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Effect of Psyllium Seed Husk on the Postprandial Glucose Control and Insulin Secretion Dynamics*

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This study was to investigate the effect of psyllium seed husk (PSYL) on postprandial glucose control and insulin secretion dynamics in Sprague-Dawley rats. In experiment 1, the rise in postprandial serum glucose was monitored during a 240-min period using a maltose loading test. In normal rats given 16.6 *mg*/100 g B.W./*ml* of PSYL orally, all the blood glucose levels during the 240-min period did not show statistically significant differences from the corresponding levels in normal rats given water. However, in streptozotocin-induced diabetic rats given the same amount of PSYL, the blood glucose level at 30 min was significantly lower than that in diabetic rats given water, and the peak time of the rise in the postprandial glucose was delayed. In experiment 2, the normal (N) and diabetic (Db) rats were given PSYL (25 *mg*/100 g B.W./*ml*/day) orally for 5 days. Blood samples were collected in order to measure the s-glucose and s-insulin levels. The final s-glucose level at day 5 in Db-PSYL was significantly lower than that in the corresponding control rats (Db-CONT) and the final s-insulin level in Db-PSYL was significantly greater than that in Db-CONT. *In vitro* 40-min pancreas perfusion was performed at day 5 in order to examine the insulin secretion dynamics. Results showed that the amounts of insulin secreted during the first phase (11-20 min) and the second phase (21-40 min) in the Db-PSYL were significantly greater than those in Db-CONT. Therefore, it is concluded that psyllium seed husk could be beneficial for controlling postprandial glucose levels in the stretozotocin-induced diabetic rats, and it may be partially mediated by insulin secretion dynamics.

Key words : Psyllium seed husk, *In vitro* pancreas perfusion, Insulin, Postprandial glucose

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INTRODUCTION

Psyllium seed husk is widely used for therapeutic purposes in certain diseases, including obesity[1] and hyperlipidemia.[2-9] Psyllium consists of a mixture of neutral and acid polysaccharides containing soluble and insoluble fibers.[10] It has been known that dietary fiber has many benefits for diabetes mellitus.[11] However, the types of fibers are crucial because their effects on diabetes could be variable.[12] Soluble fibers are more effective than insoluble fibers in reducing postprandial blood glucose and insulin levels in diabetes.[11,12] The soluble fiber provides viscous solutions that may reduce the surface area of the food particles available for digestion, altering the intraluminal activities, and reducing the rate of diffusion through the contents of the small intestine to enterocytes.[13] In many studies, psyllium has been shown to elicit a lower glycemic responses and improve glucose homeostasis[3,5,14-16] but these usually have been performed in subjects with type 2 diabetes. The purpose of this study, therefore, was to determine the effect of psyllium seed husk on the postprandial glucose control and insulin secretion dynamics in streptozotocin-induced type 1 diabetes.

MATERIALS AND METHODS

Experiment 1: Postprandial Glucose Control

Postprandial glucose control was examined by maltose loading test. Adult male Sprague-Dawley rats (300-370 g B.W.) were fed the commercial rodent pellet diet and water *ad libitum*. Diabetes was induced by intraperitoneal injection of streptozotocin (55 mg/kg B.W., Sigma Chemical Co., St. Louis, USA) dissolved freshly in 0.01 M citrate

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buffer, pH 4.5. Rats having more than 300 mg/dℓ of 12-hr fasting s-glucose level were used in diabetic groups.

Normal and diabetic rats were fasted for 12 hours. Rats in psyllium groups were orally administrated 2 g of maltose per kg B.W. and 16.6 mg/100 g B.W./mℓ psyllium seed husk. Rats in control groups were orally administrated the same dosage of maltose and water. Blood samples were taken from the tail vein after 240 minutes following the maltose load. Serum glucose levels at 0, 30, 60, 90, 120, 180, and 240 min were measured. Glucose levels in serum samples were determined by the kit (Sigma Chemical Co., Saint Louis).

