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Effects of *ispaghula husk* and guar gum on postprandial glucose and insulin concentrations in healthy subjects

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Objective: The aim of this study was to evaluate, under the same experimental conditions and in the same subjects, the effects of *ispaghula husk* and guar gum on postprandial glucose and insulin concentrations in healthy female subjects.
Design: An oral glucose load with and without fiber was administered in the morning after an overnight fast. The study of the fiber effect was planned according to a randomized and cross-over design.
Setting: The study was performed at the Department of Pharmacology, Toxicology and Nursing at the University of León (Spain).
Subjects: Ten healthy female volunteers aged 30–48 y with normal body mass indices participated in this study.
Results: A significant decrease in mean serum insulin concentrations was observed from 30 to 90 min in the presence of both fibers. The area under the insulin curve was significantly reduced by 36.1% for *ispaghula husk* and 39.4% for guar gum. The area under the glucose curve was reduced by 11.1% (significant difference) for *ispaghula husk* and 2.6% for guar gum (no significant difference).
Conclusions: According to the results obtained in this study, the administration of *ispaghula husk* may be beneficial due to its ability to reduce glucose postprandial concentration and especially insulin requirements. Individualization of the treatment would be advisable due to large individual variations observed in glycemic and insulinemic postprandial responses.
Descriptors: dietary fiber; *ispaghula husk*; guar gum; glucose; insulin; healthy female volunteers
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Introduction

In the 1970s, Burkitt and Trowell (1975) proposed the dietary fiber hypothesis, linking low fiber intake to high incidence of diabetes, colon cancer, coronary heart disease, obesity, hypertension, and certain other western diseases.

Jenkins *et al* (1976) and Kiehm *et al* (1976) reported that dietary fiber intake benefits diabetic individuals. After these initial studies, several authors have shown that the addition of specific types of non-digestible plant fiber improves glucose tolerance in healthy volunteers and in insulin-treated and non-insulin treated diabetic patients (Jenkins *et al*, 1978; Anderson *et al*, 1987).

Water-soluble plant polysaccharide fibers, such as guar gum, which are capable of forming viscous gels, appear to be more effective in improving glycemic control than water-insoluble fibers, such as cellulose and cereal fibers (Jenkins *et al*, 1978; Vinik & Jenkins, 1988). The underlying mechanisms whereby dietary fiber improves glucose homeostasis are unclear, but may include delaying gastric emptying, slowing the rate of intestinal absorption of glucose, or altering hormone secretion and/or sensitivity to a carbohydrate load (Jenkins *et al*, 1976,1978; Holt *et al*, 1979; Jenkins & Jenkins, 1985; Edwards *et al*, 1988; Weinstock & Levine, 1988).

The studies published during the two last decades regarding the efficiency of viscous fibers to lower glucose and insulin concentrations are very numerous. Among them, the most frequent are those carried out with guar gum, a fiber with a demonstrated hypoglycemic effect. The results obtained, however, are contradictory (Blackburn *et al*, 1984; Riccardi & Rivellese, 1991). In several of these

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studies examining the acute effect of dietary fiber on glucose tolerance in healthy volunteers and/or diabetic patients, lowering of blood glucose concentrations was accompanied by decreased insulin concentrations (Jenkins *et al*, 1976,1977,1978,1982; Morgan *et al*, 1979; Sandhu *et al*, 1987; Trinick *et al*, 1986; Ebeling *et al*, 1988; Pastors *et al*, 1991; Chuang *et al*, 1992; Fairchild *et al*, 1996; Gatenby *et al*, 1996; Anderson *et al*, 1999). Sometimes fiber ingestion modestly improves glycaemic control (Carroll *et al*, 1981; Lim *et al*, 1990) or, although glucose tolerance is better, insulin response remains unchanged (Groop *et al*, 1993). In other studies the improvement of blood glucose, or decreased insulin requirements, in diabetic patients (Rivellese *et al*, 1980; Jones *et al*, 1985; Holman *et al*, 1987; Thomas *et al*, 1988; Sels *et al*, 1992; Groop *et al*, 1993) and enhanced glucose tolerance in healthy subjects could not be reproduced (Groop *et al*, 1986; Behall, 1990; Sels *et al*, 1992). These apparent discrepancies can be due to differences in dietary fiber sources or in the composition of the diets employed, as well as to the interindividual variability in response (Chuang *et al*, 1992).

