# Plasma glucose and insulin responses after consumption of breakfasts with different sources of soluble fiber in type 2 diabetes patients: a randomized crossover clinical trial

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# ABSTRACT

**Background:** The amount and quality of carbohydrates are important determinants of plasma glucose after meals. Regarding fiber content, it is unclear whether the intake of soluble fibers from foods or supplements has an equally beneficial effect on lowering postprandial glucose. **Objective:** The aim of our study was to compare the acute effect of soluble fiber intake from foods or supplements after a common meal on postprandial plasma glucose and plasma insulin in patients with type 2 diabetes (T2D).

**Design:** A randomized crossover clinical trial was conducted in patients with T2D. Patients consumed isocaloric breakfasts (mean  $\pm$  SD: 369.8  $\pm$  9.4 kcal) with high amounts of fiber from diet food sources (total fiber: 9.7 g; soluble fiber: 5.4 g), high amounts of soluble fiber from guar gum supplement (total fiber: 9.1 g; soluble fiber: 5.4 g), and normal amounts of fiber (total fiber: 2.4 g; soluble fiber: 0.8 g). Primary outcomes were postprandial plasma glucose and insulin (0–180 min). Data were analyzed by repeated measures ANOVA and post hoc Bonferroni test.

**Results:** A total of 19 patients [aged 65.8  $\pm$  7.3 y; median (IQR), 10 (5–9) y of T2D duration; glycated hemoglobin 7.0%  $\pm$  0.8%; body mass index (in kg/m<sup>2</sup>) 28.2  $\pm$  2.9] completed 57 meal tests. After breakfast, the incremental area under the curve (iAUC) for plasma glucose [mg/dL  $\cdot$  min; mean (95% CI)] did not differ between high fiber from diet (HFD) [7861 (6257, 9465)] and high fiber from supplement (HFS) [7847 (5605, 10,090)] (P = 1.00) and both were lower than usual fiber (UF) [9527 (7549, 11,504)] (P = 0.014 and P = 0.037, respectively). iAUCs [ $\mu$ IU/mL  $\cdot$  min; mean (95% CI)] did not differ (P = 0.877): HFD [3781 (2513, 5050)], HFS [4006 (2711, 5302), and UF [4315 (3027, 5603)].

**Conclusions:** Higher fiber intake was associated with lower postprandial glucose at breakfast, and the intake of soluble fiber from food and supplement had a similar effect in patients with T2D. This trial was registered at clinicaltrials.gov as NCT02204384. *Am J Clin Nutr* 2017;106:1238–45.

**Keywords:** dietary fiber, plasma glucose, plasma insulin, postprandial period, soluble fiber, type 2 diabetes

# INTRODUCTION

An estimated 415 million adults worldwide are living with diabetes and it is expected that the population of patients with type 2 diabetes (T2D) will continue to grow (1). Dietary interventions are essential for blood glucose control and are strongly related to glycated hemoglobin (HbA1c) values (2). Postprandial glucose levels, depending on the degree of glycemic control, can contribute  $\leq$ 70% of HbA1c values in patients with diabetes (3, 4). Postprandial hyperglycemia has been suggested as a major risk factor for cardiovascular disease and mortality in patients with T2D (5). Postprandial glycemic response is particularly influenced by dietary carbohydrates, given both the amount and quality of carbohydrates consumed, and therefore, the fiber content (6) and glycemic index (7) of foods are important determinants of postprandial glucose responses.

The protective role of diets rich in fiber for all-cause mortality was demonstrated in patients with diabetes (8), and many studies have demonstrated the benefit of dietary or supplemented fiber consumption in glycemic control in patients with T2D (9–13). In a cross-sectional study we showed that the intake of  $\geq 5$  g of soluble fibers from food played a protective role against the metabolic syndrome in patients with T2D (12). We also demonstrated that adding a soluble fiber supplement (10 g/d) to the normal diet for 6 wk resulted in a decrease in HbA1c in patients with T2D (13). The beneficial acute effect of soluble fiber intake (psyllium,  $\beta$ -glucan, and guar) on postprandial plasma glucose response was observed in patients with diabetes (14–16) after the consumption of a high-fiber meal (17) or single beverages or foods (18, 19).

