Effect of an isocaloric diet containing fiber-enriched flour on anthropometric and biochemical parameters in healthy non-obese non-diabetic subjects

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We studied the effect of soluble fiber-enriched products on anthropometric and biochemical variables in 30 healthy non-obese, non-diabetic subjects. This was a randomized, controlled crossover, single-blind, dietary intervention study performed for 8 weeks. Subjects received an isocaloric diet with fiber-enriched products for the first 4 weeks and with regular flour products for the following 4 weeks, or *vice versa*. Weight, height, measures of fat distribution (waist, hip circumference), glucose, insulin and triglycerides were measured at baseline, after 4 and 8 weeks of intervention. BMI and insulin sensitivity indices were calculated. Weight and BMI decreased in the first period of isocaloric diet in both groups, regardless of the type of flour consumed (weight $p<0.01$, $p<0.001$ respectively; BMI $p = 0.01$, $p<0.001$ respectively). At the end of the 8 weeks, weight and BMI further decreased in the group consuming the fiber-enriched diet ($p<0.01$). Insulin resistance, estimated with the Homeostasis Model Assessment index and the Lipid Accumulation Product index, improved in all subjects after the fiber-enriched flour diet ($p = 0.03$, $p = 0.02$, respectively). In conclusion, an isocaloric diet supplemented with fiber-enriched products may improve measures of fatness and insulin sensitivity in healthy non-obese non-diabetic subjects. We might hypothesize a similar effect also in subjects with metabolic abnormalities.

Key Words: **glycemic index, fibers, fiber-enriched diet, insulin sensitivity, lipid accumulation product, HOMA-IR**

Type 2 diabetes mellitus (T2DM) is nowadays an epidemic disease affecting more than 280 million people and its prevalence is estimated to grow.(1,2) Insulin resistance is a condition favoring over time the onset of T2DM and it may be promoted by both excessive food intake and reduced physical activity. On the contrary, dietary intervention and lifestyle changes are a powerful weapon to prevent the development of T2DM in subjects at risk.(3)

Fibers reduce the risk of T2DM by lowering the glycemic index (GI) of foods(4,5) and thus the postprandial glycemic and insulinemic responses. On the contrary, high GI foods, by promoting a quick increase in postprandial blood glucose, trigger a huge insulin response with increased peripheral glucose uptake and high levels of free fatty acid in the postprandial state. When adipose tissue can no longer store these lipids, they deposit ectopically in muscle, heart, liver and pancreatic β-cells, leading to the development of insulin resistance in these normally insulin responsive tissues.(6–10)

Epidemiological data show that a fiber rich diet (from whole grains, fruit and vegetables) reduces the risk of developing insulin resistance and T2DM also in the general population.(11–16) It is noteworthy that a high intake of fibers is able to improve the metabolic profile even in subjects not affected by overt disease, thus performing a preventive action.(13,15)

The aim of this 8-week study was to evaluate the effect of a fiber enriched isocaloric diet with low GI products on anthropometrics and biochemical parameters in healthy non-obese, non-diabetic subjects as compared with an isocaloric diet containing products made with wheat flour.

Materials and Methods

Study subjects. Thirty healthy non-obese, non-diabetic volunteers (10 males and 20 females), with a mean (±SD) age of 38.3 ± 12.47 years (range 22–64 years) and body mass index (BMI) of 25.94 ± 2.46 kg/m^2 (range 20.7–29.9 kg/m^2) were recruited.

Participants were excluded if they were previously diagnosed as having T2DM, if they had a history of endocrine, gastrointestinal or psychiatric disease, if they were obese, pregnant or if they practiced physical activity at agonistic level. None of them was taking chronic corticosteroid therapy.

All participants were informed of the nature, purpose and possible risks of the study before they gave their written consent to participate. The protocol was approved by the local Ethic Committee (protocol number 2634).

Experimental design. The study was a randomized, controlled crossover, single-blind dietary intervention study lasting 8 weeks. Study design is illustrated in Fig. 1. Patients were randomly assigned to group A ($n = 15$) or group B ($n = 15$). All patients underwent anthropometric measurement and blood sampling at baseline, at 4 and 8 weeks.