Ispaghula husk is a viscous water-soluble fiber obtained from *Plantago ovata*, that has long been used as a bulk laxative with a good safety record. In the bibliographic review carried out, we have found seven studies regarding its ability to control glycemia and insulinemia. One of them was conducted in type 1 diabetic patients (Florholmen *et al*, 1982) and four in type 2 diabetic patients (Sartor *et al*, 1981; Pastors *et al*, 1991; Wolever *et al*, 1991; Anderson *et al*, 1999). Two more studies were performed in both healthy and type 2 diabetic volunteers (Fagerberg, 1982; Jarjis *et al*, 1984). The results obtained in these studies are controversial. In this way, Jarjis *et al* (1984) did not found any modification in postprandial glucose and insulin concentrations, neither in healthy subjects nor in type 2 diabetic patients. Sartor *et al* (1981) only evaluated glucose concentrations in type 2 diabetic patients after the administration of a test breakfast with and without fiber, and they found a significant decrease between 30 and 60 min in the presence of fiber. Similar results were encountered by Florholmen *et al* (1982) in type 1 diabetic patients. Fagerberg (1982) reported that psyllium reduced fasting serum glucose concentration in type 2 diabetic patients. Pastors *et al* (1991) indicate that the use of psyllium reduces postprandial glucose and insulin elevations in type 2 diabetic patients and that this fiber can produce a significant reduction in glucose after a second meal. However, Anderson *et al* (1999) found a decrease in glucose concentrations but not in insulin levels and in other study (Wolever *et al*, 1991) psyllium only reduced the glycemic response when the fiber was incorporated into or sprinkled onto a flaked bran cereal test meal.

The aim of the present study is to examine the effect, under the same conditions and in the same subjects, of *ispaghula husk* (Plantaben®), and of guar gum (Plantaguar®), on glucose tolerance and postprandial insulin concentrations in healthy female volunteers.

Methods

We have established the following criteria when we planned this study: the use of *ispaghula husk* and guar gum commercial formulations without saccharose or any other absorbable carbohydrate (Plantaben® and Plantaguar®, respectively); the administration of a psyllium dose equivalent to the maximum recommended daily (10.5 g); the administration of the same dose for guar gum so that their effects could be compared; the administration of a 50 g glucose load in aqueous solution as carbohydrate source, the most easily absorbable form; fiber was incorporated into the oral glucose load by stirring slightly with a teaspoon, as any patient would routinely prepare this treatment; the maintenance of identical environmental conditions, schedule and time were for all subjects; each subject serving as her own control.

Ten healthy female volunteers aged 30–48 y (mean 42.1 ± 5.5 y) participated in this study. They had no history of major illnesses or medication, including antimicrobial drugs, for 1 month before the beginning of the study. Written informed consent was obtained from each subject. The study protocol was approved by the Human Ethical Committee of the University and INSALUD (National Institute of Health) of León, Spain, and performed in accordance with the principles of the Helsinki Declaration.

A randomized and cross-over design was used for fiber administration. Each subject was randomly assigned to two different fibers. The study was repeated with the other fiber after an interval of at least 1 week. The randomization list was prepared using a simple random table.

On the first assay, and after an overnight fast, the subjects took 50 g glucose dissolved in 125 ml of water (Gluconaranja®), followed by 150 ml of water added to the same glass where glucose drinks had been served. On the second and third days of assays, the subjects ingested identical glucose-containing drinks supplemented with 10.5 g of the corresponding fiber (Plantaben® or Plantaguar®, Madaus, S.A., Barcelona, España).

Venous blood samples were taken from the forearm through a catheter placed in the radial vein. Blood samples were collected at 0 and 10, 20, 30, 45, 60, 75, 90 and 120 min after glucose intake for estimation of blood glucose and at 0, 30, 60, 90, and 120 min for assay of blood insulin concentrations. Glucose was measured with the Schmidt method (Schmidt, 1961) by using an autoanalyzer (Hitachi, model 704, Tokyo, Japan). Insulin concentrations were determined with an immunoradiometric assay (IRMA assay kit, Biosource Europe, S.A., Nivelles, Belgium). Arithmetic means, SDs and CVs were calculated from results measured. Areas under the concentration curves (AUC) were calculated by trapezoidal rule for blood glucose and insulin concentrations from time zero to the last determined sample time.