Although there is strong evidence regarding the benefits of high soluble fiber consumption in glucose control in patients with T2D, it is still unclear whether the effects of fiber intake from dietary sources and supplements are the same. It is known that the

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Address correspondence to CMdC (e-mail: claudiamcarv@gmail.com). Abbreviations used: HbA1c, glycated hemoglobin; HFD, high fiber from diet; HFS, high fiber from supplement; iAUC, incremental AUC; T2D, type 2 diabetes; UAE, urinary albumin excretion; UF, usual fiber.

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fibers have different characteristics, and even among the different types of soluble fiber sources from food it is possible to observe different beneficial effects on health (20, 21). A better understanding of the acute effect of soluble fiber intake on glycemic response may allow the adoption of more specific and practical dietary alternatives for patients with T2D. Our hypothesis is that a meal with a high content of soluble fiber from food determines glycemic and insulinemic responses similar to a meal with a high content of soluble fiber from supplement sources. As such, the aim of this study was to compare the acute effect of soluble fiber intake from foods or supplements after a common meal on postprandial plasma glucose and plasma insulin in patients with T2D.

## METHODS

#### Study design

This was a randomized, open-label, crossover clinical trial. Patients were randomly assigned to 3 different test meals by an online computer-generated sequence (22). The outcomes of the study were postprandial responses of plasma glucose and plasma insulin.

The study was carried out between September 2014 and December 2015 and was conducted in accordance with the guidelines established in the 1975 Declaration of Helsinki (23). The Hospital Ethics Committee of the Hospital de Clínicas de Porto Alegre (Porto Alegre, Brazil) approved the protocol, and all of the patients gave written informed consent. This clinical trial was registered at clinicaltrials.gov as NCT02204384.

#### Study protocol

Selected patients were informed about the study, signed the consent form, and were randomly assigned to a sequence of test meals. Baseline laboratory, clinical, and nutrition evaluations were performed. Patients received instructions for each morning test meal: 12-h evening fasting, avoiding physical exercise on the day before the experiments, abstaining from heavy meals and alcoholic beverages the night before the test, and abstaining from smoking. Patients also were instructed to maintain their usual medications, diet, and daily physical activities before tests and during washout periods.

Participants were assigned to each test meal in a random order on 3 different occasions separated by a 1-wk washout period. At the start of each test, 24-h recall from the previous day was facilitated by the research dietitian. Capillary blood glucose tests were performed with a glucometer before each breakfast test (Accu-Chek Active; Roche Diagnostics) (24). The capillary blood glucose was used only to rule out high glucose values at the beginning of test meals, and values >180 mg/dL precluded the initiation of the test on that day. Bioelectrical impedance analysis was performed and blood pressure was measured. Blood samples were then drawn via an indwelling cannula to obtain baseline measurements. After this, patients took their usual medications with 150 mL plain water and received the designed breakfast. They were instructed to consume the meal within 20 min and to remain seated during the test. Blood samples were collected at 0, 30, 60, 120, and 180 min after the meal, and plasma glucose and insulin were measured in all of the blood samples.

#### Patients

Consecutive outpatients with T2D at the Hospital de Clínicas de Porto Alegre Endocrine Division were selected based on the following inclusion criteria: HbA1c <9%, BMI (in kg/m<sup>2</sup>) <35, and no current insulin use. The exclusion criteria were the following: serum creatinine >2.0 mg/dL, digestive diseases (e.g., malabsorption), severe autonomic neuropathy (presence of symptomatic postural hypotension, gastroparesis, and diabetic diarrhea), recent cardiovascular event, cachexia, psychiatric disorder with comprehension impairment, and participation in other research protocols.

