Konjac-Mannan (Glucomannan) Improves Glycemia and Other Associated Risk Factors for Coronary Heart Disease in Type 2 Diabetes

A randomized controlled metabolic trial

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OBJECTIVE — To examine whether Konjac-mannan (KJM) fiber improves metabolic control as measured by glycemia, lipidemia, and blood pressure in high-risk type 2 diabetic patients.

RESEARCH DESIGN AND METHODS — A total of 11 hyperlipidemic and hypertensive type 2 diabetic patients treated conventionally by a low-fat diet and drug therapy participated. After an 8-week baseline, all were randomly assigned to take either KJM fiber–enriched test biscuits (0.7 g/412 kJ [100 kcal] of glucomannan) or matched placebo wheat bran fiber biscuits during two 3-week treatment phases separated by a 2-week washout period. The diet in either case was metabolically controlled and conformed to National Cholesterol Education Program Step 2 guidelines, while medications were maintained constant. Efficacy measures included serum fructosamine, lipid profiles, apolipoproteins, blood pressure, body weight, and nutritional analysis.

RESULTS — Compared with placebo, KJM significantly reduced the metabolic control primary end points: serum fructosamine (5.7%, $P = 0.007$, adjusted $\alpha = 0.0167$), total:HDL cholesterol ratio (10%, $P = 0.03$, adjusted $\alpha = 0.05$), and systolic blood pressure (sBP) (6.9%, $P = 0.02$, adjusted $\alpha = 0.025$). Secondary end points, including body weight, total, LDL, and HDL cholesterol, triglycerides, apolipoproteins A-1, B, and their ratio, glucose, insulin, and diastolic blood pressure, were not significant after adjustment by the Bonferroni-Hochberg procedure.

CONCLUSIONS — KJM fiber added to conventional treatment may ameliorate glycemic control, blood lipid profile, and sBP in high-risk diabetic individuals, possibly improving the effectiveness of conventional treatment in type 2 diabetes.

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Abbreviations: apo, apolipoprotein; CHD, coronary heart disease; CVD, cardiovascular disease; dBP, diastolic blood pressure; KJM, Konjac-mannan; NCEP, National Cholesterol Education Program; RIA, radioimmunoassay; sBP, systolic blood pressure; WB, wheat bran.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Hyperglycemia and diabetes are strong and independent risk factors of both all-cause and cardiovascular disease (CVD) mortality (1). These links are more pronounced when the diabetes is associated with other unfavorable risk factors such as hyperlipidemia (2), hypertension (3), or a cluster of metabolic disorders (4). Because people with diabetes have almost twice the risk of dying from CVD (69.6%) compared with people in the general U.S. population (5), the control of high glucose levels and other concomitant coronary heart disease (CHD) risk factors represents the most effective approach to prevention (6). The importance of stronger nutrition-hygienic measures has been stressed repeatedly for the public at large (4,7). When these measures prove inadequate, an aggressive drug therapy is often required to meet the conventional treatment guidelines (7). In the general population, this approach has been shown to be effective in lowering both the prevalence of hypertension (3) and serum cholesterol levels (8), but it has not reduced the incidence of diabetes (9).

Tighter fasting and postprandial glycemic control results in a considerable reduction in CHD and all-cause mortality (1), as well as fewer long-term microvascular complications both in type 1 (10) and type 2 diabetes (11). Effective dietary strategies shown to decrease postprandial plasma glucose excursions include the use of high fiber and low glycemic index diets (12,13). The mechanism is presumed to involve slowing carbohydrate absorption (13). Based on recent population studies, these types of diets have been shown to have a protective role in preventing diabetes (14,15) and CHD (16). In the case of clinical studies, however, it is the viscous water-soluble fibers, which increase the viscosity of digesta in the human gut (17), that reduce glucose and lipid CHD risk factors (18). Whether soluble fiber is able to reduce a cluster of risk factors is speculative. Studies

using soluble fiber as an adjunct to conventional treatment in individuals with two or more major CHD risk factors are scarce (19).