Statistical evaluations

The data obtained from the three treatments (without fiber and with both fibers) were compared for statistical significance by Friedman's test (treatment and subjects), at $P < 0.05$, and when the results were significant, Wilcoxon pairwise comparisons (control *vs* ispaghula husk and control *vs* guar gum) with Bonferroni correction were used. All analyses were performed by using the Statgraphics Plus for Windows 2.0 (Manugistic, Inc, Rockville, MA).

Results

Serum glucose

The rate and extent of glucose absorption decrease in the presence of both fibers when mean values are considered (Figure 1). The fiber curve shapes were similar and mean glycemic values after *ispaghula husk* were lower than after guar gum (Table 1, Figure 1). The glycemic index was 88.9 ± 11.7 and 97.5 ± 9.5% for *ispaghula husk* and guar gum, respectively.

Significant differences at 20 and 30 min were established among subjects as well as between treatments (Friedman's test, $P < 0.05$), although Wilcoxon test revealed no significant differences between fibers and fiber-free glucose load (Table 1). Finally, increased glycemic values were detected to 120 min with both fibers because two hypoglycemic episodes were present when glucose was administered alone (significant difference for guar gum *vs* glucose solution alone, Wilcoxon's test).

The decrease in area under the glucose curve (AUC) was 11.1% for *ispaghula husk* (significant difference, Wilcoxon's test) and 2.6% for guar gum, compared with the fiber-free treatment (Table 2). When accumulated areas (AUC_t, where t is the time until AUC has been calculated) were considered, significant differences were also found at 90 min between the glucose and *ispaghula husk* groups (Wilcoxon's test).

As large interindividual variations were seen in glucose concentrations, with CV ranging from 7.9 to 44.2% (Table 1), in our opinion, the employment of individual curves (Figure 2) is indicated in addition to mean curves (Figure 1).

The individual responses to glucose load were normal in seven subjects (maximum serum concentration, C_{max}, below 9.99 mmol/l), although three of them showed hypoglycemia when glucose load was administered alone, at 75 min (volunteer 7) and at 120 min (volunteers 4 and 6). In the other three individuals, C_{max} was higher than 9.99 mmol/l (volunteers 8 and 9) and close to this value at 90 min (volunteer 10). These three volunteers had diabetic familiar history. It is interesting to point out that, in the presence of both fibers, curve shapes were normalized