## **Clinical evaluation**

T2D was defined as a diagnosis of diabetes after age 35 y with no use of insulin during the first year after diagnosis (25). The diagnosis of T2D was always confirmed by the attending physician. Hypertension was defined as blood pressure >140/90 mm Hg measured on 2 occasions with a digital sphygmomanometer (HEM-705 CP; Omron Health Care Inc.) or the use of antihypertensive drugs (25). Urinary albumin excretion (UAE) was classified as normal (<14 mg/L) or elevated  $(\geq 14 \text{ mg/L})$  according to a random spot urine sample (26, 27). The elevated UAE was confirmed  $\geq 2$  times (25, 28). Cardiovascular evaluation was performed by resting electrocardiogram, and when indicated, exercise electrocardiogram, stress myocardial scintigraphy, or both were performed. The following cardiovascular events were considered: acute myocardial infarction, stroke, myocardial revascularization, or coronary angioplasty. Diabetic retinopathy was assessed by fundus examination by dilating the pupils. Peripheral neuropathy was assessed by monofilament testing in both feet. Physical activity was graded at 4 levels based on a standardized questionnaire (29) that was adapted to local habits (30). A sedentary lifestyle was considered if the patient's answer was "I read, watch television, and work in the household at tasks that don't strain me physically," corresponding to the first level of physical activity. Peripheral vascular disease was assessed by asking about the presence of intermittent claudication by use of the Rose Questionnaire (31) and palpation of peripheral pulses (posterior tibial and dorsalis pedis). Patients were classified as current smokers or nonsmokers.

# Nutritional evaluation

Body weight (patient wearing lightweight clothing without shoes) and height were measured so that the BMI could be calculated. Waist circumference was measured midway between the lowest rib margin and the iliac crest, with a nonstretch steel measuring tape (Sanny TR4010; American Medical do Brasil) (32). Body composition was assessed before each meal test in the fasted state by bioelectrical impedance analysis (InBody230; Biospace Co.).

The normal diet was evaluated by 24-h recall (USDA Automated Multiple-Pass Method) (33), and diet composition was analyzed by use of Nutribase 11 Professional Edition software version 11.22 (CyberSoft Inc.) based on the USDA National Nutrient Database for Standard Reference (34). Fiber content from both the 24-h recall and the test meals was estimated by use of the dietary fiber values for common foods table from the *CRC Handbook of Dietary Fiber in Human Nutrition* (35). The glycemic index was estimated as proposed by the FAO (36) by use of the International Tables of Glycemic Index and Glycemic Load Values, with glucose as the standard food (37).

#### Meal test composition

**Table 1** shows the nutritional composition of meal tests. The 3 breakfasts were isocaloric and had a similar distribution of carbohydrates, proteins, and lipids. Meal tests were defined as follows: a high amount of soluble fiber from dietary food sources [high fiber from diet (HFD)], a high amount of soluble fiber from supplement [high fiber from supplement (HFS)], and a meal with the usual amounts of fiber. HFD and HFS meals had similar amounts of total and soluble fibers and usual fiber (UF) had a lower amount of fiber than HFD and HFS. The supplement (sachet 5 g Fiber Mais; Nestlé Brasil) was added through use of the calculated amount in 150 mL water. It comprised 60% partially hydrolyzed guar gum and 40% inulin powder; was white in color, tasteless, and odorless; and it did not modify the appearance and texture of foods.

Breakfasts were prepared by the research dietitian (CMdC) in the kitchen of the hospital clinical research center on the day of each test meal. Frequently consumed foods were used to prepare the meals. The composition of meals was determined based on data regarding the nutritional composition of breakfast eaten commonly by 175 patients with T2D who attended the outpatient clinic of the Endocrine Division in the Hospital de Clínicas de Porto Alegre. The total fiber content of the usual breakfast of these patients ranged from 1.9 to 3.1 g (38). The same commercially available food brands were used for all of the meal tests.