Experiment 2: Insulin Secretion Dynamics

Adult male Sprague-Dawley rats (300-370 g B.W.) were fed the commercial rodent pellet diet and water *ad libitum*, and maintained in a 12 hour light-12 hour dark cycle at room temperature of 23-25 °C. Diabetes was induced as described in the experiment 1. Rats were divided into four groups (n=6/group): normal rats on psyllium seed husk (N-PSYL), normal rats on water as a control group (N-CONT), diabetic rats on psyllium seed husk (Db-PSYL), and diabetic rats on water as a control group (Db-CONT). Rats in PSYL groups were fed on natural psyllium seed husk (Procter & Gamble, Cincinnati, OH, USA, 25 mg/100 g B.W./mℓ/day) for 5 days. Initial and final body weights were measured at day 0 and day 5, respectively. Blood samples were also collected at day 0 and day 5 for the s-glucose and s-insulin measurements. At day 5, *in vitro* pancreas perfusion was performed for insulin secretion dynamics.

The perfusate preparation has been shown in the other study.[17] Briefly, the components of the perfusate were as follows: 0.18% albumin, 4.00% of dextran, 0.110 M of $CaCl_2$, 0.154 M of KCl, KH_2PO_4, $NaHCO_3$, NaCl, and $MgSO_4$. Glucose (200 mg/dℓ), a primary stimulator of insulin secretion, was added using an infusion pump during the 10-40 min of the total perfusion period. The perfusate was continually oxygenated with a 95% O_2-5% CO_2 mixture and maintained at 37 °C using an external heating source. Perfusate inflow rate was maintained at 5 mℓ/min. Pancreas was removed from the rats and perfused using an perfusion apparatus. The perfusate inflow began *via* the heparinized celiac arterial cannula. Total outflow was collected *via* a heparinized portal vein cannula, and its volume was measured. The total venous effluent was collected for 40 min with 2-5 min time intervals. The effluent samples were kept on ice until centrifuged (20 min at 4 °C, 3000 rpm). The supernatant was decanted and frozen at -20 °C until insulin amounts were assayed.

Glucose levels in serum and perfusion samples were determined by the kit (Sigma Chemical Co., Saint Louis). Insulin amounts in the serum and perfusion effluent samples were determined by the rat insulin radioimmunoassay kit (Linco Research, Inc. Saint Charles, USA). Radioisotope detection was carried out using a Cobra auto gamma counting system (Hewlett Packard Instrument Co, USA.). The cpms were counted from triplicated standard tubes and duplicated sample tubes, and the count of the nonspecific binding was subtracted. The bound/free triplicates for each point on the standard curve were averaged and plotted *vs* insulin amounts. For each sample duplicate, the bound/free was read off as insulin amounts (ng/mℓ) from the standard curve. Insulin secretion rates (ng/min) were calculated by using the measured perfusate effluent flow rate (mℓ/min) and the assayed insulin concentrations (ng/mℓ).

Statistical Analysis

All data were expressed as means ± SEM. Student's *t*-test or ANOVA followed by Scheffé test were conducted to determine a statistical significance in difference among mean values of groups. The level of significance was set at $p<0.05$.

RESULTS AND DISCUSSION

Experiment 1: Postprandial Glucose Control

Serum glucose levels of the normal rats during 0-240 min after ingesting maltose were shown in Table 1. In normal rats, serum glucose levels at single points during a whole period of 240 min did not differ statistically between the control group and psyllium group. In both groups, the peak time was 30 min, thereafter the glucose levels declined back to the base line in 240 min.

Serum glucose levels of the diabetic rats were shown

Table 1. Maltose loading test in normal rats fed psyllium seed husk

	s-Glucose levels (mg/dl)						
min	0′	30′	60′	90′	120′	180′	240′
CONT[2] (n=6)	73.6±6.5[1]	144.6±8.4	137.8±6.3	122.0±8.0	106.4±7.4	96.0±7.2	84.0±9.1
PSYL[3] (n=6)	85.5±7.0	128.8±17.5	123.8±13.5	108.0±8.4	104.3±8.6	92.5±4.5	88.5±2.5

There was no a significant difference between all the values between CONT and PSYL.