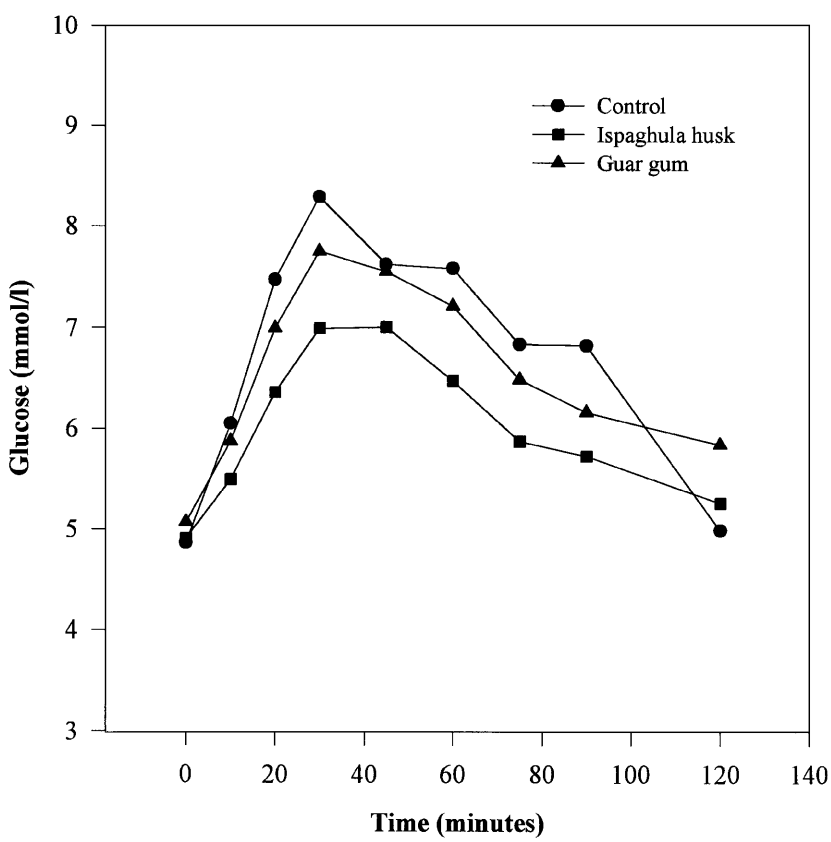

Figure 1 Mean serum glucose concentrations in 10 healthy subjects after a 50 g oral glucose load with or without fiber.

Table 1 Serum glucose concentrations (mmol/1) after a 50 g oral glucose load

	Without fiber (control)		*With* ispaghula husk		*With guar gum*	
Time (min)	$\bar{x} \pm s.d.$	*CV (%)*	$\bar{x} \pm s.d.$	*CV (%)*	$\bar{x} \pm s.d.$	*CV (%)*
0[b]	4.87 ± 0.38	7.88	4.91 ± 0.64	13.02	5.07 ± 0.67	13.11
10[b]	6.06 ± 1.08	17.90	5.50 ± 0.91	16.58	5.88 ± 1.20	20.35
20[a,b]	7.48 ± 1.37	18.35	6.37 ± 1.53	24.09	7.00 ± 1.62	23.21
30[a,b]	8.30 ± 2.02	24.32	7.00 ± 2.13	30.47	7.76 ± 1.89	24.37
45[b]	7.63 ± 2.29	29.98	7.01 ± 2.37	33.80	7.56 ± 2.25	29.77
60[b]	7.59 ± 2.76	36.38	6.48 ± 2.71	41.83	7.22 ± 2.54	35.11
75[b]	6.84 ± 2.89	42.22	5.88 ± 2.60	44.18	6.49 ± 2.31	35.58
90[b]	6.83 ± 2.76	40.35	5.73 ± 2.09	36.43	6.17 ± 2.30	37.33
120[a]	5.00 ± 1.42	28.37	5.27 ± 1.37	25.95	5.85 ± 1.59[c]	27.26

[a]Significant differences among treatments (Friedman's test, $P < 0.05$).
[b]Significant differences among subjects (Friedman's test, $P < 0.05$).
[c]Significant differences with control group (Wilcoxon modified test, for conditions see text).

Table 2 AUC values for glucose and insulin obtained after a 50 g oral glucose load

	AUC glucose (mmol/l/min)			*AUC insulin (pmol/l/min)*		
Volunteer	*Without fiber (control)*	Ispaghula husk	*Guar gum*	*Without fiber (control)*	Ispaghula husk	*Guar gum*
1	750.2	672.9	737.9	48 614.6	33 630.2	31 930.0
2	627.9	623.1	696.7	45 000.6	32 402.6	29 373.9
3	820.2	545.4	756.2	38 571.6	24 433.5	28 008.8
4	775.8	765.1	777.6	39 866.9	24 437.8	21 835.5
5	900.6	624.9	678.7	49 157.0	35 152.0	28 158.1
6	601.2	571.9	604.9	35 270.2	23 885.8	20 996.7
7	602.2	576.2	623.1	54 032.9	24 779.0	26 495.6
8	1354.9	1312.0	1391.0	75 480.7	47 492.3	43 067.4
9	972.1	877.0	899.4	108 323.6	49 887.3	53 914.8
10	825.0	723.7	801.8	39 843.3	31 704.5	29 698.2
Mean ± s.d.	823.0 ± 224.8[a,b]	729.2 ± 228.5[c]	796.7 ± 226.1	53 416.1 ± 22 438.9[a,b]	32 781.5 ± 9422.1[c]	31 347.9 ± 9978.2[c]

[a]Significant differences among treatments (Friedman's test, $P < 0.05$).
[b]Significant differences among subjects (Friedman's test, $P < 0.05$).
[c]Significant differences with control group (Wilcoxon modified test, for conditions see text).

in all subjects, volunteer 8 being the least affected (Figure 2).

