Improved Glycemic Control and Lipid Profile and Normalized Fibrinolytic Activity on a Low–Glycemic Index Diet in Type 2 Diabetic Patients

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OBJECTIVE — To evaluate the effects of varying the glycemic index (GI) of carbohydrate-rich foods on metabolic control in type 2 diabetic patients.

RESEARCH DESIGN AND METHODS — In a randomized crossover study, 20 patients, 5 women and 15 men, were given preweighed diets with different GIs during two consecutive 24-day periods. Both diets were composed in accordance with dietary recommendations for people with diabetes. The macronutrient composition and type and amount of dietary fiber were identical. Differences in GI were achieved mainly by altering the structure of the starchy foods.

RESULTS — Peripheral insulin sensitivity increased significantly and fasting plasma glucose decreased during both treatment periods. There was a significant difference in the changes of serum fructosamine concentrations between the diets ($P < 0.05$). The incremental area under the curve for both blood glucose and plasma insulin was ~30% lower after the low- than after the high-GI diet. LDL cholesterol was significantly lowered on both diets, with a significantly more pronounced reduction on the low-GI diet. Plasminogen activator inhibitor-1 activity was normalized on the low-GI diet, (−54%, $P < 0.001$), but remained unchanged on the high-GI diet.

CONCLUSIONS — A diet characterized by low-GI starchy foods lowers the glucose and insulin responses throughout the day and improves the lipid profile and capacity for fibrinolysis, suggesting a therapeutic potential in diabetes.

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Differences in glycemic responses to various carbohydrate-rich foods are related to differences in the rate at which the carbohydrate is digested and absorbed. A low glycemic response has been reported to facilitate blood glucose regulation and to improve lipid metabolism in diabetes (1,2). The glycemic index (GI) was introduced in the early 1980s as a way of ranking foods according to their glycemic effect (3). The current European dietary recommendations for patients with type 2 diabetes (4) suggest that most of the dietary energy intake should come from a combination of carbohydrates and monounsaturated fatty acids with a special emphasis on carbohydrate-containing foods rich in soluble fiber and foods with a low GI. In the healthy eating guidelines for people with diabetes in Australia and New Zealand, the GI concept is evident (5). Recent recommendations by the joint Food and Agriculture Organization (FAO)/World Health Organization Expert Consultation in a report entitled "Carbohydrates in Human Nutrition" (6) also support the choice of low-GI foods in healthy individuals. On the other hand, in the American Diabetes Association's "Nutrition Recommendations and Principles for People with Diabetes Mellitus" (7), it is stressed that the first priority should be given to the total amount of carbohydrate consumed, rather than the source of the carbohydrate. Thus, there is still no international consensus as to the clinical usefulness of the GI concept in the dietary management of diabetes. GI has been criticized for not being applicable to mixed meals, and hence the long-term effects of low-GI foods have been questioned (8–10). However, there is evidence that dietary changes that involve replacement of foods with a higher GI by those with lower indices result in improved glycemic control and reduced fasting serum lipids (2,11–16). Various properties of foods, e.g., particle size, botanical structure, and properties of the starch, have been found to influence the metabolic responses to starchy foods. Processing steps in manufacturing foods may strongly influence such food properties (17,18).

The aim of this study was to evaluate the effects of two diets with pronounced differences in GI on metabolic control in type 2 diabetic patients, to establish whether the GI approach is useful in a realistic diabetic diet for a longer period of time. The carbohydrate-rich foods in both diets were basically made from the same ingredients. Differences in GI were achieved mainly by altering the botanical food structure or the chemical starch structure of the starchy foods, thus making it

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Abbreviations: apo, apolipoprotein; GI, glycemic index; *I*, mean insulin concentration; Lp(a), lipoprotein(a); *M*, mean glucose uptake; NEFA, nonesterified fatty acids; PAI-1, plasminogen activator inhibitor-1; tPA, tissue-type plasminogen activator.

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

Table 1—*Nutrient composition*

Nutrient	Low-GI diet	High-GI diet
Carbohydrate (g/% of energy)	255/55	239/54
Starch (g)	215	205
Dietary fiber, corrected for resistant starch (g)	38	34
Glucose (g)	11	10
Fructose (g)	13	12
Sucrose (g)	9	8
Protein (g/% of energy)	84/18	78/18
Fat (g/% of energy)	57/27	60/29
Fatty acids		
Saturated (g/% of energy)	19/9	18/9
Monounsaturated (g/% of energy)	25/12	26/12
Polyunsaturated (g/% of energy))	14/7	15/7
Energy		
kcal	1,880	1,820
kJ	7,870	760

Data represent the mean for all 7 days of three analyses for each diet. Chemical analyses were performed on a menu calculated to contain 2,000 kcal (8,370 kJ). Calculations of % of energy were based on the energy levels calculated from the analysis of carbohydrates, protein, and fat. Fatty acids were calculated from the relative fatty acid composition and the energy levels calculated from the analysis of carbohydrates, protein, and fat. Energy was calculated from the analysis of carbohydrates, protein, and fat.

possible to eliminate potential effects of variations in dietary fiber or nutrients.