We therefore studied the effect of water-soluble Konjac-mannan (KJM) fiber in type 2 diabetic patients, as an adjunct to conventional treatment, on a cluster of CHD risk factors: hyperglycemia, hyperlipidemia, and hypertension. KJM was chosen as the fiber because it represents a polysaccharide with one of the highest viscosities (20). The physiologically active component is a high molecular weight glucomannan polymer that, when taken as a supplement, has been shown to have effects in lowering lipids (21–23), systolic blood pressure (sBP) (21), and glycemia (24,25). By incorporating it into commercially produced biscuits, we sought to determine whether the addition of high-viscosity fiber given in a palatable form would enhance conventional treatment outcomes, assessed primarily by total:HDL cholesterol, fructosamine, and sBP and secondarily by total, LDL, and HDL cholesterol, apolipoprotein (apo) A-1, apo B, and their ratio, glucose, insulin, and diastolic blood pressure (dBP).

Table 1—*Baseline characteristics of the study subjects according to sex*

	Men	Women
n	5	6
Age (years)	62 ± 8	59 ± 7
Body weight (% desirable)	133 ± 33	143 ± 22
Android obesity (prevalence)	5	4
Baseline risk factor values		
Serum total cholesterol (mmol/l)	6.2 ± 0.4	5.9 ± 0.5
Glycosylated hemoglobin (%)	7.4 ± 2.1	8.3 ± 3.0
sBP/dBP (mmHg)	139/78	136/82
Known duration of risk factors		
Diabetes (years, self-reported)	11.5 ± 9	18.1 ± 6
Hypertension (years)	7.1 ± 3	6.0 ± 2
Hyperlipidemia (years)	6.3 ± 3	5.6 ± 2
Drug/insulin treatment, prevalence		
Insulin	1	3
Sulfonylurea and/or metformin	5	6
Diuretics	2	4
Other antihypertensives	4	3
Lipid-lowering medications	5	6

Data are means ± SD or *n*. Values for body weight were assessed using Metropolitan Life Insurance tables of 1983. Android obesity is indicated by a waist-to-hip ratio ≥0.9 for men and ≥0.8 for women. Lipid-lowering medications include bile acid sequestrants and/or hydro-3-methyl-glutaryl CoA reductase inhibitors.

RESEARCH DESIGN AND METHODS

Subjects

A total of 11 diabetic patients (5 men, 6 women) gave written informed consent to participate in the present study, which was approved by the human ethic committees of St. Michael's Hospital and the University of Toronto. All had hyperlipidemia, hypertension, and type 2 diabetes (mean serum C-peptide 701 ± 351 pmol/l), with a minimum of 3 years since the onset of all three conditions. They were taking medications to control each of the three risk factors, consuming a National Cholesterol Education Program (NCEP) Step 2 diet, not smoking, not taking alcohol, and leading sedentary lifestyles at recruitment. Two participants had a history of atherosclerotic heart disease, but none had evidence of recent myocardial infarction, unstable angina, or congestive heart failure. Exclusion criteria were a family history of premature CHD, hypothyroidism, or renal, hepatic, or gastrointestinal disease. Table 1 provides baseline demographic, anthropometric, and clinical characteristics of the study participants.

Study design

The study used a double-blind placebo-controlled crossover design, where all subjects were maintained on the same dosage of their medications throughout. The study began with an 8-week baseline period over which participants followed an NCEP Step 2 ad libitum diet, documented by 3 nonconsecutive days of food records every 2 weeks. This was followed by the experimental phase of the study, consisting of two successive 3-week treatment periods separated by a 2-week washout interval over which another 3-day food record was obtained. During the first treatment period subjects were randomly assigned to either the KJM (NCEP Step 2 metabolically controlled diet enriched with KJM fiber) or the control treatment (the same diet enriched with wheat bran [WB] fiber). For the second treatment period, subjects were crossed over. The study began with five subjects taking the KJM treatment and six the WB control treatment.