#### Laboratory measurements

Measurements were taken at the clinical pathology laboratory of the Hospital de Clínicas de Porto Alegre. Plasma glucose was collected in tubes containing sodium fluoride and EDTA, with a total volume of 4 mL, and was measured by the enzymatic hexokinase method (Cobas 8000; Roche Diagnostics). Plasma insulin was collected in tubes with silica particles, which activate blood clotting, and separator gel, with a total volume of 5 mL. Plasma insulin was measured with the chemiluminescence method (Architect Plus ci4100; Abbott). Blood samples were allowed to clot at room temperature for 30 min and were then centrifuged (3100  $\times$  g for 10 min). After isolation, the samples were brought to the laboratory. At the beginning of the study, basal biochemical measurements were performed: HbA1c was measured by an automated precision chromatography technique (Variant II Hemoglobin Testing System, Bio-Rad Laboratories), UAE by immunoturbidimetry, serum creatinine by Jaffé's reaction, glutamic oxaloacetic transaminase and glutamic pyruvic transaminase by the ultraviolet

TABLE 1	
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Dietary characteristics of breakfast tests: composition and individual foods<sup>1</sup>

	Meals			
	HFD	HFS	UF	
Macronutrients and fiber	r			
Total energy, kcal	379.9	361.3	368.3	
Protein, g	15.4	15.6	15.8	
en%	15.4	16.6	16.8	
Fat, g	12.4	12.8	12.9	
en%	27.9	30.7	30.8	
Carbohydrate, g	56.7	50.0	49.6	
en%	56.7	52.7	52.4	
Fiber, g				
Total	9.7	9.1	2.4	
Soluble	5.4	$5.4^{2}$	0.8	
Insoluble	4.3	3.7	1.6	
Glycemic index	44.2	44.9	59.5	
Glycemic load	20.0	18.7	25.8	
Foods consumed				
	Papaya, 180 g	Pear, 50 g	Pear, 50 g	
	Orange, 150 g	Cream cracker, 5 g	Cream cracker, 5 g	
	Semi-skim milk, 150 mL	Semi-skim milk, 200 mL	Semi-skim milk, 200 mL	
	Rye bread, 25 g	Rye bread, 50 g	White bread, 50 g	
	Margarine, 10 g	Margarine, 5 g	Margarine, 5 g	
	Lean ham, 15 g	_	_	
	Mozzarella cheese, 15 g	Mozzarella cheese, 15 g	Mozzarella cheese, 15 g	
	Instant coffee, 5 g	Instant coffee, 5 g	Instant coffee, 5 g	
	Plain water, 150 mL	Plain water, 150 mL	Plain water, 150 mL	
	_	Fiber supplement, 5 g	_	

<sup>1</sup> en%, percentage from energy; HFD, high fiber from diet; HFS, high fiber from supplement; UF, usual fiber.

<sup>2</sup>Including 4.3 g soluble fiber from each sachet (5 g).

(Cobas 8000). Total HDL cholesterol and triglycerides were measured by the enzymatic colorimetric method (Cobas 8000), and LDL cholesterol was estimated by use of Friedewald's formula (39). The Chronic Kidney Disease Epidemiology Collaboration equation was used to estimate the glomerular filtration rate (40).

#### Statistical analyses

# Sample size

A sample size of 19 patients (90% power,  $\alpha$ : 0.025, considering 10% losses) was estimated based on a noninferiority hypothesis of glycemic response of HFD and HFS meal tests. This estimate was based on a glucose difference of 5 mmol/L  $\cdot$  min (or 90 mg/dL  $\cdot$  min) (41). In addition, a sample size of 14 patients (90% power,  $\alpha$ : 0.05, considering 10% losses) was estimated based on the assumption that both HFD and HFS meals have a lower postprandial glycemic response (41 mmol/L  $\cdot$  min or 738 mg/dL  $\cdot$  min) than the UF meal (42). The sample size with the greater number of participants was used and was

calculated with the use of WINPEPI (PEPI-for-Windows) version 11.61 software.

# Data analysis

Incremental AUCs (iAUCs) for plasma glucose and plasma insulin were calculated with the trapezoid rule, ignoring the area beneath the plasma fasting concentration (43). iAUCs and the absolute insulin and glucose values at each point (the effect of time and each different meal analyzed separately) were compared by repeated-measures ANOVA via a general linear model, and a categorical variable called "type of meal sequence" was included as a factor in all of the analyses. A post hoc Bonferroni test was used to identify the differences that were detected by ANOVA.

