 weeks of guar or placebo administration.

THE AMERICAN JOURNAL OF CARDIOLOGY JULY 1, 1988 53

PLASMA CHOLESTEROL REDUCTION WITH GUAR GUM

weeks. This reduction from baseline values amounted to a 14.7% and 17.5% reduction in total and LDL cholesterol, respectively. When the group E change is compared with the liquid placebo group change, an overall greater reduction of 13.2% (p < 0.001) in total and a 13.8% (p < 0.02) in LDL cholesterol is noted. There was no significant change in triglycerides, HDL cholesterol, HDL₂ cholesterol, total cholesterol/HDL cholesterol ratio (Table III).

Other variables: Adherence to the guar gum regimen was determined by packet count and the mean adherence was >90%. There was no difference in adherence between the solid and liquid form or between guar and placebo. The subjects were monitored for side effects and the most commonly reported were flatulence and loose bowel movements. One subject in the medium viscosity guar group withdrew from the study because of gastrointestinal symptoms.

Analysis of 3-day diet records revealed no significant baseline differences in total calories consumed, in dietary composition when analyzed as percent of calories from carbohydrate, fat and protein or in dietary cholesterol. Average daily dietary cholesterol intake at baseline in the combined medium viscosity guar group averaged 362 mg and 345 mg in the combined placebo group. At 4 weeks the change in cholesterol intake was +26 mg and -55.5 mg for the guar and placebo groups, respectively. At 8 weeks the average dietary cholesterol change from baseline was -38 mg for the guar group and +3 mg for the placebo group. Percent of calories from fat or saturated fat did not change in any group from baseline to 4 or 8 weeks. Blood chemistries, including calcium, potassium, glucose, creatinine, uric acid, serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase, were analyzed, and no significant change was noted after 8 weeks of medium viscosity guar therapy.

DISCUSSION

Guar gum is a galactomannan with a molecular weight of approximately 220,000 that is derived from the seed of the plant Cyamopsis tetragonoloba. It is commonly administered by mixing the guar powder in a liquid. For convenience, a solid form may be desirable. A "crispbread" form of guar has been compared with a hydrated form.⁶ In this 2-week study of 11 patients with hyperlipidemia type II or IV, the mean daily amount of crispbread ingested was 12 ± 2 g, and 11 ± 2 g in the hydrated guar group.⁶ The crispbread form had the greatest compliance rate, and less flatulence and stool looseness was noted compared with the hydrated form.

In our study, 80% of both guar groups and 80% of 1 placebo group preferred the liquid form. The sticky nature of the guar cracker in the mouth was a common reason for the liquid preference.

Previous studies with guar therapy have demonstrated plasma total cholesterol changes ranging from a reduction of 3.4% to 16.6% (Table I). Triglyceride and HDL cholesterol values have revealed a consistent pattern of no significant change. In many of these studies, Our study is relatively unique in that the subjects represent persons who fall into the National Institutes of Health definition of "moderate risk" and were not selected because of a hyperlipidemia type. Kahn et al⁷ studied 24 healthy volunteers but the mean total cholesterol was approximately 180 mg/dl, well below the moderate risk range. In the study by Kahn et al, total cholesterol decreased 16.6% when guar was given in a capsule form.

In our study, 4 weeks of guar therapy resulted in a total cholesterol reduction that was 6 to 11% greater than the reduction seen in the placebo groups for the medium and high viscosity grades, respectively. The power of the results may be somewhat attenuated due to the variability in lipid changes in the placebo group C at 4 weeks. This variability was in part due to the small sample size of this group (n = 6). Nevertheless, at 4 weeks a significant reduction in total cholesterol (p = 0.035) was noted when both placebo groups and both guar groups were combined for analysis. A return toward baseline for total and LDL cholesterol was observed at 8 weeks; this reduced the significance of the longer term total cholesterol reduction (p = 0.120). These alterations in plasma lipids do not appear to be caused by changes in diet composition or compliance to the guar dose.