1) Mean±SEM

2) rats were orally administrated 2 g of maltose per kg B.W. and 1 ml/100 g B.W. of water.

3) rats were orally administrated 2 g of maltose per kg B.W. and 16.6 mg/100 g B.W./ml of psyllium seed husk.

in Table 2. Serum glucose level of diabetic rats in the control group was 339.2±15.0 mg/dℓ at 0 min and 417.7± 19.2 mg/dℓ at 240 min, indicating s-glucose at the end of the period never returned to their base line. The peak time was 30 min with the s-glucose level of 622.4±14.0 mg/dℓ. On the other hand, serum glucose levels of diabetic rats administered psyllium at 0 min and 240 min were 365.5± 12.5 and 357.0±21.0 mg/dℓ, respectively. These results demonstrated that s-glucose levels reached to the base line in 240 min. The peak time in the psyllium group was 60 min with the s-glucose level of 603.5±63.5 mg/dℓ, showing a slower uprising when compared to the diabetic rats in the control group.

The s-glucose levels at 30 min were significantly different between the diabetic rats in the control group (622.4±14.0 mg/dℓ) and those in psyllium groups (546.0± 22.0 mg/dℓ) ($p<0.05$) (Table 2). Therefore, the postprandial rise of glucose was significantly reduced and delayed by psyllium in diabetic rats. It had been reported that psyllium had reducing effects on the rise of blood glucose after the meal[5,14] and decreased glycemic index.[18] It has been reported that the water-soluble, gel-forming fiber such as guar gum, gum tragacanth reduce the expected rise in glucose levels after the glucose solution or meal ingestion in normal subjects and individuals with type 1 and 2 diabetes.[11] Possible explanation for the mechanisms for the postprandial glucose response after psyllium feeding is that the properties of psyllium as a soluble fiber modify the digestion and absorption of maltose in the small intestine. Indeed, Sierra *et al.*[16] reported that the consumption of psyllium decreased glucose absorption by 12.2% in type 2 diabetes patients. Another explanation is that psyllium may enhance the acute phase of insulin secretion from the pancreas, which could be supported by the results from the following Experiment 2.

Table 2. Maltose loading test in diabetic rats fed psyllium seed husk

	s-Glucose levels (mg/dl)						
min	0′	30′*	60′	90′	120′	180′	240′
CONT[2] (n=6)	339.2±15.0[1]	622.4±14.0	609.6±36.9	582.0±30.5	539.8±24.0	471.4±17.9	417.7±19.2
PSYL[3] (n=6)	365.5±12.5	546.0±22.0	603.5±63.5	474.0±30.0	436.0±36.0	399.5±21.5	357.0±21.0

* There was a significance difference between the values between CONT and PSYL using Student's *t*-test at $p<0.05$.
1) Mean±SEM.
2) rats were orally administrated 2 g of maltose per kg B.W. and 1 ml/100 g B.W. of water.
3) rats were orally administrated 2 g of maltose per kg B.W. and 16.6 mg /100 g B.W./ml of psyllium seed husk.

Experiment 2: Insulin Secretion Dynamics

The mean body weights at day 0 (initial) in N-CONT and N-PSYL were 333.2±17.7 g and 300.0±9.0 g, respectively, and did not differ significantly between these two groups. The mean body weights at day 5 (final) showed no difference statistically between the two groups as 348.7±13.7 g in N-CONT and 316.5±12.5 g in N-PSYL. In diabetic rats, no significant differences were found in the mean initial body weights and mean final body weights between Db-CONT and Db-PSYL (initial B.W. of 337.2±21.2 g and 367.0±22.6 g, respectively; final B.W. of 318.2±19.6 g and 339.4±16.2 g respectively).

Initial and final s-glucose levels were shown in Table 3. The initial s-glucose level at day 0 and final s-glucose level at day 5 were comparable between N-CONT and N-PSYL groups, respectively. The initial s-glucose levels were not different between Db-CONT and Db-PSYL groups (396.00±21.2 mg/dℓ and 376.50±20.69 mg/dℓ, respectively). However, the final s-glucose levels were significantly different as 421.33±14.96 mg/dℓ in Db-CONT and 331.83±18.07 mg/dℓ in Db-PSYL ($p<0.05$).