An isocaloric diet with products made of regular flour (from here on named "placebo") was administered to patients of group A for 4 weeks, thereafter an isocaloric diet with products made of soluble fiber-enriched flour was administered for further 4 weeks. The fiber enriched diet was given to patients of group B firstly for 4 weeks followed by further 4 weeks of placebo diet.

Anthropometric measures. At each follow-up visit anthropometric measures were taken with participant in light clothing

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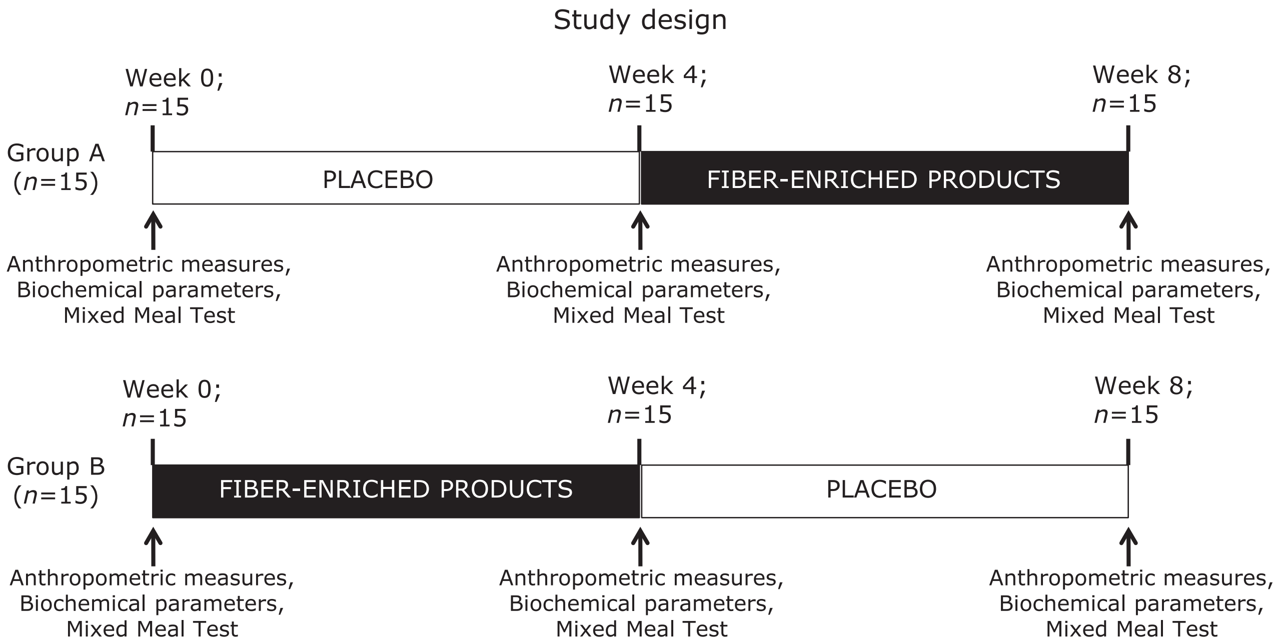

Fig. 1. Study design. The study was a randomized, controlled crossover, single-blind dietary intervention study lasting 8 weeks. Patients were randomly assigned to group A (n = 15) or group B (n = 15) and underwent anthropometric measurement and blood sampling at baseline, at 4 and 8 weeks.

without shoes. Weight and height were recorded to the nearest 0.1 kg and 0.5 cm using standard scales and stadiometers, respectively. Waist and hip circumference were measured using a flexible tape: the horizontal circumference at the level of the umbilicus and the largest horizontal girth between waist and thigh respectively. BMI and waist to hip ratio (WHR) were calculated.

Blood samples. Blood samples were taken from an arm vein after a 12-h overnight fast for the analysis of glucose, insulin, triglycerides, total and HDL cholesterol, as previously reported.[17] LDL cholesterol was calculated with the Friedewald formula. Moreover, all patients were given a standard Mixed Meal Test (MMT, 314 kcal, 59.3% carbohydrates, 20.38% proteins, 20.16% lipids) and blood samples were taken after 30, 60, 90, 120 and 180 min to analyze glucose, insulin and FFA levels. All determinants were performed at baseline, 4- and 8-week in both group.