Diet

Both treatments consisted of a 3-day rotating NCEP Step 2 diet with three meals per day provided under metabolic conditions. All foods were preweighed, packaged, and couriered to participants for consumption at home or at work. The mean macronutrient profile conformed with an NCEP Step 2 diet. Energy intakes for weight maintenance were provided according to Lipid Research Clinics Tables with adjustment for physical activity (26). Total dietary fiber was administrated at 2 g/412 kJ (100 kcal), with a mean daily intake, according to energy intake, ranging from 24 g to a plateau of 50 g for those consuming 2,500 kcal/day or more. The actual diet consumed is presented in Table 3.

The two treatments differed only in the type of fiber. Participants on the KJM treatment received KJM-enriched biscuits,

Table 2—*Composition (g/100 g) of KJM and WB biscuits at a moisture content of 2.8 g/100 g*

Biscuit type	Protein	Fat	Available carbohydrate	KJM flour	Ash	Total dietary fiber: Dietary fiber	Total dietary fiber: Glucomannan from KJM flour	Energy (kJ/100 g)
WB	6.8	14.4	66.5	—	1.4	2.8	—	1,011
KJM	6.2	13.9	61.2	15.3	1.3	2.3	10.6	944

Available carbohydrate values are calculated as follows: 100 − (moisture + protein + fat + total dietary fiber + ash). Added sucrose was between 37 and 40% of the total available carbohydrate. Average values for dietary fiber in WB and flour were analyzed by the method of Prosky et al. (35). The glucomannan value represents 69% glucomannan polymer derived from KJM flour.

whereas those on the control treatment received an equal quantity of WB (placebo) biscuits. Subjects were instructed to eat an equal amount of biscuits along with an 8-oz beverage as a snack, three times daily, including once at bedtime. Both types of biscuits were produced and provided by Dicofarm (Rome, Italy; KJM biscuits are commercially available in Italy as Dicoman biscuits). They had similar nutrient profiles (Table 2) and were indistinguishable in taste and appearance. KJM biscuits contained ~15% KJM flour, of which 69% was the active high-viscosity glucomannan, 15% other polysaccharides, and 16% excipients by weight. Because KJM flour comprised half (1 g/412 kJ [100 kcal]) of the total fiber on the KJM treatment, ~0.7 g/412 kJ (100 kcal) was glucomannan. WB biscuits, in contrast, had a lower proportion of fiber than KJM biscuits (Table 2). Therefore, ~14 g/day of WB fiber derived from standardized American Association of Cereal Chemist hard red wheat bran was added to the WB control diet to compensate for these fiber differences.

Any food from the metabolic diet together with study biscuits not consumed were brought to the clinic for weighing to measure compliance. Dietary changes found to occur during the first 3-week treatment period were duplicated before food delivery for the second treatment period for each participant.

Table 3—*Average intake of energy and nutrients before and during study periods*

	Baseline	KJM	WB	*P*
Total energy (kJ/day)	7,671 ± 1,760	8,907 ± 2,250	9,134 ± 1,006	0.23
Total fat (% of energy)	24.8 ± 6.2	23.4 ± 2.1	23.9 ± 1.6	0.6
Saturated fat (% of energy)	8.2 ± 2.4	4.1 ± 0.4	3.9 ± 0.2	0.73
Monosaturated fat (% of energy)	7.3 ± 1.3	12.4 ± 1.9	12.6 ± 1.4	0.35
Polyunsaturated fat (% of energy)	9.1 ± 2.1	7.1 ± 0.2	7.6 ± 0.3	0.24
Cholesterol (mg/4,184kJ)	87 ± 17	44 ± 18	36 ± 11	0.12
Total protein (% of energy)	18.7 ± 4.2	15.5 ± 1.7	14.9 ± 2.1	0.86
Available carbohydrate (% of energy)	56.5 ± 14.3	60.5 ± 8.6	61.2 ± 6.5	0.4
Sugar (% of energy)	13.2 ± 17.2	11.2 ± 0.6	10.4 ± 0.3	0.17
Total fiber (g/day)	27.4 ± 14.2	39.3 ± 11.4	40.1 ± 12.5	0.9
Water soluble (g/day)	8.1 ± 2.7	23.1 ± 4.1	8.3 ± 2.4	<0.001
Water insoluble (g/day)	17.8 ± 4.2	16.7 ± 3.6	29.8 ± 4.8	<0.001
Sodium (mg)	4,540 ± 1,350	2,820 ± 348	2,708 ± 420	0.878
Potassium (mg)	1,430 ± 850	3,960 ± 450	4,240 ± 664	0.659
Calcium (mg)	630 ± 442	1,150 ± 185	1,370 ± 246	0.552