When the AUC parameter is considered (Table 2), the highest decreases were 33.5% (volunteer 3) for *ispaghula husk* and 24.6% (volunteer 5) for guar gum. AUC values always fall for *ispaghula husk*, whereas for guar gum values are in some cases slightly higher than the corresponding glucose AUC, but in all cases both fibers caused the normalization of the curve (disappearance of hypoglycemic episodes, low responses etc).

Serum insulin
Decreases in mean serum insulin concentrations were observed from 30 to 120 min in the presence of both fibers (Table 3 and Figure 3), being significant from 30 up to 90 min between fibers and fiber-free glucose load (Wilcoxon's test), and among subjects (Friedman's test, $P < 0.05$). Insulinaemic index was 64.0 ± 10.9 and 60.6 ± 8.8% for *ispaghula husk* and guar gum, respectively.

Insulin AUC was reduced by 36.1% when *ispaghula husk* was administered, and 39.4% after guar gum. Differences in AUC were significant between both fibers and glucose alone (Wilcoxon's test, Table 2). Accumulated AUC were lower for both fibers than for glucose load without fiber from 30 up to 120 min. These differences were significant between guar gum – glucose and ispaghula husk – glucose groups, except for this last one at 30 min (Wilcoxon's test).

Ispaghula husk and guar gum effects on insulin liberation are very similar, but guar gum appears to be more effective. Large interindividual variations were also observed in insulin concentrations, with CV ranging from 24.0 to 83.7% (Table 3).

The individual insulinemic responses in all subjects were smaller in the presence of fibers (Figure 4) and curve profiles were similar, although guar gum reduces insulin concentrations more effectively than *Plantago ovata*. Mean and individual data provide similar arguments in this case.

