

*Original Article***A randomized controlled study for evaluation of psyllium effects on kinetics of carbohydrate absorption**

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**Abstract**

**BACKGROUND:** This study was performed to evaluate the effects of psyllium on kinetics of alimentary carbohydrate absorption in diet-treated type 2 diabetic patients.

**METHODS:** This was a double blind, prospective, controlled clinical trial. Twelve patients (6 in each group) participated in the present study. After an overnight fast, a standard 435 kcal breakfast was given to participants. Fasting, 1- and 2-hour postprandial plasma glucose was measured in the case and control groups. Cow's milk containing 5 grams of psyllium granules for the case and without psyllium for the control groups was also delivered.

**RESULTS:** Plasma glucose changes in the first hour were significantly different between control and case groups (53.8 versus 17.8 respectively,  $P = 0.037$ ). Also, mean 2-hour postprandial plasma glucose was 167.67 and 117.67 mg/dl for control and case groups, respectively ( $P = 0.05$ ).

**CONCLUSIONS:** This pilot study revealed that psyllium may effectively reduce postprandial plasma glucose possibly by retarding GI carbohydrate absorption. Larger studies are needed to confirm the results of this study and define its role compared to acarbose or meglitinides.

**KEYWORDS:** Psyllium, postprandial hyperglycemia, type 2 diabetes mellitus.

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Recently, postprandial hyperglycemia has been considered as an independent cardiovascular risk factor similar to hypertension, hyperlipidemia, and smoking<sup>1-3</sup>. Several lines of evidence have implicated targeting postprandial glucose control for better cardiovascular risk reduction<sup>4-7</sup>. Currently, there are few available drugs aimed at postprandial glucose control<sup>8</sup>. Rapidly acting insulin secretagogues (e.g., nateglinide,

repaglinide) have recently been introduced to improve the control of postprandial hyperglycemia<sup>7</sup>, but with the price of increasing insulin production and risk of hypoglycemia. Prandial oral antidiabetic agents such as alpha-glucosidase inhibitors (acarbose, miglitol) have been introduced to improve the control of postprandial hyperglycemia and may also have other benefits<sup>9-13</sup>, but their use have some limitations<sup>14-16</sup>. Fiber, in particular viscous

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dietary fiber, has positive effects on human health both in the prevention and in treatment of chronic diseases. A high fiber diet has preventive effects against constipation, colon diverticulosis, carcinoma of the large bowel and stomach, type 2 diabetes, metabolic syndrome and cardiovascular disease <sup>17</sup>. Increased dietary fiber is recommended by health authorities worldwide <sup>18</sup>. Recent research has focused on the use of dietary fibers, especially soluble dietary fibers (such as guar gum, locust bean gum, and psyllium fibers), resistant starch, and slowly digestible carbohydrates. These have been shown to alter food structure, texture, and viscosity, and hence the rate of starch degradation during digestion. The past 30 years of intensive clinical research with guar, psyllium, oat and other fiber-rich foods have repeatedly demonstrated the health benefits of dietary fiber in lowering insulin requirements and improving blood glucose control in diabetics, as well as reducing serum lipid levels in hyperlipidemia. Accumulating epidemiological evidence also supports a link between high-fiber diets and reduced risk of heart disease and cancer <sup>18</sup>. Water-soluble dietary fibers have been found to decrease postprandial glucose concentrations and decrease serum cholesterol concentrations <sup>19</sup>. Psyllium is a bulk-forming laxative containing high fiber and mucilage. Psyllium or ispaghula husk (the husk of the seeds of *Plantago ovata*) is a mixture of neutral and acid polysaccharides containing galacturonic acid with a ratio of soluble/insoluble fiber of 70/30. Some foods could potentially be enriched with psyllium, like breads, breakfast cereals, pasta and snack foods <sup>20</sup>. Some studies showed glucose absorption decreased significantly in the presence of psyllium <sup>21</sup>. Psyllium also significantly reduced total and LDL cholesterol and uric acid <sup>21</sup>. These studies indicate a beneficial therapeutic effect of psyllium (Plantaben) in the metabolic control of type 2 diabetics as well as in lowering the risk of coronary heart disease without adversely affecting either mineral or vitamins A and E concentrations <sup>21</sup>. However, the mechanism of fibers' action is not fully understood and the ef-

fect is not always consistent with the expected results. One reason could be the large intra- and inter-fiber variability due to its complex structural and physicochemical characteristics <sup>18</sup>. The fiber also must be mixed with the administered glucose or food <sup>22</sup>. The beneficial effect of dietary fiber in the management of type 2 diabetes, has not been fully demonstrated <sup>22,23</sup>. This study was performed to address the effects of psyllium on kinetics of alimentary carbohydrate absorption in diet-treated type 2 diabetic patients.