Data are means ± SD. KJM and WB diets are based on actual intake (n = 11). Baseline values are based on the mean of four 3-day food records. Differences between KJM and WB study periods were calculated by Student's t test for paired data.

Laboratory methods

Serum blood samples were immediately separated and stored in four aliquots at −70°C after collection. They were thawed at the end of the study for analysis of total cholesterol, HDL, and triglycerides measured enzymatically (27,28). LDL content was estimated by the formula of Friedewald et al. (29). Apo A1 and B were determined by rocket immunoelectrophoresis (30). Fasting blood glucose was analyzed by a hexokinase method using a Cobas Mira Autoanalyzer (Roche Diagnostic, Mississauga, Ontario, Canada). Serum fructosamine was analyzed in triplicate using the Cobas Fara II (31), and plasma insulin was measured in duplicate by radioimmunoassay (RIA) with reagent from ICN Biomedicals (Horsham, PA) (32). Finally, C-peptide was determined by RIA (33).

Physical measurements were obtained by standard techniques. Blood pressure was taken and expressed as the mean of three measurements to the nearest 2 mmHg on both arms. Fasting body weight was determined using a beam scale in light clothing, with an emptied bladder and in bare feet. Waist and hip circumferences were measured by soft nonstretchable tape on the narrowest and widest parts of the trunk.

Energy and nutrient analysis of the diets was calculated using U.S. Department of Agriculture data (34). Nutrient composition of the treatment biscuits was analyzed using the Prosky method to determine fiber content (35).

Statistical analyses

Results are expressed as means ± SEM, except for age, anthropometric measurements, and nutrient intake (means ± SD). Data were analyzed by the Statistical Analysis System (SAS) (36). Differences in serum lipids, apolipoproteins, glycemia, blood pressure, and body weight between the beginning (week 0) and end (week 3) of each treatment (control and KJM) were assessed by two-tailed Student's t test for paired data (proc univariate). Analysis of covariance with the facility of the general linear model procedure (proc glm) was used to test for differences in these same parameters between the two treatments. Adjustment for multiple comparisons was made by the Bonferroni-Hochberg procedure (37) for primary (fructosamine, total:HDL cholesterol ratio, and sBP) and secondary (body weight, total, LDL, and HDL cholesterol, apo A-1, B, and A-1:B ratio, glucose, insulin, and dBP) end points separately. P values for each end point were ordered sequentially and contrasted with the corresponding adjusted comparison-wise critical α-levels. Null hypotheses were rejected only if the P values were less than their corresponding α-values (37). Control of individual variation from the repeat measures aspect of the design was addressed by incorporating the random subject effect as well as the starting measurement. Diet, sex, and phase effects were also incorporated in this model. To test for confounding effects of body weight on study parameters, Pearson correlations were performed (proc corr).