RESEARCH DESIGN AND METHODS

Study design

In a randomized crossover study, patients with type 2 diabetes were given two diets with different food structure with either a low or a high GI during two consecutive 24-day periods. Throughout the study, the participants were free-living, and they continued their customary life and activities without any change in degree of physical activity. Admission and change of diets took place on the same day of the week. The participants started in randomized order with either of the two different diets. All patients had given their informed consent before entering the study, and the study design was approved by the Ethical Committee of the Medical Faculty of Uppsala University, Uppsala, Sweden.

Subjects

The study comprised 20 patients, 5 women and 15 men, with mean ages of 65 (range 56–76) and 67 (50–77) years, respectively. The mean body weight (mean ± SD) of the 20 patients on admission was 76.3 ± 7.5 kg, with a BMI of 25.3 ± 2.7 kg/m^2. Individuals with a BMI >27 were not included. The average HbA_{1c} on admission was 7.2 ± 1.4%. The known duration of the diabetic disease varied between 0.5 and 17 years. Four of the patients were treated with diet only and the other 16 were treated with diet in combination with oral antidiabetic drugs. One took metformin only and the other 15 took sulfonylurea, nine in combination with metformin. No insulin-treated subjects were included. All medication remained unchanged throughout the study.

Diets

The two test diets were planned with the aim of achieving large differences in the GI of the starchy foods, in particular, but with no differences in the amounts of energy, protein, fat, carbohydrate, starch, and dietary fiber. The diets were composed in accordance with the previous dietary recommendations for patients with diabetes (19–21). The nutrient composition of the test diets had been calculated and analyzed chemically (Table 1). According to the database from the Swedish National Food Administration, the energy derived from protein, fat, and carbohydrate was 16, 28, and 55%, respectively. Based on the sources of carbohydrate in the diets, a mean GI was calculated. On the average, GI was calculated on the basis of data for 94 ± 2.5% (92–96) of all the carbohydrates in the diets. The average GIs of the low- and high-GI diets, as expressed in rela-

Table 2—*GIs of starchy foods included in the two test diets*

Starchy food	Contribution% (carbohydrate basis)	Low-GI diet (ref. no.)	High-GI diet (ref. no.)
Whole grain barley bread	23	58 (22)	
Whole meal barley bread	23		100 (22)
White durum pasta	21	67 (23)	
White durum bread	21		100 (23)
Parboiled rice	21	65*	
Sticky rice	21		86*
Whole grain barley porridge	3	35 (24)	
Whole meal barley porridge	3		98 (25)
Whole red lentils	2	36 (26)	
Ground red lentils	2		70†
Whole white beans	2	40 (26)	
Ground white beans	2		74†
Whole red kidney beans	2	36 (30)	
Ground red kidney beans	2		70 (30)
Whole brown beans	2	40‡	
Ground brown beans	2		74‡
Ordinary maize starch muffins	1	68*	
High-amylose maize starch muffins	1		96*
Ordinary maize flour	0.5	50*	
High-amylose maize flour	0.5		81*

The structure of the starchy foods was changed with the purpose of varying the GI (with white bread as reference) of the diets while maintaining an identical gross nutrient composition. All other dietary constituents were kept identical in both test diets. *GI predicted from in vitro assay according to Granfeldt et al. (30). †Estimated assuming an increase in GI due to milling, as in red kidney beans. ‡Properties assumed to be similar to those in the corresponding white bean product (27). Ordinary maize products are 25% amylose; high-amylose products are 70% amylose.