Insulin sensitivity data. Insulin sensitivity was estimated at baseline and after each 4-week period through three indices: Matsuda Index,[18,19] homeostasis model assessment of insulin resistance (HOMA-IR)[20] and lipid accumulation product (LAP) index.[21] The Matsuda index expresses whole body insulin sensitivity through glucose and insulin concentration measured during an Oral Glucose Tolerance Test. We applied the Matsuda Index to the Mixed Meal Test. The formula used was as follows: 10.000/√[(FPG (mg/dl) × FPI (μU/ml) × Mean test glucose concentration (mg/dl) × Mean test insulin concentration) (μU/ml)], where FPG was fasting plasmatic glucose and FPI was fasting plasmatic insulin. HOMA-IR index estimates insulin resistance (mainly in the liver) from fasting glucose and insulin: [FPG (mg/dl) × FPI (μU/ml)]/405. The LAP index is based on waist circumference (WC) and triglyceride (TG) concentration and reflects the ectopic lipid deposits that primarily cause insulin resistance and therefore is an indirect measure of body insulin resistance. The formula used was different for men and women, as follows: for men = [WC (cm) – 65] × [TG (mM)]; for women = [WC (cm) – 58] × [TG (mM)].

Diet. Usual daily caloric intake and fiber consumption was assessed by a 3-day food record during the first visit and the calculation was performed using WindFood program (ver. 3.0.0, Medimatica, Teramo, Italy). An isocaloric, balanced diet (55–60% carbohydrates, 25–30% lipids, 15–20% proteins) was developed for each patient according to his own daily total energy expenditure, calculated multiplying the basal energy expenditure (calculated by Harris-Benedict formula), for physical activity levels (1.3 if they were sedentary, 1.4 if they were moderately active, 1.5 if they were highly active).[22] To determine physical activity levels all participants completed the International Physical Activity Questionnaire. Participants have been trained not to change their physical activity habits for the whole duration of the study.

The diet included every day 125 g of fresh pasta (such as "spaghetti"), 50 g of biscuits, 120 g of bread. These products could be made either with regular flour or with fiber-enriched flour. The fibers used were: guar guam, glucomannan, inulin and wheat fiber, for a total daily fiber supplement of 34 g. The products were delivered to each participant at home for free and regular intake of these products was verified.

The participants were randomized to follow the placebo diet for the first 4 weeks and the soluble fiber-enriched diet for the following 4 weeks (Group A, n = 15, 5 males and 10 females, BMI 25.99 ± 2.31 kg/m^2), or *vice versa* (Group B, n = 15, 5 males and 10 females, BMI 25.99 ± 2.31 kg/m^2).

Statistical analysis. The normality of data distribution was assessed by the Kolmogorov-Smirnoff test.

All measures at basal and after each 4-week period were compared in each group by using Student's t test analysis. The statistical analysis was performed using WinSTAT Program (ver. 2009. 1; Cambridge, MA). The results are presented as mean ± SD. Data were considered significant for $p<0.05$.

Results

All participants completed the study. No significant differences in both anthropometric and biochemical parameters, were observed between the two groups at baseline (Table 1). Anthropometric and biochemical characteristics of participants at baseline and during the intervention are shown in Table 2. The isocaloric diets given to the study participants were almost the same in term

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Table 1. Subjects characteristics at baseline