RESULTS — All participants followed the experimental protocol with little difficulty. According to 3-day food records collected over the baseline and washout periods, subjects ate their usual low-fat (<25% energy) and high-fiber (>27 g/day) diets (Table 3). In addition, during the treatment periods, returned food and biscuits from metabolic diets indicated that subjects consumed an average of 93 and 95% of diet calories prescribed on the KJM and WB control treatments, respectively, and 88% (137 g/day) and 91% (142 g/day) of the KJM test and WB placebo biscuits, respectively. Consumption patterns translated into an insignificant decrease in body weight during both treatment periods (Table 4). There was no correlation between changes in weight and serum lipids, glucose, or blood pressure (data not shown). The only side effect experienced was a transient complaint of flatulence and

soft stools reported by 37 and 24% of participants during the KJM and the WB control treatments, respectively, but none refused to continue the study.

Serum lipids

Blood lipids were improved during KJM treatment compared with the WB control treatment (Table 4). The primary lipid endpoint, total:HDL cholesterol, decreased significantly by 5.7 ± 2.3% (P = 0.034, α = 0.05) during KJM treatment compared with an insignificant increase of 4.7 ± 4.4% (P = 0.316, α = 0.017) during the WB control treatment. The resultant between-treatment decrease of 10 ± 4.0% in those on the KJM treatment was significant (P = 0.028, α = 0.05). The secondary end points of total and LDL cholesterol also fell significantly by 16 ± 2.7% (P = 0.001, α = 0.005) and 25 ± 3.9% (P = 0.001, α = 0.005), respectively, during KJM treatment compared with 4.9 ± 3.7% (P = 0.20, α = 0.006) and 4.8 ± 5.9% (P = 0.45, α = 0.008), respectively, during the WB control treatment. Resultant between-treatment differences of 11 ± 4.2% (P = 0.025, α = 0.005) and 19 ± 6.8% (P = 0.033, α = 0.006) were insignificant, however, after correction by the Bonferroni-Hochberg procedure. The combined fall in total cholesterol and LDL in those on the KJM treatment indicated reclassification of the lipid status from elevated to normal cholesterolemia (<5.2 mmol/l) (2) for 6 of 11 subjects. Values for LDL, however, were derived from only 9 subjects, because 2 of 11 participants had serum triglyceride levels >4.5 mmol/l, not allowing for calculation by the Friedewald equation.

Similar results were observed for apo B and the apo B:A-1 ratio. During KJM treatment, both fell significantly by 14 ± 3.4% (P = 0.002, α = 0.006) and 8.6 ± 2.3% (P = 0.004, α = 0.007), respectively, compared with 3.0 ± 5.0% (P = 0.57, α = 0.013) and 3.0 ± 4.8% (P = 0.55, α = 0.01) during the WB control treatment. These changes, however, resulted in insignificant between-treatment differences of 11 ± 4.3% (P = 0.025, α = 0.005) and 5.6 ± 4.5% (P = 0.24, α = 0.008) after correction by the Bonferroni-Hochberg procedure.

In contrast, such effects were not seen for HDL, apo A-1, or triglycerides. During KJM and WB control treatments, HDL and apo A-1 decreased insignificantly, for insignificant between-treatment changes. Similarly, during both treatments, triglycerides increased insignificantly, with no significant difference between treatments.

Glycemic control

Improvements in glycemic control were observed in those on the KJM treatment compared with those on the WB control treatment (Table 4). The primary glycemic end point, serum fructosamine, was reduced insignificantly during both the KJM and control treatments by 6.1 ± 2.4% (P = 0.03, α = 0.025) and 0.5 ± 1.4% (P = 0.751, α = 0.05), respectively, after correction by the Bonferroni procedure. The resultant between-treatment decrease of 5.7 ± 1.7% in those on the KJM treatment was nevertheless significant (P = 0.007, α = 0.017). No significant between-treatment differences were seen for the secondary end points of insulin and glucose,

Table 4—*Changes in primary and secondary end points of metabolic control during and between the KJM and WB control study periods*