tion to that of white wheat bread, were 56.8 ± 3.6 (52.9–60.9) and 82.7 ± 3.1 (76.9–85.1) U, respectively. The value for the diet with the low GI was on the average 31% (26.2 ± 3.8 U) lower than that for the high-GI diet. GI values were calculated on the foodstuffs, and their GI values are given in Table 2. The diets were based on common foods, and both diets were basically prepared from the same ingredients. The difference in GI was mainly achieved by manipulating the structure of the starchy foods (Table 2). For most food items, the GIs had previously been measured in healthy subjects (22–27) or derived by using data from the literature (28,29). With regard to foods for which GI data were missing, the GIs were predicted by using an enzymatic in vitro procedure (30). This method is based on enzyme incubation of chewed samples and allows evaluation of products as eaten. A hydrolysis index is calculated from the area under the hydrolysis graph with the test product and expressed as a percentage of the corresponding area with white bread as a reference. Hydrolysis indices thus calculated have been shown to predict GIs for a large number of cereal- and legume-based foods with good accuracy ($r = 0.877$, $P < 0.005$) (30). Except for the foodstuffs with different GIs, all other ingredients in the two diets were kept identical. Both diets were based on a 1-week menu that was repeated during each test period. Four different energy levels were used: 1,600 kcal (6.7 MJ), 2,000 kcal (8.4 MJ), 2,400 kcal (10.1 MJ), and 2,800 kcal (11.8 MJ). The relative contents of nutrients were identical at different levels of energy intake. Dietary instructions were given by a dietitian before entry into the study. The participants were provided with all the food throughout the study period. The food was individually prepared in a metabolic kitchen, and the estimated energy intake of the participants was calculated on the basis of their initial body weight in an attempt to keep the body weight constant throughout both diet periods. The female patients received 30 kcal (125 kJ) per kilogram of body weight, and the male patients, 35 kcal (145 kJ). If a patient gained or lost weight, the energy level was adjusted. An example of a menu for 1 day on the low- and the high-GI diets, respectively, is given in Table 3. The food was collected by the subjects three times a week. In a written 1-week menu, they were told which dishes and food items should be eaten for breakfast, lunch, dinner, and in-between meals. All prepared dishes were ready to be heated.

Table 3—*Menu for 1 day on the low- and high-GI diets at the 2,000-kcal level*

Meal	Low-GI day	High-GI day
Breakfast		
	Pasta porridge:	127 g bread made from
	73 g durum pasta*	durum wheat*
	18 g margarine	18 g margarine
	30 g strawberries	30 g strawberries
	3 g sugar	3 g sugar
	150 ml low-fat milk	150 ml low-fat milk
Lunch		
	54 g durum pasta*	95 g bread made from
		durum wheat*
	Salmon sauce:	Salmon sauce:
	5 g flour	5 g flour
	10 g margarine	10 g margarine
	100 ml low-fat milk	100 ml low-fat milk
	50 g salmon	50 g salmon
	10 g leek	10 g leek
	45 g green beans	45 g green beans
	45 g bread made of	45 g bread made of
	whole barley seeds*	ground barley seeds*
	3 g margarine	3 g margarine
	105 g orange	105 g orange
Dinner		
	Chili con carne:	Chili con carne:
	40 g white beans, whole*	40 g white beans, ground*
	50 g minced meat	50 g minced meat
	30 g onion	30 g onion
	3 g garlic	3 g garlic
	60 g tomato, crushed	60 g tomato, crushed
	10 g tomato, puree	10 g tomato, puree
	15 g margarine	15 g margarine
	47 g parboiled rice*	47 g sticky rice*
	Tomato salad:	Tomato salad:
	65 g tomato	65 g tomato
	5 g canola oil	5 g canola oil
	2 g vinegar	2 g vinegar
Snack		
	75 g bread made of	75 g bread made of
	whole barley seeds*	ground barley seeds*
	6 g margarine	6 g margarine
	150 ml low-fat milk	150 ml low-fat milk
	Apple rice:	Apple rice:
	32 g parboiled rice*	34 g sticky rice*
	5 g honey	5 g honey
	40 g apple	40 g apple
	5 g lemon juice	5 g lemon juice

*Foods with different GI values.

Instructions were given on how to store and prepare the food. The participants were requested to eat all the food that they received. No other food items except water, mineral water, coffee, and tea were allowed. If, for some reason, a participant was not able to eat all of the food, he or she was instructed to return the food to the metabolic ward to be weighed and subtracted from the calculated amount in the diet.

Chemical analysis of the diets

For analysis of the nutrient composition, duplicate portions for each day were prepared separately on three occasions. Each portion was homogenized with water, and

samples were removed and stored at −18°C. For measurements of carbohydrates, dietary fiber, and protein, the samples were freeze-dried. The content of insoluble and soluble dietary fiber was analyzed by a gravimetric method according to Asp et al. (31,32). Starch was determined as described by Holm et al. (33), and the other carbohydrates were measured by enzymatic methods (Roche Diagnostics, Mannheim, Germany). The total fat content and fatty acid composition were also determined. A quantity of 10 g of the homogenate (see above) was extracted with 50 ml methanol, 100 ml chloroform, and 150 ml of 0.2 mol/l sodium dihydrogen phosphate; 10 ml of the chloroform phase was evaporated to dryness; and the total fat content was determined by weighing. Another aliquot of the chloroform phase was used for determination of the fatty acid composition. The fatty acids were transesterified to methyl esters and analyzed by gas-liquid chromatography as described above (34).