	Basal - Group A	Basal - Group B	*p*
Sex (F)	10	10	
Age	35.27 ± 11.5	41.4 ± 13.0	0.66
Weight (kg)	70.75 ± 11.37	72.38 ± 11.99	0.84
Height	164.53 ± 11.45	166.9 ± 10.08	0.64
BMI (kg/m^2)	25.99 ± 2.31	25.90 ± 2.68	0.59
Waist (cm)	81.53 ± 8.24	81.06 ± 8.48	0.94
Hip (cm)	102.37 ± 7.42	101.83 ± 5.19	0.19
WHR	0.79 ± 0.06	0.79 ± 0.08	0.26
Fasting glucose (mg/dl)	81.87 ± 9.05	81.47 ± 6.81	0.29
HbA1c (mg/dl)	4.89 ± 0.34	4.89 ± 0.31	0.69
Insulin (μmol/L)	7.97 ± 3.99	7.03 ± 3.06	0.33
Trglycerides (mg/dl)	90 ± 37.46	86.87 ± 26.52	0.2
Total cholesterol (mg/dl)	194.06 ± 40.09	203.07 ± 29.05	0.24
HDL cholesterol (mg/dl)	57.13 ± 11.55	61.53 ± 13.80	0.51
LDL cholesterol (mg/dl)	118.93 ± 36.38	124.16 ± 21.61	0.06
Matsuda index	8.23 ± 3.39	8.55 ± 2.60	0.33
HOMA index	1.60 ± 0.84	1.41 ± 0.61	0.25
LAP index	22.76 ± 16.95	20.81 ± 9.76	0.47
Usual diet (kcal/day)	2,082.34 ± 332.06	2,058.77 ± 357.50	0.78
Isocaloric diet (kcal/day)	1,937.99 ± 282.75	1,934.07 ± 246.73	0.64

Comparison of demographic, anthropometric and biochemical parameters between partecipants assigned to Group A and B. Data ara mean ± SD.

Table 2. Group A and Group B anthropometric and biochemical characteristics at baseline, after 4- and 8-weeks

Group A	Basal	Placebo (weeks 0–4)	p^{1*}	Fiber enriched diet (weeks 4–8)	p^{2**}
Weight (kg)	70.75 ± 11.37	69.40 ± 11.53	0.001	68.0 ± 11.48	0.019
BMI (kg/m^2)	25.99 ± 2.31	25.42 ± 2.31	0.001	25.20 ± 2.23	0.021
Waist (cm)	81.53 ± 8.24	79 ± 7.84	0.013	78.2 ± 7.85	0.222
Hip (cm)	102.37 ± 7.42	100.8 ± 6.47	0.032	99.53 ± 6.86	0.00013
WHR	0.79 ± 0.06	0.78 ± 0.06	0.133	0.78 ± 0.06	0.81
Fasting glucose (mg/dl)	81.86 ± 9.05	79.26 ± 6.44	0.155	81.53 ± 7.58	0.154
HbA1c (mg/dl)	4.89 ± 0.34	4.71 ± 0.38	0.004	4.73 ± 0.33	0.33
Insulin (μmol/L)	7.97 ± 3.99	7.05 ± 3.62	0.145	6.48 ± 3.08	0.336
Triglycerides (mg/dl)	90 ± 37.46	102.06 ± 36.85	0.06	96.46 ± 39.40	0.54
Total cholesterol (mg/dl)	194.06 ± 40.09	192.33 ± 40.14	0.64	179.06 ± 39.49	0.0024
HDL cholesterol (mg/dl)	57.13 ± 11.55	52.53 ± 8.08	0.009	51.53 ± 11.40	0.64
LDL cholesterol (mg/dl)	118.93 ± 36.38	119.38 ± 37.92	0.89	108.24 ± 35.56	0.007
Matsuda index	8.23 ± 3.39	8.97 ± 4.25	0.42	9.19 ± 3.31	0.879
HOMA index	1.60 ± 0.84	1.39 ± 0.78	0.118	1.24 ± 0.68	0.526
LAP index	22.76 ± 16.95	22.34 ± 14.51	0.829	19.14 ± 10.95	0.125
Group B	**Basal**	**Fiber enriched products (0–4 weeks)**	$p^{1\#}$	**Placebo (4–8 weeks)**	$p^{2\#\#}$
Weight (kg)	72.38 ± 11.99	70.86 ± 11.08	0.003	70.08 ± 10.56	0.051
BMI (kg/m^2)	25.90 ± 2.68	25.32 ± 2.35	0.001	25.07 ± 2.33	0.75
Waist (cm)	81.06 ± 8.48	78.56 ± 7.86	0.00069	78.43 ± 7.62	0.85
Hip (cm)	101.83 ± 5.19	100.60 ± 4.98	0.089	100.63 ± 5.07	0.95
WHR	0.79 ± 0.08	0.77 ± 0.08	0.13	0.77 ± 0.07	0.92
Fasting glucose (mg/dl)	81.47 ± 6.81	79.8 ± 9.37	0.38	81.53 ± 7.83	0.16
HbA1c (mg/dl)	4.89 ± 0.31	4.85 ± 0.30	0.55	4.83 ± 0.33	0.6
Insulin (μmol/L)	7.03 ± 3.06	6.00 ± 2.11	0.22	7.15 ± 3.40	0.22
Triglycerides (mg/dl)	86.87 ± 26.52	85.66 ± 23.76	0.86	90.53 ± 20.23	0.44
Total cholesterol (mg/dl)	203.07 ± 29.05	186.86 ± 31.69	0.002	207.06 ± 27.90	0.0004
HDL cholesterol (mg/dl)	61.53 ± 13.80	58.20 ± 9.79	0.15	60.6 ± 9.11	0.17
LDL cholesterol (mg/dl)	124.16 ± 21.61	111.53 ± 24.95	0.002	128.36 ± 22.29	0.0001
Matsuda index	8.55 ± 2.60	9.75 ± 4.44	0.26	8.67 ± 3.23	0.4
HOMA index	1.41 ± 0.61	1.19 ± 0.44	0.15	1.59 ± 0.75	0.19
LAP index	20.81 ± 9.76	17.95 ± 8.41	0.08	18.66 ± 8.17	0.46