	KJM			WB			Between-treatments		
Risk factor	Week 0	Week 3	Change (%)	Week 0	Week 3	Change (%)	Change (%)	P	α
Primary end points									
Total:HDL cholesterol (mmol/l)	6.08 ± 0.53	5.69 ± 0.48	−5.7 ± 2.3*	6.06 ± 0.56	6.21 ± 0.53	4.7 ± 4.4	−10 ± 4.0	0.028*	0.05
Fructosamine (mmol/l)	3.36 ± 0.1	3.17 ± 0.2	−6.1 ± 2.4	3.25 ± 0.2	3.25 ± 0.2	−0.5 ± 1.4	−5.7 ± 1.7	0.007*	0.017
sBP (mmHg)	139.5 ± 5.0	131.6 ± 4.9	−5.5 ± 1.4*	128.8 ± 4.0	130.4 ± 4.7	1.4 ± 2.7	−6.9 ± 2.5	0.021*	0.025
Secondary end points									
Cholesterol (mmol/l)									
Total	6.10 ± 0.29	5.11 ± 0.28	−16 ± 2.7*	5.81 ± 0.19	5.48 ± 0.19	−4.9 ± 3.7	−11 ± 4.2	0.025	0.005
LDL	3.89 ± 0.25	3.04 ± 0.24	−25 ± 3.9*	3.56 ± 0.18	3.29 ± 0.18	−4.8 ± 5.9	−19 ± 6.8	0.033	0.006
HDL	1.07 ± 0.08	0.94 ± 0.06	−11 ± 2.2	1.04 ± 0.10	0.95 ± 0.08	−8.9 ± 2.4*	−2.2 ± 3.1	0.492	0.01
Triglyceride (mmol/l)	2.53 ± 0.23	2.88 ± 0.29	18.7 ± 12.8	2.69 ± 0.44	2.96 ± 0.37	25.1 ± 14.7	−6.4 ± 13.9	0.657	0.017
Apolipoprotein (g/l)									
Apo A-1	1.47 ± 0.07	1.37 ± 0.06	−6 ± 3.1	1.48 ± 0.08	1.48 ± 0.10	0.7 ±3.8	−6.7 ± 4.3	0.154	0.007
Apo B	1.50 ± 0.09	1.28 ± 0.08	−14 ± 3.4*	1.48 ± 0.08	1.40 ± 0.07	−3.0 ± 5.0	−11 ± 4.3	0.025	0.005
Apo B/Apo A-1	1.05 ± 0.09	0.96 ± 0.08	−8.6 ± 2.3*	1.05 ± 0.10	0.99 ± 0.08	−3.0 ± 4.8	−5.6 ± 4.5	0.235	0.008
Glycemic control									
Glucose (mmol/l)	9.63 ± 0.89	8.62 ± 0.95	−11.0 ± 3.0*	9.29 ± 0.74	8.99 ± 0.78	−1.5 ± 6.1	−9.7 ± 6.1	0.141	0.006
Insulin (pmol/l)	142 ± 32	140 ± 31	2.1 ± 11	154 ± 38.6	150 ± 32.8	9.58 ± 9.8	−7.5 ± 12.4	0.559	0.013
dBP (mmHg)	79.1 ± 2.0	77.5 ± 1.8	−1.6 ± 2.8	78.3 ± 1.6	78.4 ± 2.7	0.4 ± 3.6	−2.0 ± 5.2	0.706	0.025
Body weight (kg)	85.6 ± 19	85.0 ± 19	−0.6 ± 0.5	85.9 ± 19	85.3 ± 19	−0.6 ± 0.4	−0.1 ± 0.4	0.899	0.05

Data are means ± SEM except for body weight, which is means ± SD (n = 11). Between-treatment differences were assessed by analysis of covariance (PROC GLM). Comparisonwise α-level was adjusted for multiple end point comparisons with the Bonferroni-Hochberg procedure for primary and secondary end points separately. LDL values are for nine subjects, since two subjects had triglycerides >4.5 mmol/l, preventing calculation by the Friedewald equation. *Significant after adjustment of α-level by the Bonferroni-Hochberg procedure. Null-hypotheses were rejected only if the P values were less than their corresponding α-value. P values for during-treatment changes were assessed by paired Student's t test.

although during the KJM treatment, fasting glycemia fell significantly by 11 ± 3.0% (P = 0.004, α = 0.008) compared with 1.5 ± 6.1% (P = 0.804, α = 0.013) in those on the control treatment.