Laboratory methods

The participants were admitted to a metabolic ward for 2 days at the beginning and end of each dietary period for laboratory measurements. On the 1st day, blood samples were drawn after an overnight fast for determination of plasma glucose, serum fructosamine, plasma insulin, C-peptide, serum lipoproteins, serum apolipoproteins, nonesterified fatty acids (NEFAs), fatty acid composition of the serum cholesterol esters, serum tocopherols, and plasminogen activator inhibitor-1 (PAI-1) activity. In addition, blood samples were drawn at fixed time points throughout the day from 0730 to 1800 (profile day) for assay of plasma glucose and plasma insulin at 60, 120, 180, 240, 300, 360, 480, and 540 min after breakfast and of C-peptide, serum cholesterol, serum triglycerides, and NEFA concentrations at 120 and 300 min after breakfast. The subjects followed the study diets on the profile day, with breakfast at 0800, lunch at 1215, dinner at 1615, and snacks at 1000 and 1400. On the 2nd day, the insulin sensitivity was evaluated by a euglycemic-hyperinsulinemic clamp technique. The subjects were weighed three times a week in indoor clothing without shoes. Plasma glucose concentrations were determined by the glucose oxidase method (35). The determination of serum fructosamine was performed using a Roche reagent kit (07-366694) (Roche, Basel), based on nitroblue tetrazolium reduction in alkaline medium, in a Cobas Bio centrifugal analyzer. Plasma insulin assays were performed by the enzyme-immunological test for quantitative determination of human insulin in vitro (enzyme-linked immunosorbent assay/1-step sandwich assay; Boehringer Mannheim Immunodiagnostics for the ES300). Plasma C-peptide was measured according to the method of Heding (36). NEFAs were determined with a Wako NEFA C-kit (994-75409) (Wako, Neuss, Germany), modified for use in a Monarch apparatus (Instrumentation Laboratories, Lexington, MA). Lipoprotein concentrations in serum were determined after an overnight fast. VLDL, LDL, and HDL were isolated by a combination of preparative ultracentrifugation (37) and precipitation with a sodium phosphotungstate and magnesium chloride solution (38). Triglyceride and cholesterol concentrations were measured in serum and in the isolated lipoprotein fractions by enzymatic methods using the IL Test cholesterol method 181618-10 and the IL Test triglyceride enzymatic-colorimetric method 181610-60 in a Monarch apparatus (Instrumentation Laboratories). The concentrations of serum apolipoprotein (apo) A-1 and B were determined by immunochemical assay (Orion Diagnostica, Espoo, Finland) in a Monarch apparatus (Instrumentation Laboratories). Lipoprotein(a) [Lp(a)] was measured by a Pharmacia apo(a) radioimmunoassay method (Pharmacia, Uppsala, Sweden). This is based on the direct sandwich technique, in which two monoclonal antibodies are directed against separate antigenic determinants on the apo(a) in the sample. The concentration is expressed in U/l. According to the manufacturer, 1 U of apo(a) is approximately equal to 0.7 mg Lp(a). The fatty acid compositions of the serum cholesterol esters were determined by gas-liquid chromatography as described earlier (34). The concentrations of α- and γ-tocopherol in serum were assayed by high performance liquid chromatography using a fluorescence detector, as described by Öhrvall et al. (39). PAI-1 activity in plasma was measured with Spectrolyse/pL kits from Biopool AB (Umeå, Sweden), using polylysine as a stimulator (40). The euglycemic-hyperinsulinemic clamp technique according to DeFronzo et al. (41) was used as described in detail by Pollare et al. (42). Insulin sensitivity is expressed as the insulin sensitivity index ($M/I_{60–120}$), which is a measure of the tissue sensitivity to insulin expressed per unit of insulin obtained by dividing the mean glucose uptake (M) by the mean insulin concentration (I) during the last 60 min of the clamp study.

Statistical analyses

The analyses take into account the design of the experiment, the scales, and the distributions of variables (43). For continuous variables with normal distributions (for some variables after logarithmic transformation), an analysis of variance model with factors for treatment, participant, and time was used. Comparisons were made of the two dietary periods, and each dietary period was also compared with the results on admission. The mean value of period one and period two minus the baseline value was used as the basis of a test of different carryover effects between the two treatments. The test was performed as a t test between the two sequences. For continuous variables with normal distributions, a t test for different carryover effects at the 10% level was used. If this test was not significant, a t test for different treatment effects at the 5% level was used. If the carryover tests were significant, only data from the first dietary period were used in comparisons of treatment effects. If the usual assumptions for t tests did not hold, or if the data were on an ordinal scale, the t test was replaced by the Mann-Whitney U test. Since no carryover effects were identified, data from both periods with a high-GI diet were added, irrespective of the order of treatment, as were both periods with a low-GI diet. An analysis of covariance with change in body weight as a covariate was carried out to separate the effects of treatment from those of changes in body weight. Some of the data were unbalanced, since a few values were missing. In consequence, the results are presented as least-square means, which form the basis of the statistical tests and estimates in the analyses and take the imbalance into account.