Other than total and LDL cholesterol, guar-induced changes in lipid and lipoprotein values have not been impressive. Investigators have reported a nonsignificant reduction in triglyceride and HDL cholesterol levels. This lack of significant triglyceride reduction may be deceiving. Bosello et al⁸ have reported a 30.4% (p <0.01) reduction in triglycerides in hyperlipidemic subjects but an even greater reduction in apolipoprotein C-III-0 of 55.3% (p <0.001). This may be of mechanistic importance since Windler et al⁹ have reported that C-III-0 inhibited uptake of rat hepatic VLDL by perfused rat liver. Thus, significant changes may occur in lipoprotein metabolism not reflected by the cholesterol content of VLDL, LDL and HDL.

To investigate this possibility we measured the cholesterol content of HDL subspecies HDL₂ and HDL₃. Low HDL₂ cholesterol values have been related to arteriographically determined extent of coronary artery disease and rate of disease progression.^{10,11} In our investigation no significant change in HDL₂ or HDL₃ cholesterol content was noted.

The duration of the guar effect is an important issue. A significant reduction of total and LDL cholesterol was demonstrated during an 8-week trial with the maximum reduction at 3 weeks. During a 12-week trial a significant reduction in total and LDL cholesterol was noted at 6 weeks but no significant change was seen at 12 weeks.^{6,12} Subsequent to a placebo-controlled guar trial, 13 patients chose to continue to receive guar therapy and a sustained decrease in total cholesterol values was noted after 12 months of therapy.¹³ The return toward baseline values in our study did not appear to be erlipidemia

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The mechanism of action of guar is unclear but it may involve its viscosity and "coating" of the intestinal mucosa, limiting the intestinal bulk phase diffusion and thus interfering with adsorption of lipids.^{14,15} Gee,¹⁶ Blackburn¹⁷ and their co-workers found, in rat jejunum, that the presence of a polysaccharide gum in the fluid surrounding the villi may give rise to a thickening of this rate-limiting layer.

The response of the high viscosity group E supports the concept that viscosity is an important variable in guar's ability to lower plasma cholesterol values. After 4 weeks of therapy group E revealed significant reductions in total and LDL cholesterol. These were 13.2% and 13.8% greater than the placebo group compared with the medium viscosity group that achieved a 6.0% and 7.4% greater reduction in total and LDL cholesterol compared to the placebo group. Triglycerides, HDL cholesterol and HDL₂ cholesterol did not change significantly. The high viscosity guar was not formulated in a cracker and therapy was not continued past week 4.

Blood chemistries revealed no significant alterations. Side effects were all related to the gastrointestinal system and similar to those reported by other investigators. The 2 most common complaints were loose stools and increased flatulence. These symptoms tended to decrease after several weeks of guar therapy. The interaction of guar's affect on the absorption of medications was not investigated.

In summary, short-term therapy with 15 g of guar daily was effective in obtaining a clinically important reduction in plasma total and LDL cholesterol; this can be compared to the mean 8.5% and 12.6% reduction seen in the Coronary Primary Prevention Trial.¹⁸ The availability of a cholesterol-lowering dietary additive allows the addition of a third stage to the classic 2-stage approach to plasma lipid reduction, that is, diet-exercise-weight reduction, and lipid-lowering medications. Dietary supplements such as guar gum are relatively inexpensive and may provide an intermediate step in plasma lipid management between that of lifestyle alteration and drug therapy. This can be particularly important in patients with established coronary artery disease and total cholesterol values that are not elevated sufficiently to warrant classic pharmacotherapy.¹⁹

Further investigation with guar therapy is warranted. Among the questions that should be addressed are long-term effectiveness, effect of guar therapy on the absorption of medications, effect of guar therapy on the bioavailability of micronutrients, optimal viscosity and delivery mode and development of approaches to maintain long-term compliance.

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