Table 3. Serum Glucose levels in normal and diabetic rats fed psyllium seed husk

s-Glucose levels (mg/dl)	Normal rats		Diabetic rats	
	CONT[2] (n=6)	PSYL[3] (n=6)	CONT (n=6)	PSYL (n=6)
Initial level at day 0	74.83±2.37[a,1]	76.00±4.00[a]	396.00±21.2[b]	376.50±20.69[b]
Final level at day 5	72.40±2.32[a]	79.00±5.00[a]	421.33±14.96[b]	331.83±18.07[c]

Within the same row, values with different superscripts are significantly different by Scheffé test at $p<0.05$.
1) Mean±SEM.
2) Rats were fed on pellet diet and water for 5 days.
3) Rats were fed on pellet diet and psyllium seed husk (25 mg/100 g B.W./ml/day) for 5 days.

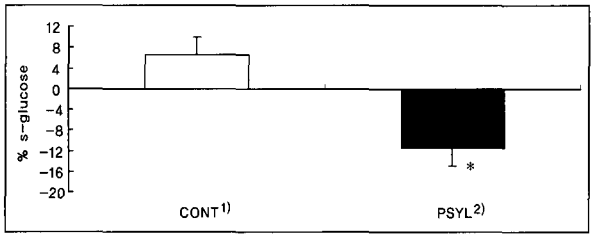

Fig. 1 Percent changes in s-glucose of the diabetic rats fed psyllium husk.

Values represent Mean±SEM (n=6/group).
% s-glucose={(Final glucose level - Initial glucose level)/Initial glucose level}×100
* $p<0.05$ using Student's *t*-test
1) Rats were fed on pellet diet and water for 5 days.
2) Rats were fed on pellet diet and psyllium seed husk (25 mg/100 g B.W./ml/day) for 5 days.

These data indicated the blood glucose lowering effect of PSYL. Fig. 1 showed the percent change in glucose levels between the initial and final levels in the diabetic rats, which was negative in Db-PSYL while positive in Db-CONT ($p<0.05$ between the Db-CONT and Db-PSYL groups). Although several studies have been reported in which psyllium reduced the blood glucose levels, but those reports were conducted in type 2 diabetes.[3,5,14-16] Results in our study clearly showed the s-glucose lowering effect of PSYL even in the type 1 diabetes.

Initial and final s-insulin levels were shown in Table 4. The initial and final s-insulin levels were comparable between N-CONT and N-PSYL groups, respectively. In diabetic rats, the initial s-insulin levels were also similar between Db-CONT and Db-PSYL groups (0.474±0.053 ng/mL and 0.477±0.040 ng/mL, respectively). However, the final s-insulin levels in diabetic rats were significantly different between the Db-CONT (0.288±0.038 ng/mL) and Db-PSYL groups (0.409±0.042 ng/mL) ($p<0.05$). These data demonstrated that psyllium protected against a decrease in s-insulin level and delayed the progression of diabetes. The results from this study were consistent with the study with db/db diabetic mice fed psyllium.[19]

The stimulation-secretion coupling in the pancreatic β-cells is affected by glucose[20] as well as amino acids,[22] Mn,[23] Mg,[24] and Ca.[25] Therefore, the biochemical environment of pancreas may modulate the secretion from the pancreas. In addition, the nervous system is involved in the regulation of insulin secretion from the pancreas.[26-31] Indeed, it has been reported that the insulin secretion is modulated by the sympathetic nervous system[26,30] and parasympathetic nervous system.[29] Besides, the pancreatic islet cells are highly innervated through the autonomic nervous system, and the nerve fibers terminate in the pericapillary space within the capillary basement membrane, or the nerve fibers are closely apposed to endocrine cells in the pancreas.[20] Therefore, the neural inputs could be important in the regulation of insulin secretion from the pancreas. Other factors influencing insulin secretion could be other hormones.[27),28] The method used in this study was able to determine the direct effect of glucose on the insulin release from the pancreas without any above primary and secondary metabolic, neural, and hormonal influences on the secretory process, since *in vitro* perfusion used allows the anatomical isolation.