Blood pressure

An improvement in blood pressure was also observed in those on the KJM treatment compared with those on the WB control treatment (Table 4). The primary blood pressure endpoint, sBP, decreased significantly in those on KJM supplementation by 5.5 ± 1.4% (P = 0.003, α = 0.017) compared with 1.4 ± 2.7% (P = 0.62, α = 0.03) in those on the WB control treatment, producing a significant between-treatment difference of 6.9 ± 2.5% (P = 0.021, α = 0.025) or 9.4 ± 3 mmHg. During both treatments, however, dBP remained virtually unchanged with no significant difference between treatments. The result was a reclassification in sBP status from moderately high to normotensive (<135 mmHg) in 5 of 11 subjects after the KJM treatment.

CONCLUSIONS — The present study indicates that the addition of 0.7 g/412 kJ (100 kcal) of high-viscosity glucomannan in biscuit form to conventional CHD treatment (a low–saturated fat diet combined with drug therapy) improved metabolic control beyond the effect of conventional treatment alone in high-risk individuals with type 2 diabetes. We observed amelioration in three major CHD risk factors—hyperglycemia, hypertension, and hyperlipidemia—relative to a matched placebo control treatment, as measured by the primary end points of fructosamine, sBP, and total:HDL cholesterol, respectively. Differences in secondary glycemic, blood pressure, and lipid end points were insignificant after adjustment for multiple comparisons by the Bonferroni-Hochberg procedure. With greater power derived from a larger sample size, significance might have been achieved in these cases.

To achieve similar metabolic benefits, the most recent dietary recommendations of the American Diabetes Association have a change in emphasis from encouraging carbohydrate and less processed fiber foods to increased consumption of monounsaturated fat (38). The reasoning is that fiber has only very modest effects on LDL cholesterol and does nothing to raise HDL cholesterol levels. Nevertheless, the diet usually prescribed for the management of CHD risk factors in people with diabetes resembles an NCEP Step 1 or 2 diet. The recommendations for these diets are as follows: for NCEP Step 1, <30% of total calories from fat, <10% from saturated fat, and <10% from polyunsaturated fat, with <300 mg/day of cholesterol; and for NCEP Step 2, the same except <7% of total calories from saturated fat with <200 mg/day of cholesterol. In the two well-controlled clinical studies in this area, limitations of the diets are evident. Hunninghake et al. (39), following hypercholesterolemic subjects on an NCEP Step 2 diet for 3 months, found that LDL was reduced by only 5%. Schaefer et al. (40) found a reduction in LDL in subjects provided an NCEP Step 2 diet on a metabolic basis to be as much as 17%, but with adverse effects on other lipid parameters and no effect on the total:HDL cholesterol ratio. A high intersubject variability in LDL reductions was also noticed. These results are in agreement with our findings, but we also detected an improvement in lipid ratios in those on KJM treatment. The suggestion is that an NCEP Step 2 diet supplemented with KJM may confer additional benefits over this diet alone.

Lipids

Improvements in blood lipid control have previously been shown when NCEP Step 2 diets were supplemented with soluble fiber from different dietary sources (41) or fiber supplements (18,42). Although such studies have reported reduced total and LDL cholesterol concentrations, few, as has been the case for NCEP diets, have reported improved lipoprotein ratios. Out of the three lipid trials that used KJM (21–23), the former two did not show a significant change in these ratios. In contrast, Venter et al. (23) found 4.5 g/day glucomannan significantly improved both LDL and the LDL:HDL ratio in 18 hypercholesterolemic subjects. These last findings are supported by those of the present study, in which a significant 10 ± 4.0% decrease in the total:HDL cholesterol ratio was noticed in those on the KJM treatment compared with control subjects. The mechanism by which our KJM-supplemented biscuits had this lipid-lowering effect is not clear. It is likely similar to the mechanism proposed for other soluble fibers. Possibilities include an inhibition of cholesterol absorption in the jejunum (43), bile acid absorption in the ileum (44), or less postprandial stimulation of hydro-3-methyl-glutaryl CoA reductase (41). Other options include the generation of short-chain fatty acids by colonic microflora, predominantly propionate, which may decrease hepatic cholesterol synthesis (45).