A per-protocol analysis was performed. Variables with nonnormal distribution (Shapiro-Wilk test) were log transformed before analysis (insulin data) and the corresponding results were described as absolute values. Data are presented as means  $\pm$  SDs, means  $\pm$  SEs (for figures), means (95% CIs), and median and IQR (25th–75th percentiles). Significance was defined as  $P \leq 0.05$ . SPSS Statistics software version 21.0 (IBM Corporation) was used for the statistical analyses.

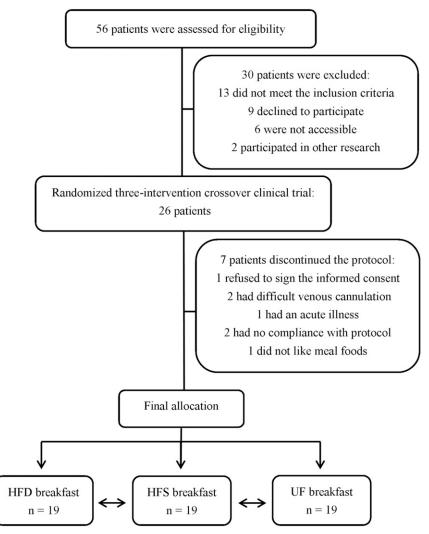


FIGURE 1 Flowchart of the study of 19 patients with type 2 diabetes. HFD, high fiber from diet; HFS, high fiber from supplement; UF, usual fiber.

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# RESULTS

A total of 19 patients with T2D completed the experimental protocol. **Figure 1** is a flowchart of patient inclusion. The baseline clinical, laboratory, and anthropometric characteristics of 19 participants are shown in **Table 2**. Regarding anti-hyperglycemic oral agents, 8 patients (42.1%) used metformin only, 7 patients (36.8%) used metformin plus glibenclamide, and 3 patients (15.8%) used metformin and glibenclamide plus 3 other antihyperglycemic oral agents: linagliptin (n = 1), dapa-gliflozin (n = 1), or empagliflozin (n = 1). Diet was the only diabetes treatment in 1 patient. Most patients received antihypertensive (n = 16; 84.2%) and lipid-lowering drugs (n = 16; 84.2%).

All of the test meals were consumed fully within 11.9  $\pm$  3.1 min. Two patients (10.5%) reported changes in their usual bowel function (i.e., need to evacuate) after the consumption of an HFD meal. The participants' pretest fasting plasma glucose and plasma insulin, BMI, weight, and the previous day's dietary intake were not different between meal tests (**Table 3**).

One meal test was repeated in 3 patients because the blood sample hemolysis precluded insulin measurements and the original test meal randomization was not maintained. There was no interaction between the "type of meal sequence" and iAUCs.

iAUCs for plasma glucose (mg/dL  $\cdot$  min) of 3 consumed test meals were compared (ANOVA; P = 0.023): iAUCs of HFD (mean: 7861, 95% CI: 6257, 9465) and HFS (mean: 7847, 95% CI: 5605, 10,090) were lower than the iAUCs of UF meals (mean: 9527, 95% CI: 7549, 11,504) (P = 0.014 and P = 0.037, respectively); the iAUCs of HFD and HFS meals did not differ (P = 1.00) (**Figure 2**A). No substantial group  $\times$  time interaction was observed (Figure 2A).

No differences were demonstrated between insulin iAUCs ( $\mu$ IU/mL · min) of tested breakfasts (ANOVA; *P* = 0.877): HFD (mean: 3781, 95% CI: 2513, 5050), HFS (mean: 4006, 95% CI: 2711, 5302), and UF (mean: 4315, 95% CI: 3027, 5603) (Figure 2B). No substantial group × time interaction was observed (Figure 2B).