The amount of insulin secretion during the 40 min of perfusion period was shown in Table 5. In normal rats, the amounts of insulin secretion during the first 10 min of the equilibration period were comparable between N-CONT and N-PSYL groups. During the next 11-20 min of the first phase of secretion and 21-40 min of the second phase of the secretion, significant differences in N-CONT and N-PSYL groups were not seen either. Therefore, PSYL may not influence the insulin secretion from the pancreas of normal rats.

On the other hand, the insulin secretion dynamics in diabetic rats was appeared quite different in the normal rats. The amounts of insulin secretion during the first 10 min of the equilibration period were 3.07±0.53 ng/300g B.W. in Db-CONT and 7.84±1.51 ng/300 g B.W. in Db-PSYL ($p<0.05$ between Db-CONT and Db-PSYL groups). The amount of insulin secreted during this perfusion period in Db-PSYL was about 2.6 times greater than that in Db-CONT. During the next 11-20 min of the first phase, the amount of insulin secretion in CONT group was 6.17±2.34 ng/300 g B.W. and was 14.53±1.14 ng/

Table 4. Serum insulin levels in normal and diabetic rats fed psyllium seed husk

s-Insulin levels (ng/ml)	Normal rats		Diabetic rats	
	CONT[2] (n=6)	PSYL[3] (n=6)	CONT (n=6)	PSYL (n=6)
Initial level at day 0	0.759±0.056[a,1]	0.863±0.092[a]	0.474±0.053[b]	0.477±0.040[b]
Final level at day 5	0.615±0.097[a]	0.620±0.156[a]	0.288±0.038[b]	0.409±0.042[c]

Within the same row, values with different superscripts are significantly different by Scheffé test at $p<0.05$.
1) Mean±SEM.
2) Rats were fed on pellet diet and water for 5 days.
3) Rats were fed on pellet diet and psyllium seed husk (25 mg/100 g B.W./ml/day) for 5 days.

Table 5. Amounts of insulin secretion from the perfused pancreas of normal and diabetic rats

Period	Normal rats		Diabetic rats	
	CONT[2] (n=6)	PSYL[3] (n=6)	CONT (n=6)	PSYL (n=6)
Equilibration[4] (0-10 min)	16.02±2.90[a,1]	18.29±4.72[a]	3.07±0.53[b]	7.84±1.51[b]
First phase[5] (11-20 min)	128.08±13.89[a]	116.09±16.10[a]	6.17±2.34[b]	14.53±1.14[c]
Second phase[5] (21-40 min)	104.08±13.33[a]	101.88±32.88[a]	1.94±0.97[b]	7.23±0.72[c]

Within the same row, values with different superscripts are significantly different by Scheffé test at $p<0.05$.
Unit of insulin secretion amount : ng/period/300 g B.W.
1) Mean±SEM.
2) Rats were fed on pellet diet and water for 5 days.
3) Rats were fed on pellet diet and psyllium seed husk (25 mg/100 g B.W./ml/day) for 5 days.
4) period of no glucose stimulation
5) period of 200mg/dl glucose stimulation

300 g B.W. in PSYL ($p<0.05$ between Db-CONT and Db-PSYL groups). The pancreas in Db-PSYL secreted insulin about 2.4 times greater than that in Db-CONT during this perfusion period. During the second phase, the amount of insulin secretion in the CONT group was 1.94±0.97 ng/300 g B.W. and was 7.23±0.72 ng/300 g B.W. in PSYL ($p<0.05$ between Db-CONT and Db-PSYL groups). During this last period of 21-40 min, the total amount of insulin secreted in Db-PSYL was about 3.7 times greater than that in Db-CONT. These data showed that PSYL significantly stimulated the insulin secretion from the pancreas in the diabetic rats, although the absolute amount was still in the lower range when compared to those in the non-diabetic normal rats.