Data are espressed mean ± SD. p^{1*}, Placebo vs Basal; p^{2**}, Fiber enriched diet vs Placebo; $p^{1\#}$, Fiber enriched diet vs Basal; $p^{2\#\#}$, Placebo vs Fiber enriched diet.

of mean calorie amount and percentage of nutrients. The isocaloric diet resulted lower in energy (Group A: –144.35 kcal/day, p = 0.02; Group B: –124.71 kcal/day, p = 0.01) and higher in fiber content (Group A: +7.64 g; p<0.001; Group B: +8.29; p<0.01) as compared to usual diet in both groups. The daily amount of fiber was significantly higher in the fiber-enriched diet period than in placebo one (Group A: +41.62 g, Group B: +42.27; p<0.001 for both groups).

Anthropometric measures. Weight and BMI resulted significantly lower in Group A after the 4-week placebo period (change from baseline –1.35 kg, p<0.01; –0.57 kg/m^2, p<0.01, respectively). We observed a further decrease in weight and BMI in this group after the period of fiber-enriched diet (change from placebo –1.4 kg, p = 0.01; –0.22 kg/m^2, p = 0.02, respectively). In Group B we observed a significant reduction of weight and BMI after the fiber enriched period (change from baseline –1.52 kg, p<0.01; –0.58 kg/m^2, p<0.01, respectively), and an additional slight decrease of weight after the period of placebo diet (–0.78 kg, p = 0.05).

Both groups displayed a reduction in waist circumference after the first 4-week period (Group A, –2.53 cm, p<0.05 vs basal; Group B, –2.5 cm, p<0.001 vs basal) regardless of the type of flour consumed. No further changes were observed in the following 4-week period. Hip circumference was reduced only in Group A, both after the placebo period (–1.57 cm, p<0.05 vs basal) and after the fiber-enriched diet (–0.8 cm, p<0.001 vs placebo). WHR did not change in both group.

Glucose metabolism and insulin-resistance indices. Fasting glucose and fasting insulin did not change significantly in both groups during the 8 weeks of the study. Matsuda Index increased in both groups after the fiber-enriched diet but without reaching statistical significance. HOMA-IR and LAP indices decreased in both gropus after the fiber-enriched diet, although not significantly. A further analysis has been performed by considering all participants jointed at baseline. HOMA-IR index was significantly lower after the total isocaloric plus fiber-enriched diet as compared with basal (–0.35, p<0.03) (Fig. 2). Similarly, the LAP index significantly decreased at the end of the 8-week study (–1.86, p<0.02) (Fig. 3). No change was observed in Matsuda index (data not shown).