RESULTS

Body weight

The intention was to keep the subjects' weight stable during the entire study. Adjustments in the energy levels were therefore made if there were any changes in body weight. Owing to the large volume of the diets, it was not always possible to completely adjust the energy intake to avoid a reduction of the body weight. Consequently, there was a slight and similar reduction in body weight during both diet

Table 4—*Effects on glucose and insulin metabolism after 3 weeks on low- and high-GI diets*

	Baseline	Low GI	% Change	High GI	% Change	*P*
Fasting plasma glucose (mmol/l)	10.3 ± 3.2	8.8 ± 3.1	−14.6*	9.0 ± 3.1	−13.3*	0.471
HbA_{1c} (%)	7.2 ± 1.4	6.7 ± 1.3	−5.9†	6.9 ± 1.3	−3.6	0.107
Fructosamine (μmol/l)	353 ± 78	347 ± 72	−1.8	356 ± 75	0.8	0.050
Fasting plasma insulin (mU/l)	13.6 ± 8.4	12.5 ± 4.5	−8.3	12.7 ± 5.0	−6.3	0.930
Insulin sensitivity (*M/I*)	4.3 ± 2.8	5.6 ± 2.8	30†	5.2 ± 2.5	21‡	0.305

Data are means ± SD. *P* includes values for differences between the low- and high-GI diets. Significant changes during the dietary periods when compared with baseline: *$P < 0.001$; †$P < 0.01$; ‡$P < 0.05$.

periods, 1.5 ± 7.21 kg on the high-GI diet and 1.4 ± 7.08 kg on the low-GI diet. All results presented have therefore been adjusted for changes in body weight.

Glucose and insulin metabolism

The fasting plasma glucose concentration fell significantly by ~14% ($P < 0.001$) during both the low- and the high-GI period (Table 4). The incremental area under the plasma glucose response curve during the 9-h profile day was 31% lower ($P < 0.05$) after the period with the low-GI diet than after the high-GI period (Fig. 1). The changes in the serum fructosamine concentrations differed significantly ($P = 0.05$) between the two diet periods (Table 4). The incremental area under the curve for plasma insulin during the day was 27% lower ($P < 0.01$) after the low-GI diet (Fig. 2), while the peripheral insulin sensitivity measured by the clamp technique (*M/I*) increased significantly during both periods (Table 4). The C-peptide levels were significantly higher after the high-GI diet, compared with the low-GI diet, at 120 ($P = 0.001$) and 300 ($P < 0.01$) min after breakfast.

Serum lipoprotein lipids

The serum cholesterol concentration was markedly reduced after both dietary periods when compared with the value on admission (Table 5).The reduction in subjects on the low-GI diet was significantly more pronounced than that in those on the high-GI diet (−5%, $P < 0.01$). Serum triglycerides were reduced to the same extent on both diets. HDL cholesterol levels were also decreased after both diet periods. LDL cholesterol was reduced by 29% ($P < 0.001$) after the low-GI diet and by 22% ($P < 0.001$) after the high-GI diet when compared with that on admission. When comparing the two periods, LDL cholesterol was 8% ($P < 0.01$) lower in the low-GI diet than in the high-GI diet (Table 5).

Serum apolipoprotein concentration

The concentration of apoB was markedly decreased after both diet periods, significantly more after the low- (−24%) than after the high- (−19%) GI period. The serum concentration of apoA-1 was also significantly decreased after both periods, slightly more after the period with the low-GI diet. The concentrations of Lp(a) decreased to a similar extent during both diet periods (Table 5).

NEFA concentration

There were no changes in the fasting values of NEFA, but there were significant differences between the dietary periods during the day, the NEFA levels being ~40% higher at 120 and 180 min and 31% lower at 300 min on the low-GI period compared with the high-GI period (Fig. 3).

Fatty acid composition of the serum cholesterol esters

The fatty acid composition of the serum cholesterol esters was similar after the two dietary periods. Compared with admission, the proportions of α-linoleic acid and docosahexanoic acid had increased, and those of palmitoleic and stearic acid had decreased, indicating good compliance to both diets (data not shown).

Serum tocopherols

The serum tocopherol concentration changed significantly and to about the same extent during both treatment periods. The concentration of α-tocopherol was increased after both dietary periods: by 9% ($P < 0.05$) after the low-GI period, and by 14% ($P < 0.05$) after the high-GI period, while that of γ-tocopherol was increased by 43% ($P < 0.001$) after the low- and 41% ($P < 0.001$) after the high-GI period.