We performed the same postprandial comparisons for glucose and insulin iAUCs, including an antihyperglycemic agent, isolated or combined, as a categorical variable. There was no interaction between the type of antihyperglycemic medication and iAUCs for each evaluated test meal, and the results did not change for both glucose and insulin responses (data not shown).

## DISCUSSION

The present study demonstrated that in patients with T2D, the consumption of breakfast with a high amount of soluble fiber from foods or supplements had the same effect on postprandial glycemic response. Furthermore, the postprandial plasma glucose response was smaller with HFDs than with the breakfast containing UF. We observed an 18% difference in plasma glucose iAUCs between the breakfasts that were rich in fiber, irrespective of the source, compared to the one with UF. In fact, a difference >16% between postprandial glucose iAUCs was considered clinically relevant (43). Postprandial insulin increased after all of the meal tests, but there was no difference between their iAUCs.

To the best of our knowledge, no previous study in patients with T2D has been designed to compare the acute glycemic and

# TABLE 2

Baseline characteristics of 19 patients with T2D<sup>1</sup>

Characteristics	Value
Sociodemographic	
Women, $n$ (%)	10 (52.6)
White, self-reported ethnicity, $n$ (%)	15 (78.9)
Age, y	$65.8 \pm 7.3$
Years of study	$9.7 \pm 4.7$
Current smoking, $n$ (%)	4 (21.0)
Current alcohol beverage intake, $n$ (%)	9 (47.4)
Clinical	
Diabetes duration, y	10 (5–9)
Sedentary lifestyle, n (%)	10 (52.6)
Hypertension, $n$ (%)	16 (84.2)
Systolic blood pressure, mm Hg	$131 \pm 8$
Diastolic blood pressure, mm Hg	$73 \pm 7$
Diabetic retinopathy, $n$ (%)	7 (36.8)
Peripheral vasculopathy, $n$ (%)	2 (10.5)
Elevated urinary albumin excretion, n (%)	5 (26.3)
Cardiovascular events, $n$ (%)	3 (15.8)
Angioplasty, n (%)	1 (5.3)
Stroke, $n$ (%)	2 (10.5)
Laboratory	
Fasting plasma glucose, mg/dL	$135.8 \pm 20.7$
Glycated hemoglobin, %	$7.0 \pm 0.8$
Total cholesterol, mg/dL	$167.2 \pm 43.0$
HDL cholesterol	
Men, mg/dL	$41.0 \pm 10.7$
Women, mg/dL	$50.3 \pm 12.3$
LDL cholesterol	$92.3 \pm 33.2$
Triglycerides, mg/dL	130.0 (96.0-130.0)
Urinary albumin excretion, mg/L	5.0 (3.0-25.8)
Creatinine, mg/dL	$0.8 \pm 0.2$
GFR, mL $\cdot$ min <sup>-1</sup> $\cdot$ 1.73 m <sup>-2</sup>	$78.8 \pm 15.3$
Glutamic oxaloacetic transaminase, U/L	$20.3 \pm 7.2$
Glutamic pyruvic transaminase, U/L	$22.4 \pm 13.0$
Thyrotropin, µIU/mL	$2.2 \pm 1.0$
Anthropometric	
BMI, kg/m <sup>2</sup>	$28.2 \pm 2.9$
Skeletal muscle mass, kg	$25.6 \pm 4.9$
Body fat mass, kg	$26.1 \pm 6.5$
Body fat, %	$35.7 \pm 6.5$
Waist circumference	
Men, cm	$102.7 \pm 9.9$
Women, cm	$94.9 \pm 8.6$
Dietary intake	
Total energy, kcal	$1702 \pm 168$
Protein, g	61 (47-92)
en%	$18.8 \pm 1.5$
Fat, g	67 (43-77)
en%	$36.9 \pm 2.0$
Carbohydrate, g	192 (143-211)
en%	$44.2 \pm 2.2$
Fiber, g	
Total	$16.9 \pm 2.4$
Soluble	$5.3 \pm 0.8$
Insoluble	$11.5 \pm 1.7$
Glycemic index	$54.2 \pm 1.4$

<sup>1</sup> Values are means  $\pm$  SDs, medians (25th–75th percentiles), or number of patients with analyzed characteristic (%). en%, percentage of energy; GFR, glomerular filtration rate; T2D, type 2 diabetes.