## Methods

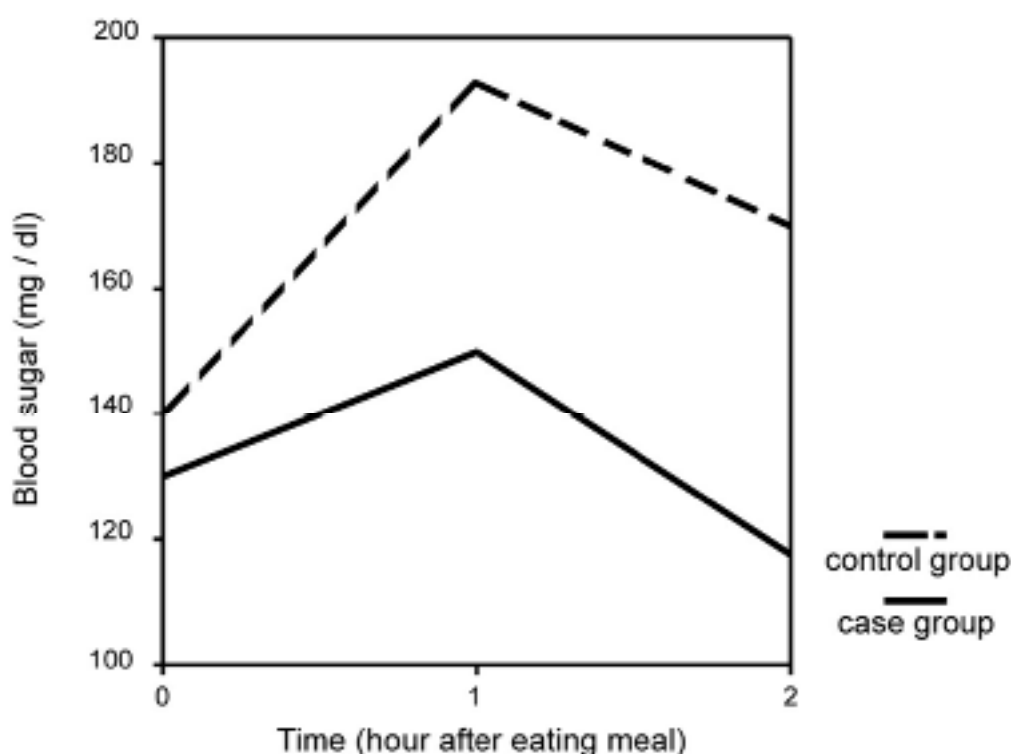
This study was a double blind, prospective, controlled, clinical trial on type 2 diabetic patients. The participants were randomized into two groups from type 2 diabetic patients referred to Isfahan endocrine and metabolism research center. Eligibility criteria were diet-treated diabetics without history of diabetic complications like renal failure, intake of digoxin <sup>24,25</sup>, carbamazepine or lithium <sup>26,27</sup> (because of their absorptive interaction with psyllium) and also psyllium intake as recent as two weeks. Twelve patients (4 males and 8 females) participated in the present study; 6 in the case group and 6 in the control group (2 males and 4 females in each group). After an overnight fast, participants were enrolled and a fine intravenous catheter was inserted and fasting plasma obtained for glucose. Then, standard 435 kcal breakfasts containing 90 g white bread (240 kcal), 30g medium-fat cheese (75 kcal), and a glass of low-fat cow's milk (120 kcal) were given to participants. Milk in the case group contained 5 grams of psyllium granules (Gol Daru, Iran). The psyllium was added to hot milk for 10 minutes and then provided to the participants. In the control group, milk without psyllium was administered as placebo. Participants of the two groups were blind to the psyllium contents of their milk. The laboratory team and the responsible physician were also blind to case or control participants. Postprandial plasma was obtained at 60 and 120 minutes after eating breakfast and measured for glucose concentration using colorimetric

method (Chem Enzyme, Iran). Results included plasma glucose levels and demographic information collected in questionnaires. Mean plasma glucose at each step was compared between the two groups by independent t-tests and within each group by paired t-tests. Mean plasma glucose changes during each step were also compared between the two groups by t-test. The SPSS software version 11.5 was used for statistical analysis. Data are shown as mean (standard deviation; SD) and P values less than 0.05 are considered statistically significant.

## Results

The mean weight of participants was 72 kg and 68 kg in the case and control groups, respectively and average age was 56 and 57, respectively. Diabetes duration was from 1 to 8 years. Differences in mean (SD) fasting plasma glucose (FPG) was non-significant between control and case groups (138.3 (29.8) mg/dl and 130 (39.7) mg/dl, respectively  $P = 0.69$ ). Mean

(SD) 1-hour postprandial plasma glucose was 192.2 (53) and 147.8 (37.3) mg/dl in control and case groups, respectively ( $P = 0.12$ ). Mean (SD) 2-hour postprandial plasma glucose was significantly different; 167.7 (52.6) and 117.7 (18.5) mg/dl in control and case groups, respectively ( $P = 0.05$ , figure 1). Also, the difference in mean increment of plasma glucose after 1 hour, (1 hour postprandial plasma glucose minus FPG) was significant with 53.83 (34) mg/dl in the control group but only 17.83 (13.5) mg/dl in the case group, ( $P = 0.03$ ). Mean (SD) change of plasma glucose after 2 hours in comparison with 1 hour postprandial, (2 hours postprandial minus 1 hour postprandial plasma glucose) was -24.5 (11.5) mg/dl in control group in comparison with -30.2 (36.3) mg/dl in case group ( $P = 0.72$ ). Finally, the ratio of plasma glucose increment (plasma glucose increment divided by FPG) was also calculated for each participant and presented in table 1.