PAI-1 activity

PAI-1 activity decreased substantially on the low-GI diet by 58% ($P < 0.01$), but remained unchanged on the high-GI diet. When comparing the two periods, the PAI-1 activity was 53% ($P < 0.001$) lower after the low-GI than after the high-GI diet. (Fig. 4).

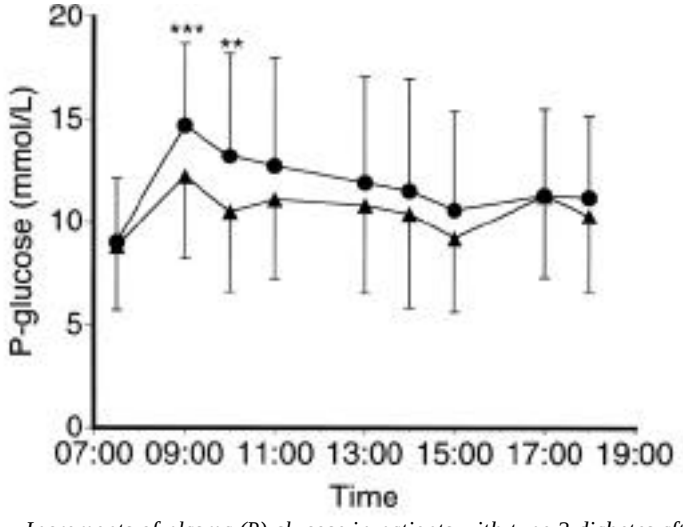

Figure 1—*Increments of plasma (P) glucose in patients with type 2 diabetes after the period of low-GI diet* (▲) *compared with that after the high-GI diet* (●). *Areas under the curve (area units) for the low- and the high-GI diet were 1,495 ± 671.8 and 2,124.8 ± 1,468.96, respectively. **P < 0.01, ***P < 0.001.*

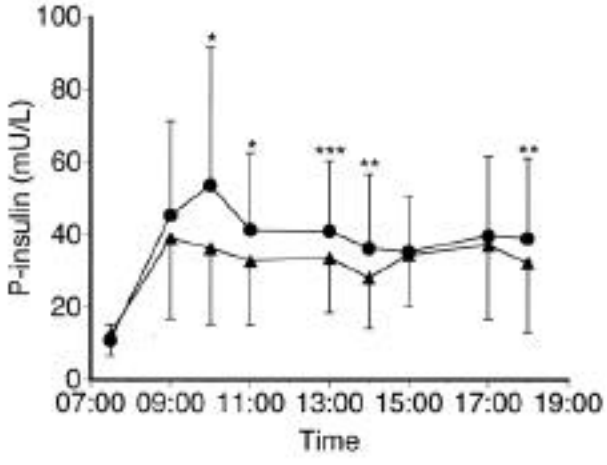

Figure 2—*Increments of plasma (P) insulin in patients with type 2 diabetes after the period of low-GI diet* (▲) *compared with that after the high-GI diet* (●). *Areas under the curve (area units) for the low- and the high-GI diet were 12,927 ± 6,729.2 and 17,724 ± 10,318.0, respectively. *P < 0.05, **P < 0.01, ***P < 0.001.*

CONCLUSIONS — Our study shows that a strictly controlled diet for people with diabetes, with a low GI for the major starchy foods, results in a considerably improved metabolic profile when compared with a corresponding high-GI diet. The glucose and insulin responses throughout the day were lower, the LDL cholesterol level was decreased, and the PAI-1 activity levels were normalized after the period with the low-GI diet. There was a dramatic reduction in plasma glucose, serum cholesterol, and LDL cholesterol, as well as an increase in insulin sensitivity, even after the diet period with the high GI. This is probably due to the fact that both diets were composed in accordance with the dietary recommendations (19–21), i.e., low in fat, modified in fat quality, and high in dietary fiber, which apparently differed from the habitual diet of the participants. The improvement in insulin sensitivity was more accentuated, however, on the low-GI diet (+30%) than on the high-GI diet (+21%). In this study, the average GIs of the low- and high-GI diets were 57 and 83 U, respectively. Compared with many controlled dietary studies using the GI concept, the GI of our low-GI diet was even further reduced (2,12,13,44).