TABLE 3

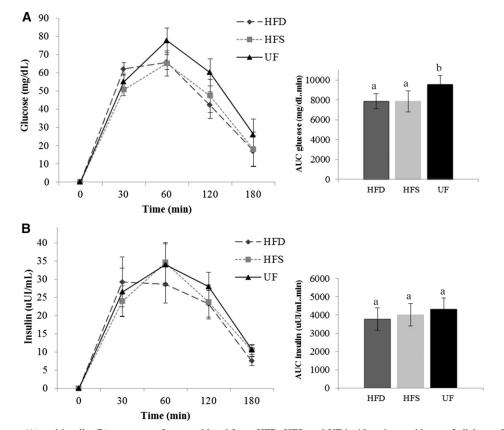
Plasma glucose, plasma insulir	, and other analyzed vari	bles in each tested breakfast	t meal in 19 patients with T2D <sup>1</sup>
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	Meals			
	HFD	HFS	UF	$P^2$
Fasting plasma glucose, mg/dL	131.7 ± 21.8	$131.3 \pm 20.8$	128.1 ± 23.5	0.741
Fasting plasma insulin, $\mu$ IU/mL	$10.5 \pm 6.1$	$10.2 \pm 6.2$	$9.4 \pm 4.8$	0.356
BMI, kg/m <sup>2</sup>	$28.1 \pm 3.1$	$28.2 \pm 3.1$	$28.3 \pm 3.0$	0.815
Body weight, kg	$72.3 \pm 10.9$	$72.3 \pm 10.5$	$72.4 \pm 10.6$	0.638
24-h recall, kcal	$1872.6 \pm 838.9$	$1825.2 \pm 763.7$	$1739.5 \pm 776.0$	0.607
Protein, g	85 (53-95)	69 (57–92)	78 (47–112)	0.941
Fat, g	53 (39-75)	54 (40-86)	51 (40-79)	0.738
Carbohydrate, g	202 (153-298)	206 (153-249)	211 (158-225)	0.728
Fiber, g				
Total	$20.1 \pm 2.0$	$20.8 \pm 2.3$	$18.8 \pm 1.8$	0.768
Soluble	$6.8 \pm 3.4$	$6.4 \pm 3.3$	$6.0 \pm 2.8$	0.690
Insoluble	$13.3 \pm 6.2$	$14.4 \pm 7.6$	$12.8 \pm 5.5$	0.693
Glycemic index	$55.8 \pm 7.0$	$54.6 \pm 5.2$	$53.4 \pm 4.9$	0.309
Glycemic load	78.8 (60.5–116.6)	83.5 (71.8–103.9)	76.4 (72.9–101.5)	0.588

<sup>1</sup> Values are means  $\pm$  SDs and medians (25th–75th percentiles). HFD, high fiber from diet; HFS, high fiber from supplement; T2D, type 2 diabetes; UF, usual fiber.

 $^{2}P$  value for ANOVA for repeated measures.

insulin responses after the intake of soluble fiber from foods or supplements in a common meal. A low postprandial response of plasma glucose after the consumption of soluble fiber was demonstrated in patients with diabetes (14–18). Most of these studies evaluated the response of insulin and glucose after the consumption of single foods: beverages (14, 18), single cereal bars (16), or single breads (19). Evaluation of the plasma glucose response in a real-life context confers additional clinical applicability to our results. The postprandial responses to meals in the present study were evaluated in a mixed meal instead of a



**FIGURE 2** Glucose (A) and insulin (B) responses after tested breakfasts: HFD, HFS, and UF in 19 patients with type 2 diabetes. Values are means  $\pm$  SEMs, adjusted for the categorical variable "type of meal sequence." No substantial group  $\times$  time interaction was observed in either (A) or (B). Different letters in bars indicate significant statistical difference (P < 0.05) between incremental AUC test meals. ANOVA for repeated measures and post hoc Bonferroni test. HFD, high fiber from diet; HFS, high fiber from supplement; UF, usual fiber.

single food or beverage. The composition of the breakfast was based on the contents of the usual morning meals consumed by our outpatients with T2D (38). Meal tests were conducted under well-standardized conditions: patients had good chronic glucose control, similar baseline plasma glucose levels, and spent the same amount of time eating the breakfasts. The macronutrient composition of the 3 breakfasts was similar, except for the type and amount of fiber, as expected. Finally, the total dietary intake in the previous day in each tested breakfast did not differ.