Glycemic control

Improvements in diabetes control after soluble fiber supplementation have also been shown (46). KJM, in particular, has been shown to have a beneficial effect after both acute (25) and long-term (24,25) administration. Our findings support these observations. In those on KJM treatment compared with control subjects, a 5.7 ± 1.7% reduction was observed in serum fructosamine, a short-term marker of diabetes control, with no effect on either fasting glucose or insulin concentrations. These results were not altered by excluding four subjects treated with insulin. An effect of the gel-forming KJM on digestion may explain this finding. It has been suggested that decreases in glucose and insulin levels after the consumption of water-soluble fibers are related to slower rates of food absorption in the small intestine associated with increased viscosity (47). KJM has been shown to have very high viscosity, ~5 times higher than guar gum (47) and considerably more than pectin (23). Consequently, in some studies it has been given at half the dosage relative to these other fibers (47).

Blood pressure

Finally, although few studies have demonstrated an effect of fiber on blood pressure, significant reductions in both sBP and dBP have been reported after consumption of guar granulates (48) and soluble dietary fiber supplements (49). The same effect has been shown for KJM, but only in sBP (21). This last finding agrees with results from the present study, in which KJM treatment significantly reduced sBP by 6.9% compared with WB control treatment but did not affect dBP. The commonly recommended oat bran, in contrast, has been shown to affect neither sBP nor dBP (50). A possible mechanism for the blood pressure–lowering effect of soluble fibers may involve increased insulin sensitivity (18), which may reduce blood pressure by influencing sodium absorption in the distal tubule, increasing sympathetic nervous system activity and peripheral vascular resistance (51). Unfortunately, this parameter was not measured.

The effect of KJM fiber supplements on the three CHD risk factors persists even in subjects who are concurrently taking con-

ventional drug therapy. Consistent with our findings, a combination of fiber and drugs has been shown to be more effective clinically in improving metabolic control than the drug given alone. Tuomilehto et al. (52) found that the viscous soluble fiber guar gum and gemfibrozil administered together reduced total cholesterol and the LDL:HDL ratio significantly more than gemfibrozil and placebo. Elsewhere this same effect has been noticed for blood glucose and blood pressure. A significant reduction was found in postprandial blood glucose after consumption of sulfonylurea (glibenclamide) and glucomannan with a test meal compared with sulfonylurea alone with the same test meal (53). Similarly, a significant decrease in dBP was noticed after administration of guar gum compared with placebo in patients receiving drug treatment for hypertension (19). Together these findings suggest that highly viscous soluble fiber may augment or potentiate the effect of drugs.

In conclusion, the application of KJM supplementation in our high-risk diabetic study group demonstrated simultaneous improvement in all three diet-modifiable risk factors, indicating a reduction in overall CHD risk (54). One of the benefits we foresee from this study is that KJM-supplemented therapy may lower required drug dosages and improve overall cost-effectiveness and acceptability of treatment. Although we agree that food should be the normal way to achieve an adequate fiber intake, we also consider that fiber-supplemented foods have advantages in the treatment of individuals at high risk for CHD and represent a possible intermediate step between diet and drug therapy. To maximize the therapeutic potential of KJM in CHD prevention, however, studies with larger sample sizes are needed. A determination of the optimal fiber dose in different categories of people and the rheological-biological relationship of KJM are also warranted.

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