In a meta-analysis of 11 medium- to long-term studies using the GI approach, Miller (45) concluded that the GI of the diabetic diet was, on average, lowered from 91 to 75 (white bread = 100). In one of the more successful studies, the GI value was reduced to 52, which is comparable with the value for our low-GI diet (15). It has been suggested that the GI of the diet in free-living subjects with type 2 diabetes is distributed with a mean of 85 ± 5 U (70–97.8) (46). This is comparable with the GI of the high-GI diet in the present study. The present study confirms and extends the results of some of the previous long-term studies evaluating the effects of a similar GI reduction (2,13,15,44). The difference in the area under the day-long curve for plasma glucose and plasma insulin corresponded very well with the predicted difference in mean GI, which was 26 U. The higher NEFA levels on the low, as compared with the high, GI diet 2 and 3 h after breakfast are probably secondary to a lower plasma insulin concentration, which, however, cannot explain the lower NEFA value on the low-GI diet after 5 h. Compared with the value on admission, serum lipoprotein lipid and apolipoprotein concentrations were substantially reduced on both diets. This study shows that a reduction of GI from a level comparable to that of a diabetic diet, according to the current recommendations of the American Diabetes Association (21), is associated with a significantly more pronounced reduction of LDL cholesterol and apoB. The extent of the total reduction of serum and LDL cholesterol compared with that on admission is comparable to that obtained by treatment with hydroxy-methyl-glutaryl (HMG)-CoA reductase inhibitors, such as simvastatin (47) and pravastatin (48), which lowered plasma cholesterol by 25 and 20% and LDL cholesterol by 35 and 26%, respectively, in recent trials.

This is the first time that lowering the dietary GI has been shown to improve the capacity for fibrinolysis. Earlier studies have demonstrated that dietary changes

Table 5—*Serum lipoprotein and serum apo concentrations at baseline and after 3 weeks on diets with low- and high-GI diets*

	Baseline	Low GI	% Change	High GI	% Change	*P*
Serum cholesterol (mmol/l)	5.79 ± 0.78	4.23 ± 0.73	−27*	4.46 ± 0.87	−23*	0.002
Serum triglycerides (mmol/l)	1.80 ± 1.00	1.25 ± 0.58	−30*	1.22 ± 0.57	−32*	0.877
HDL cholesterol (mmol/l)	1.06 ± 0.26	0.88 ± 0.28	−17†	0.87 ± 0.27	−19†	0.700
HDL triglycerides (mmol/l)	0.10 ± 0.05	0.09 ± 0.06	−10	0.07 ± 0.04	−35	0.086
VLDL cholesterol (mmol/l)	0.56 ± 0.48	0.37 ± 0.21	−34	0.41 ± 0.27	−27	0.494
VLDL triglycerides (mmol/l)	1.28 ± 0.98	0.94 ± 0.47	−27	0.99 ± 0.57	−23	0.117
LDL cholesterol (mmol/l)	4.03 ± 0.78	2.87 ± 0.70	−29*	3.13 ± 0.90	−22*	0.003
LDL triglycerides (mmol/l)	0.42 ± 0.10	0.33 ± 0.09	−20*	0.34 ± 0.09	−18†	0.573
LDL/HDL cholesterol	3.96 ± 1.15	3.66 ± 1.57	−8	3.84 ± 1.24	−3	0.121
ApoA-1 (mg/dl)	125.8 ± 16.24	99.3 ± 17.95	−21*	102.5 ± 15.56	−19*	0.036
ApoB (mg/dl)	104.3 ± 16.25	78.9 ± 15.61	−24*	84.3 ± 14.67	−19*	0.006
Apo(a) (U/l)	39.8 ± 296.2	307.0 ± 329.61	28*	304.2 ± 335.36	27*	0.222

Data are means ± SD. *P* includes values for differences between the low- and high-GI diets. Significant changes during the dietary periods when compared with baseline: *$P < 0.001$; †$P < 0.01$.

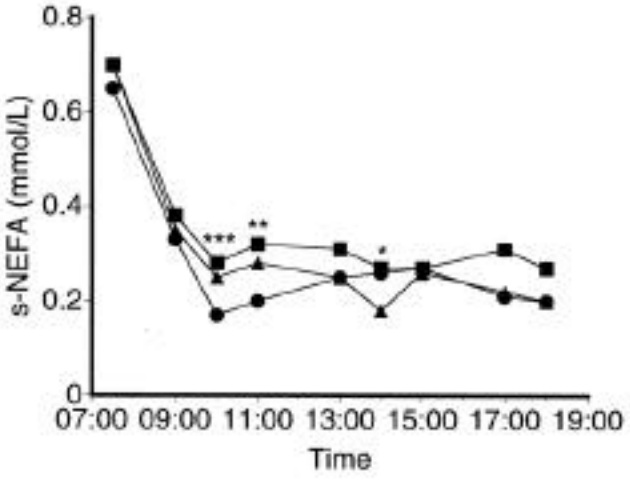

Figure 3—*Responses of serum (s) NEFAs after two diets with different food structures and GIs in patients with type 2 diabetes. This figure represents admission (■) compared with the low-GI diet (▲) and the high-GI diet (●). *P < 0.05, **P < 0.01, ***P < 0.001.*