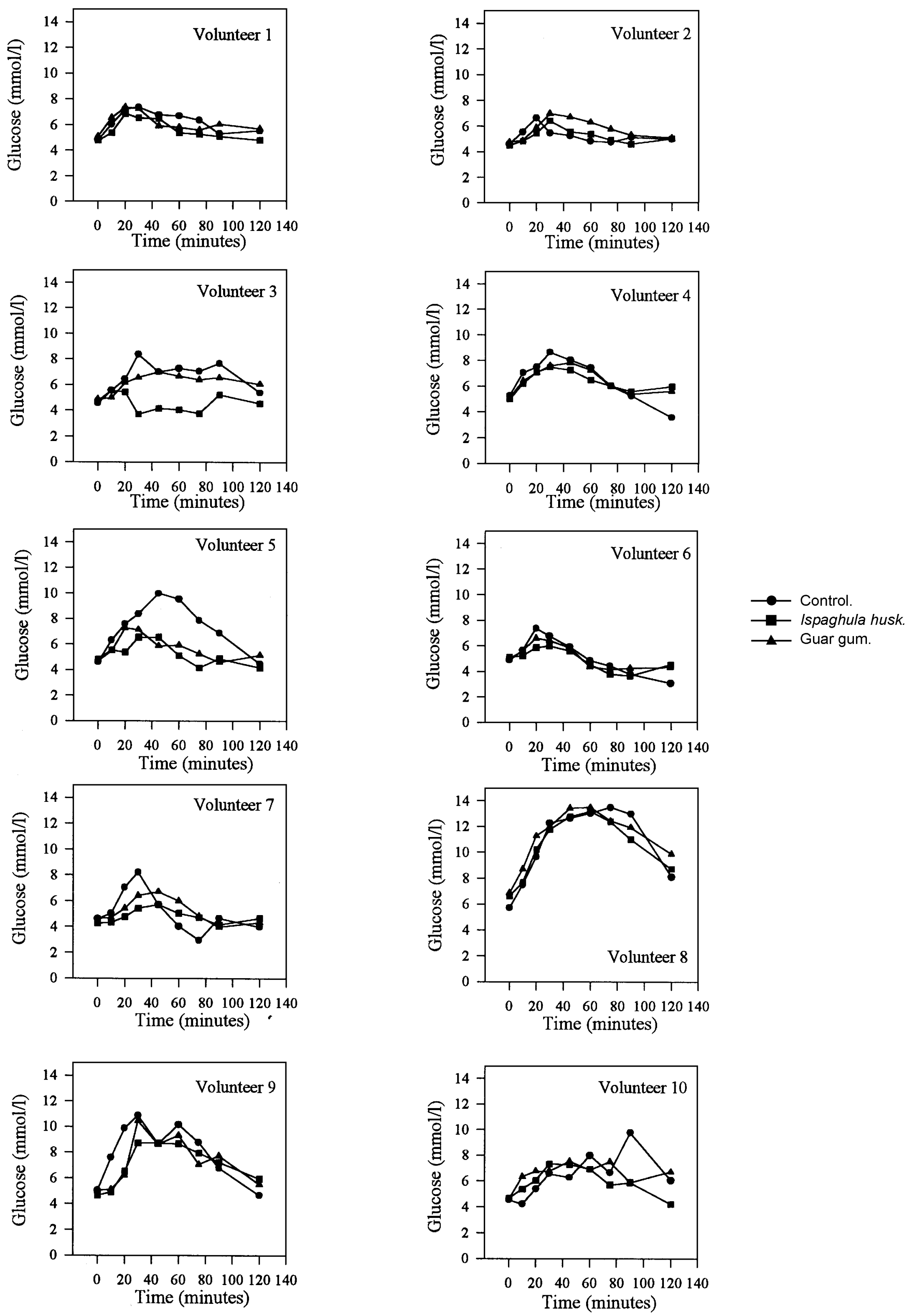

Figure 2 Individual serum glucose–time curves in 10 healthy subjects after a 50 g glucose load with or without fiber.

Table 3 Serum insulin concentrations (pmol/l) after a 50 g oral glucose load

	Without fiber (control)		*With* ispaghula husk		*With guar gum*	
Time (min)	$\bar{x} \pm s.d.$	*CV (%)*	$\bar{x} \pm s.d.$	*CV (%)*	$\bar{x} \pm s.d.$	*CV(%)*
0	68.43 ± 19.71	28.81	85.33 ± 21.10	24.72	75.25 ± 26.63	69.27
30[a,b]	469.77 ± 112.52	23.95	316.90 ± 122.29[c]	38.59	330.65 ± 82.92[c]	52.63
60[a,b]	585.26 ± 418.91	71.58	345.04 ± 165.55[c]	47.98	325.71 ± 146.23[c]	83.65
90[a,b]	555.97 ± 413.43	74.36	279.74 ± 112.35[c]	40.16	257.90 ± 145.20[c]	76.16
120	270.65 ± 153.86	56.85	216.73 ± 98.39	45.40	206.71 ± 127.21	46.54

[a]Significant differences among treatments (Friedman's test, $P < 0.05$).
[b]Significant differences among subjects (Friedman's test, $P < 0.05$).
[c]Significant differences with control group (Wilcoxon modified test, for conditions see text).