Lipid profile. Total cholesterol decreased significantly in both groups after the fiber-enriched period (Group A: –1.73 mg/dl, p<0.01 vs placebo; Group B: –16.21 mg/dl, p<0.01 vs basal). Notably, in Group B total cholesterol returned to baseline level (p<0.001 vs fiber-enriched period) after the placebo period. A significant decrease in LDL cholesterol concentration was observed in Group A and Group B after the fiber-enriched period (Group A: –13.27 mg/dl, p<0.01 vs placebo; Group B –12.63 mg/dl, p = 0.002 vs basal). In Group B, LDL cholesterol returned to baseline level after the placebo period. In Group A we observed a slight decrease in HDL level after the placebo period (–4.6 mg/dl; p<0.01 vs basal). Neither the placebo nor the fiber enriched isocaloric diet affected fasting triglycerides in both groups.

Adverse events. The inclusion of 34 g/daily of fiber for the 4 weeks of intervention was well tolerated by all participants. Mild adverse effects reported were abdominal tension, meteorism and flatulence that resolved within the first few days of the fiber-enriched period.

Discussion

In this study, we observed that an isocaloric diet including 34 g/day fiber supplement by expressly made alimentary preparation over 8 weeks ameliorated anthropometrics parameters such as weight and waist circumference and improved insulin resistance (i.e., reduced HOMA-IR index) in healthy non-obese, non-diabetic subjects.

The proprietary fiber mix added to products consumed in our study has been previously shown to markedly reduce the GI[23] of food containing it. The novelty of our study was to explore the effect of a prolonged intake of such products on both anthropometric and biochemical parameters, as well as on specific indices of insulin resistance. We hypothesized that improving anthropometric and biochemical parameters in healthy subjects could have a preventive effect on the development of metabolic abnormalities.

In our study, we observed changes in anthropometrics measures in both groups: the first decrease in weight and BMI could be due to the fact that the isocaloric diet was lower in respect to the usual daily caloric intake of study subjects. It is difficult to distinguish the net effect of fiber-enriched products as opposite to the isocaloric diet alone, however it is to note that a further significant weight loss was observed when adding fiber-enriched flour. Moreover, a greater reduction in waist circumference was observed as effect of the fiber-enriched diet.

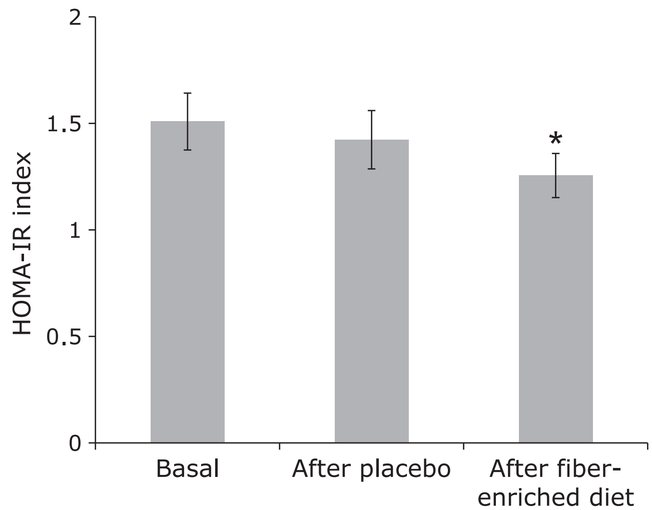

Fig. 2. HOMA-IR index in all subjects. HOMA-IR index was evaluated during the 8-week isocaloric diet at baseline after placebo and after fiber-enriched product consume. Data are expressed as mean ± SD; *p<0.05 vs basal.

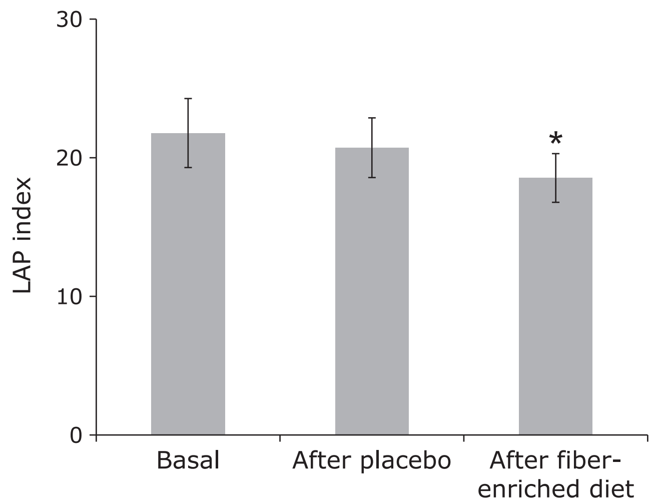

Fig. 3. LAP index in all subjects. LAP index was evaluated during the 8-week isocaloric diet at baseline after placebo and after fiber-enriched product consume. Data are expressed as mean ± SD; *p<0.05 vs basal.