such as a reduction of the fat intake and an increase in fiber intake may improve the fibrinolytic activity. Consequently, a longer period on a low-fat high-fiber diet markedly increased the plasma tissue-type plasminogen activator (tPA) (49,50). In an epidemiological study (51), a high intake of fruit and vegetables was associated with reduced PAI-1 levels. When the normal diet was enriched with dietary fiber, such as guar gum and oat husk, there was a decrease in the PAI-1 activity (52,53). According to Boman et al. (54), a low dietary fiber intake appears to be associated with high PAI-1 activity. It should be stressed that there were no differences in the amount and source of dietary fiber between the low and high-GI diets in the present study. In one study, a diet high in complex carbohydrate and dietary fiber and low in fat showed highly significant reductions in the levels of plasminogen, tPA, and PAI-1. However there was no information about the source of the carbohydrates (55). A positive association between the VLDL triglyceride concentration, plasma insulin level and PAI-1 activity has been suggested (56). In this study, there were no differences in the triglyceride concentrations at the end of the two dietary periods, while the incremental area under the curve for plasma insulin during a characteristic day on the low-GI diet was significantly lower. The results thus suggest that the reductions in PAI-1 activity may have been due to the reduced insulin levels rather than to decreased triglyceride levels.

The low and high-GI diets were basically made from the same ingredients. The high GIs of the carbohydrate-rich foodstuffs were mainly achieved by manipulating the structure of the starchy foods. The results emphasize the importance of food form (17,18). However, although the test diets were based on identical ingredients, the low-GI foods can be expected to contain somewhat larger amounts of resistant starch (57). Like dietary fiber, resistant starch will be fermented by the colonic microflora. The metabolic effects of the short-chain fatty acids formed remain to be established. However, in a study by Thorburn et al. (58), increased colonic fermentation was associated with improved glucose tolerance.

In our study, there was a certain reduction in body weight after both dietary periods. It was almost impossible to adjust the energy levels to ensure total weight stability, presumably because of the large volume of the diets and their effect on satiety. The participants could not eat any more, and they stated that they had never eaten so much before without gaining weight. This demonstrates that the diet usually eaten by many diabetic patients probably is relatively energy dense, with more dietary fat, and low in dietary fiber.

When it comes to the practical application of the GI concept in the management of diabetes, it is important to look at the diet as a whole. The GI is useful only when comparing different foodstuffs within the same food group and should not be used as an isolated concept. As judged from the present study, advice concerning fat content and fat quality should be complemented by advice regarding the carbohydrate quality, in order to prevent cardiovascular disease. To make the choice easier for the patients, this advice should focus on food items and their effects. People with diabetes should thus be encouraged to eat traditional foods with low GIs, such as pasta, parboiled rice, whole grain breads, and different kinds of beans. Today the choice of low-GI foods is limited, especially when it comes to breakfast products such as bread and cereal products. There is therefore a need for development of new foods with a low GI. The food industry has the ability as well as the responsibility to modify the GI of different products and to create low-GI foods.

The present data indicate that the GI is a useful concept in the management of diabetes. In addition to improving glucose homeostasis, a low-GI diet seems to improve lipid metabolism, and is therefore also useful in the management of hyperlipidemia. In addition, this study has also

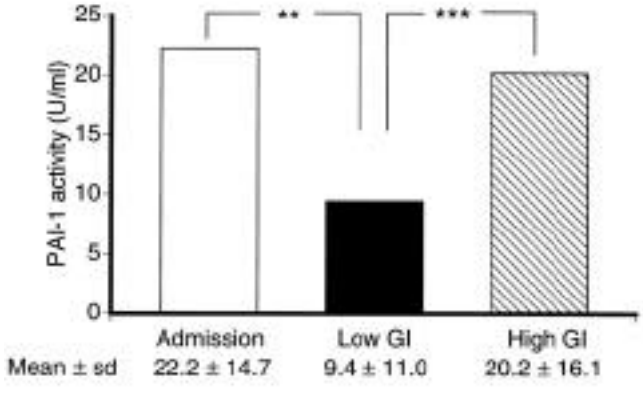

Figure 4—*Comparison of the effects on the activity of PAI-1 of two diets with different food structures and GIs in patients with type 2 diabetes. PAI-1 activity values on admission and after the low- and high-GI diets were 22.2 ± 14.7, 9.4 ± 11.0, and 20.2 ± 16.1, respectively. **P < 0.01, ***P < 0.001.*

shown that a diet with a low GI improves the capacity for fibrinolysis. A low-GI diet thus has several advantages in the treatment of insulin resistance syndrome.

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