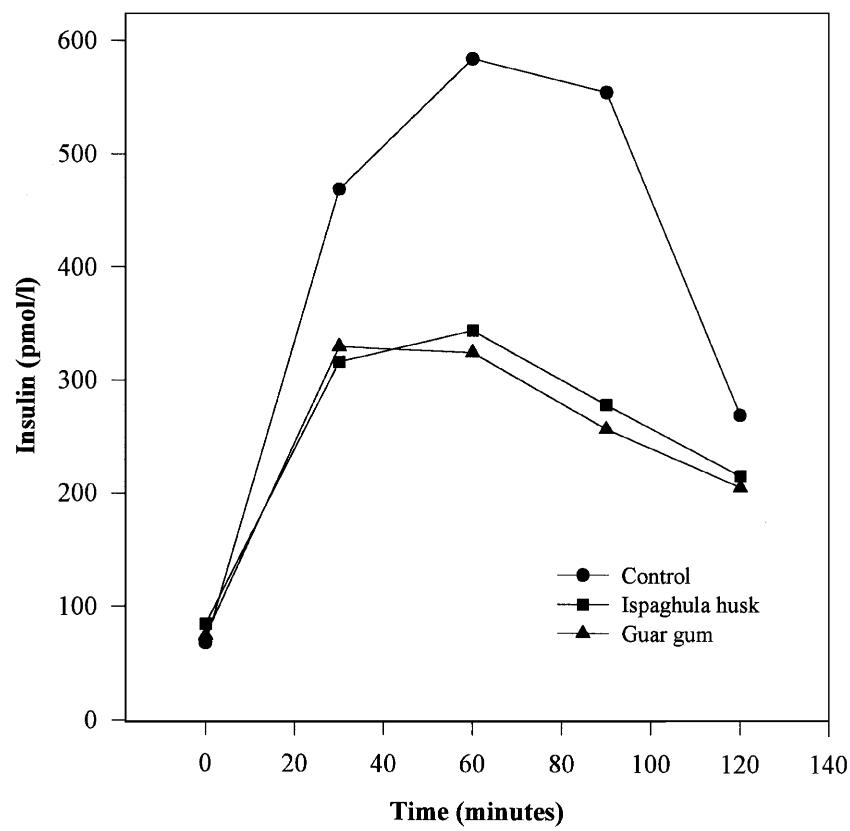

Figure 3 Mean serum insulin concentrations in 10 healthy subjects after a 50 g oral glucose load with or without fiber.

Discussion

Five previous studies have been carried out with two different preparations of *ispaghula husk* in insulin-dependent (Florholmen *et al*, 1982) and in non-insulin-dependent diabetic patients (Sartor *et al*, 1981; Anderson *et al*, 1999; Pastors *et al*, 1991) and in both healthy and non-insulin-dependent diabetic subjects (Jarjis *et al*, 1984). In the first four studies, postprandial glycemia was significantly reduced after a standardized breakfast with 3.6 g (Florholmen *et al*, 1982), 6.6 g (Sartor *et al*, 1981), 6.6 g (Anderson *et al*, 1999) and 5.1 g fiber (Pastors *et al*, 1991), respectively. In contrast, no significant differences were found after a 50 g glucose load administered with 3.5 or 7 g fiber (Jarjis *et al*, 1984). These differences could be at least partly attributed to carbohydrate sources (test meal or glucose solution) and the way that fiber was administered. It is recognized that both the composition and physicochemical properties of foods in a meal are important in regulating the glycemic response (Simpson *et al*, 1985; Jenkins *et al*, 1983).