Different mechanisms have been related to the beneficial effect of soluble fiber on postprandial glucose responses. The effects of soluble fiber on the stomach and small intestine increase in the viscosity and gel forming of gut contents, reduction in glucose diffusion through the unstirred water layer, delay in small bowel transit, reduction in the accessibility of  $\alpha$ -amylase by its substrates, and prolonged absorption of carbohydrates in part by increasing incretin levels—seem to be involved. In addition, soluble fiber intake has been associated with increased insulin sensitivity (21).

Other studies conducted in patients with T2D have evaluated the acute insulin response after consuming foods containing fiber but without testing different sources of fibers as we did (15–19). Only one study (17), conducted in a small sample of 8 patients with T2D, evaluated glucose and insulin responses after consuming a common meal. Cereal meals with 3 different amounts of  $\beta$ -glucan (4.0, 6.0, and 8.4 g) were compared with a standard continental breakfast. Similar to our study, there was a smaller increment in the glucose AUCs of breakfasts with soluble fiber, but the insulin AUC was not described. In our study we observed an increase in insulin after all meal tests but without differences between them. Long-term fiber consumption has been associated with decreased levels of fasting insulin (44), but our study was designed to evaluate the acute postprandial insulin response. Our insulin data were in accordance with a recent meta-analysis on the effects of soluble fiber (psyllium) in postprandial insulin levels in patients with T2D (14) that showed no substantial differences in postprandial insulin.

A potential limitation of the present study includes reliance on the manufacturers' labeled food composition information instead of on laboratory analyses of food nutrients. Moreover, an issue that did not permit generalization of our data could be the good glycemic, lipid, and blood pressure control practiced by our patients, which was present at baseline. In patients with worse metabolic control, the effect of soluble fiber may be more important if we postulate that  $\leq$ 70% of HbA1c depends on postprandial glucose (3, 4). Finally, our studied sample size was calculated based on the postprandial response of glucose, not taking the insulin response into account. We could not discount the absence of differences in insulin responses after breakfasts being related to the sample size calculation.

The present study adds to our understanding of the effect of different sources of soluble fiber on glucose responses after a common meal and provides support for encouraging people with T2D to increase their soluble fiber intake, regardless of the source. The absolute difference (4.6 g) of soluble fiber between both meal tests rich in fiber and the UF meal test is proved to lower on the postprandial glucose of these patients. Higher fiber intake from dietary foods represents a low-cost option besides providing important nutrients, such as vitamins and minerals, for improved health.

In conclusion, higher fiber intake was associated with lower postprandial glucose at breakfast, and the intake of soluble fiber from food and supplements had a similar effect in patients with T2D. This may be a useful and practical strategy for improving the postprandial metabolic profile in these patients. Our results must be confirmed in long-term clinical trials, taking into account total daily intake.

This manuscript is dedicated to the memory of our dear friend, colleague, mentor, and coauthor MJA, who died in May 2017. The authors' responsibilities were as follows—CMdC, TPdP, JCdA, LVV, and MJA: designed the research; CMdC, TPdP, VMTM, and LVV: conducted the research; CMdC: analyzed the data; CMdC and MJA: wrote the article; LVV: had primary responsibility for the final content; and all authors: read and approved the final manuscript. CMdC received a scholarship from CAPES, and TPdP received grants from Projeto Nacional de Pós-Doutorado (PNPD/CAPES). The remaining authors reported no conflicts of interest related to the study.

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