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Among the effects of the fiber-enriched intervention diets, there was an improvement of all insulin resistance indices, mainly the HOMA-IR index, a marker of insulin resistance mostly of the liver. These data are in agree with similar studies in which fiber supplement[24,25] or high-fiber diet[26] ameliorated body insulin resistance in healthy subjects, as assessed by HOMA-IR index or glucose clamp. Possible mechanisms involved in the improvement of insulin sensitivity include slow intestinal absorption of glucose and colonic fermentation of fibers. The fermentation of undigested carbohydrates by the colonic bacteria may contribute to the reduction of postprandial glycemia.[27] The products of colonic fermentation of fibers, short chain fatty acids, increase in serum and may have positive effects on lipid and glucose metabolism in liver.[28,29]

In our study the LAP index significantly improved after the isocaloric plus fiber-enriched diet. The association between fiber supplementation and LAP index was never studied before. The LAP index is an accurate predictor of the risk of developing metabolic syndrome[30] and the fiber supplement in our study may contribute to reduce it. The improvement of LAP index in all patients after the fiber-enriched period reflects the possible reduction of ectopic lipid deposits that are in part responsible for insulin-resistance.[12–16]

Similar studies tested the effects of a fiber supplement on insulin resistance and glucose metabolism.[24,25] However, in these studies researchers instructed patients not to change their habitual diet, and no changes in anthropometric measures were observed; nevertheless an improvement of insulin sensitivity was found. A previous study conducted with 19 healthy non-obese subjects showed that low glycemic index high fiber meal lowered the glycemic and insulinemic response after eating it.[31] Moreover, another study demonstrated that a 10.5 g/die psyllum supplementation lowered fasting plasma glucose and insulin over a 6 month-intervention.[32] Total cholesterol decreased significantly in both groups after the fiber-enriched diet: lowering total and LDL cholesterol is a characteristic of fibers that is important in preventing cardiovascular events.[33] Prior study demonstrated the efficacy of fibers on lipidic parameters in hypercolesterolemic or hypertensive or diabetic subjects. In fact, according to the main international guidelines for obesity and cardiovascular disease prevention, the first approach to lower cardiovascular risk could be the improvement of lifestyle with physical activity and diet, such as increased fiber content.[34]

In conclusion, this study suggests that the daily consume of 34 g fibers by eating products made of soluble fiber-enriched flour during a 4-week isocaloric diet period improves anthropometrics parameters and insulin resistance indices in healthy non-obese, non-diabetic subjects. This fiber-enriched diet was well tolerated by the participants of our study, with very few and minor side effects.

It is known that diets composed of aliments that are able to reduce postprandial glucose are preferred in patients suffering from metabolic syndrome and T2DM. Quality and not only quantity of a diet may contribute to an appropriate body weight control. Our diet is not restrictive and included pasta and bakery products added with a specific fiber mix without significant change in their organoleptic characteristics. These products were able to modify body composition (such as waist circumference) and body weight. It is well known that changing these parameters plays a preventive role on the development of metabolic diseases.

Larger and prospective studies will be useful to demonstrate that these low GI products with flavor and consistency of traditional ones, could play a possible preventive role in healthy population, as well as a possible therapeutic role in subjects with metabolic abnormalities.

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Abbreviations

BMI	body mass index
FPG	fasting plasmatic glucose
FPI	fasting plasmatic insulin
GI	glycemic index
HOMA-IR	homeostasis model assessment of insulin resistance index
LAP	lipid accumulation product index
WC	waist circumference
T2DM	type 2 diabetes mellitus
TG	triglycerides
WHR	waist to hip ratio

Conflict of Interest

No potential conflicts of interest were disclosed.

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