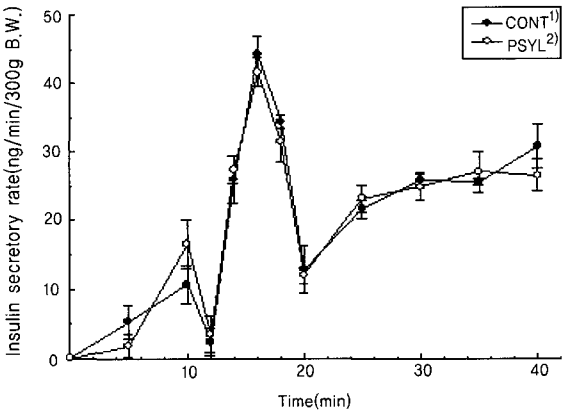

Fig. 2 Insulin secretion dynamics in the normal rats fed on psyllium seed husk.

Values represent Mean±SEM (n=6/group).
Glucose (200 mg/dl) was given at 10 min during a 40 min-perfusion period.
1) Rats were fed on pellet diet and water for 5 days.
2) Rats were fed on pellet diet and psyllium seed husk (25 mg/100 g B.W./ml/day) for 5 days.

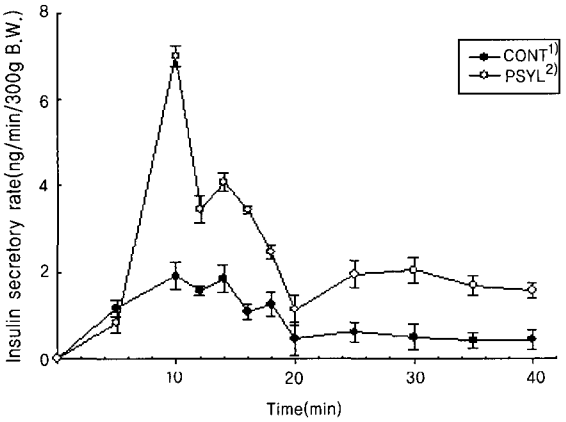

Fig. 3 Insulin secretion dynamics in the diabetic rats fed on psyllium seed husk.

Values represent Mean±SEM (n=6/group).
Glucose(200 mg/dl) was given at 10 min during a 40 min-perfusion period.
1) Rats were fed on pellet diet and water for 5 days.
2) Rats were fed on pellet diet and psyllium seed husk (25 mg/100 g B.W./ml/day) for 5 days.

In Fig. 2, the dynamics of insulin secretion from the pancreas of normal rats was shown. In both N-CONT and N-PSYL groups, the first peaks during the equilibration period (0-10 min) were clearly seen, indicating the normal secretory pattern. The first (11-20 min) and second (21-40 min) phases of insulin secretion were also observed in both groups, which were the typical secretory pattern. Insulin secretion in this study showed a biphasic pattern, which was consistent with the pattern observed in other studies reported by Curry *et al.*.[32),33)] A peak of insulin secretion during the first secretory phase was seen at around 16 min in both of the N-CONT and N-PSYL groups, showing a normal pattern of insulin dynamics. In Fig. 3, the dynamics of insulin secretion from the pancreas of diabetic rats was shown. In Db-CONT groups, all the peaks appeared to be blunted. However in the Db-PSYL group, the first peak was shown around at 10 min and followed by the second peak although it was characterized as much lower than the first peak in the curve. In light of the present results, it is possible that psyllium could protect the pancreatic β cells from further deterioration or even enhance the remaining β cell function. It has been reported that propionic and butyric acids, the end products of fiber fermentation in the large intestine, may have insulinotropic effects.[34)] However, which constituent of psyllium acts as an insulin stimulating factor could not be elucidated in this study. Moreover, the long-term effects of psyllium need to be studied while this short-term study may have implications in terms of reducing blood glucose levels and insulin secretion.

In conclusions, our results showed that the psyllium seed husk had a beneficial effect for the postprandial blood control, thus psyllium seed husk can be used as a diet supplement with meal. Psyllium appears to restore the insulin secretory dynamics, however, further studies with pancreatic β-cells are needed to clarify its effects and the mechanism involved.

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