**Figure 1.** Plasma glucose changes in case and control groups.

**Table 1.** Mean (SD) of plasma glucose and its changes before and after breakfast in psyllium-treated type 2 diabetic patients and control group.

	Psyllium treated N = 6	Control group N = 6	P values
FPG (mg/dl)	130.0 (39.7)	138.3 (29.8)	.690
1hpp (mg/dl)	147.8 (37.3)	192.2 (53.0)	.120
2hpp (mg/dl)	117.7 (18.5)	167.7 (52.6)	.050
1hpp- FPG (mg/dl)	17.8 (13.5)	53.8 (34.0)	.037
1hpp- FPG Ratio	.1585 (.16)	.3854 (.24)	.085
2hpp-1hpp (mg/dl)	-30.2 (36.3)	-24.5 (11.5)	.724
2hpp-1hpp Ratio	-.1717 (.18)	-.1339 (.06)	.655
AUC	16300.0 (3563.4)	20710.0 (5493.1)	.130

#### Abbreviations:

FPG: fasting plasma glucose, 1hpp and 2hpp: 1 and 2 hours postprandial plasma glucose, AUC: area under the curve of plasma glucose, 1hpp-FPG Ratio: One hour post prandial minus fasting plasma glucose divided by fasting plasma glucose, 2hpp-1hpp Ratio: Two hour post prandial minus one hour post prandial plasma glucose divided by one hour post prandial

#### Discussion

The present study was designed to address the effects of psyllium on the kinetics of carbohydrates absorption in type 2 diabetic patients by the assessment of postprandial plasma glucose. As the results revealed, psyllium led to a significant retardation and decrement of postprandial glucose excursions. On the one hand, fasting plasma glucose in the case and control groups were similar (138 mg/dl in control group versus 130 mg/dl in the case group). On the other hand, 1-hour postprandial plasma glucose was 44.34 mg/dl (30%) less in the case group, and 2-hour postprandial plasma glucose in the case group was also 50 mg/dl (42%) less than that in the control group. One different aspect of the present study from other studies was the evaluation of the effects of a single dose of psyllium on the kinetics of carbohydrate absorption based on the plasma glucose changes. This allowed us to compare psyllium with other drugs specifically targeting postprandial plasma glucose. In a similar study, Pastors et al reported psyllium, as a meal supplement, reduced proximate and second-meal postprandial glucose and insulin concentrations in non-insulin-dependent diabetics<sup>28</sup>. In this study, like others, psyllium was tolerated well without any complication.  $\beta$ -cell dysfunction in type 2 diabetic patients is characterized by sluggish insulin production.

Many of these patients are able to maintain near normal fasting plasma glucose, but facing an acute demand, like food intake, their  $\beta$ -cells fail and hyperglycemia occurs. This can be avoided by strategies such as advising diabetic patients to decrease portion size and increase frequency of meals. Also, strategies that retard carbohydrate digestion and absorption can compensate this sluggish  $\beta$  cell function. Drugs like acarbose, which inhibit  $\alpha$  glucosidase, an enzyme essential for terminal step of complex carbohydrate digestion, can help to this option. The above-mentioned relation of postprandial hyperglycemia to cardiovascular mortality uncovers the importance of such strategies. One option for therapy may be rapid-acting insulin injection or stimulating diet-induced insulin production by the  $\beta$ -cells, which meglitinides do but with undesired side-effects<sup>29-34</sup>. Alternatively, these goals can be achieved by slowing ingestion, digestion or absorption of carbohydrates in the gut, which can be achieved by consuming fiber with diet. Wolever<sup>35</sup> determined advantage of taking a soluble fiber supplement separate from food, as opposed to incorporated with food. In that study, psyllium reduced the glycemic response in normal subjects when sprinkled onto or incorporated into the cereal, but not when taken before the cereal. Increasing the amount of psyllium from zero to 20% resulted in a linear dose-

dependent reduction of the glycemic index. In subjects with diabetes, the blood-glucose-lowering effect of the psyllium flake cereal was similar to that in normal subjects <sup>35</sup>. In our study, we mixed psyllium with hot milk and asked participants to drink that with a meal. Anderson reported that the addition of psyllium to a traditional diet for persons with diabetes is safe and well tolerated, and improves glycemic and lipid control in men with type 2 diabetes and hypercholesterolemia <sup>19</sup>. Sierra <sup>21</sup>, Rodriguez-Moran <sup>36</sup> and many others have re-

ported similar results. In conclusion, our pilot study revealed that psyllium can effectively reduce postprandial plasma glucose, possibly by retarding carbohydrate absorption. Efficacy of psyllium may parallel acarbose and repaglinide, without their costs or complications. Larger multi-central studies are needed to confirm the results of this study, define its role compared to acarbose or meglitinides and to search its effects on cardiovascular mortality.

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