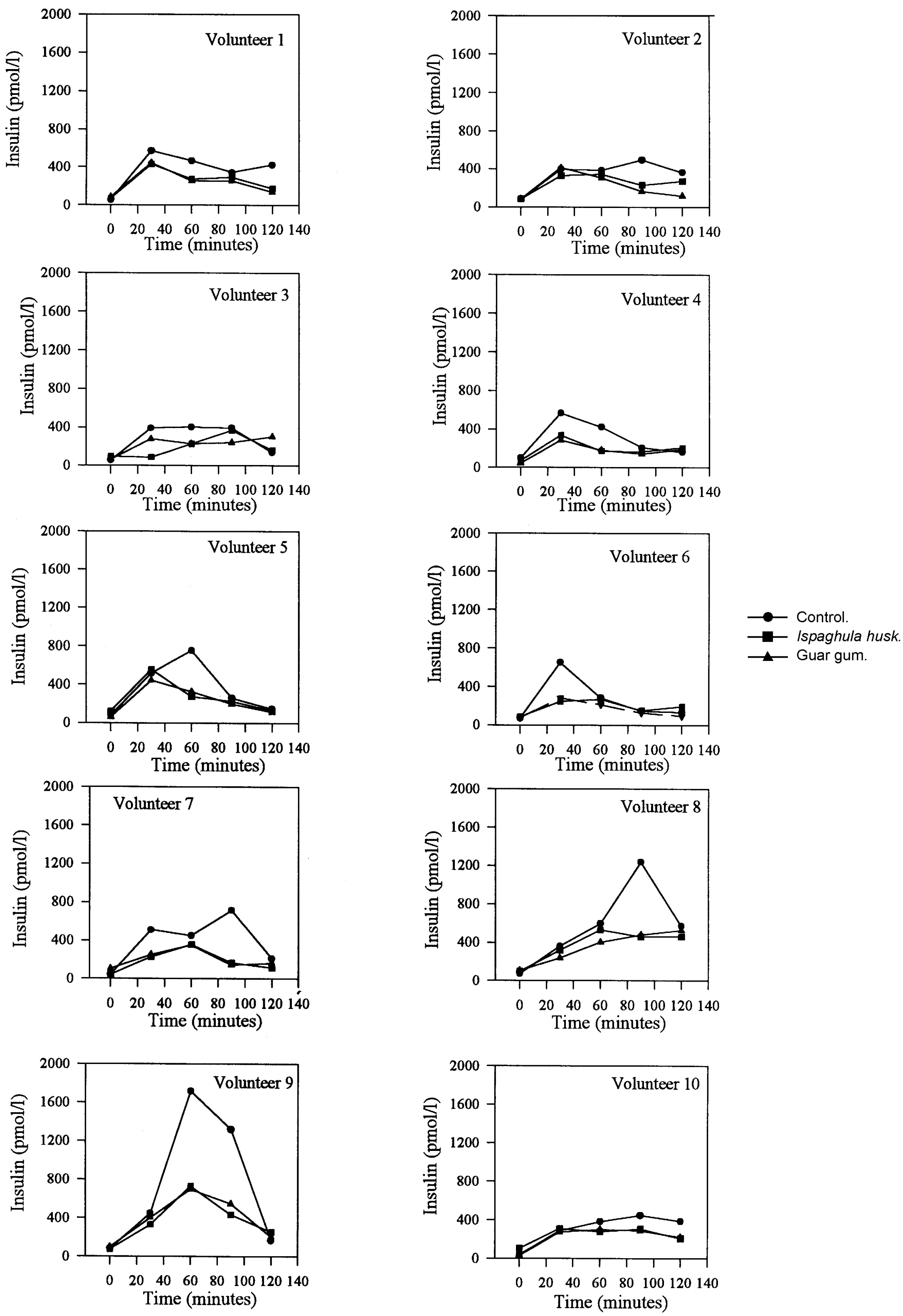

Figure 4 Individual serumm insulin–time curves in 10 healthy subjects after a 50 g glucose load with or without fiber.

Our results differ from those reported by Jarjis *et al*, (1984), because those authors did not find any significant effect of *ispaghula husk* (3.5 and 7 g) on glucose tolerance or insulin concentrations in normal volunteers after a 50 g glucose load. On the other hand, our results are partly consistent with those obtained by those authors for gum guar, although a lower dose (2.5 g) than ours (10.5 g) was used. In our opinion, the guidelines followed to mix fiber and glucose provide the explanation for these divergences: Jarjis *et al* (1984), prepared the glucose solution containing either *ispaghula husk* or gum guar by stirring vigorously at least 12 h before its administration to become fully hydrated.

Mixing fiber and glucose as they describe could be appropriate for gum guar but not for *ispaghula husk*. Vigorous stirring and allowing to stand overnight may affect its rheological properties. In this respect, Jenkins *et al* demonstrated in 1978 that delay in gastrointestinal transit time, including the component of gastric emptying rate, is related to the viscosity of fiber substances in the stomach. Guar gum improves glucose tolerance to a carbohydrate load, whereas this effect is abolished when hydrolyzed nonviscous guar is used. In contrast, Kasper *et al* (1985), did not find a delay in gastric transit time after the addition of pectin, guar or bran to a liquid test meal, despite a significant increase in viscosity. Other authors, like O'Connor *et al* (1981), have described the importance of viscosity in the efficacy of fiber formulations.

Brenelli *et al* (1997) indicate that temperature, the process of acidification, alkalinization and exposure to intestinal ions induce different viscosity changes in gums having similar initial viscosity, establishing a relationship between a minor decrease of gum viscosity *in vitro* and a reduction of postprandial hyperglycemia.

The results obtained in this study with guar gum are similar to those shown by Ellis *et al* in 1991 in healthy volunteers. These authors found that there were no effects of various wheat breads containing guar gum samples (with different molecular weight and particle size) on the post-prandial blood glucose responses, but they encountered significant decreases in the postprandial plasma insulin concentrations. Smith and Holm (1982) reported that guar gum decreased glucose concentrations in type 1 and 2 diabetic patients, but this effect did not appear in healthy subjects.

When we showed our results, we mentioned the large individual variations observed in glycemic and insulinemic postprandial responses. Judging from the results of the present study, individualization of the treatment would be needed for it to be more effective. Finally, and even when long-term studies in diabetic patients would be required, *ispaghula husk* seems to be a suitable candidate for the treatment of these patients in the pharmaceutical preparation used in this study.

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