Pinitol from Soybeans Reduces Postprandial Blood Glucose in Patients with Type 2 Diabetes Mellitus

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ABSTRACT The effect of 3-O-methyl-D-chiro-inositol (D-pinitol), purified from soybean, on the postprandial blood glucose response in patients with type 2 diabetes mellitus was examined. Fifteen Korean subjects with type 2 diabetes mellitus (seven men, eight women; 60.3 ± 3.1 years old) ingested cooked white rice containing 50 g of available carbohydrate with or without prior ingestion of soy pinitol. Pinitol was given either as a 1.2 g dose at 0, 60, 120, or 180 minutes prior to rice ingestion, or as a 0.6 g dose at 60 minutes prior to rice ingestion. Capillary blood glucose levels were monitored for 4 hours after rice consumption. The ingestion of 1.2 g of pinitol 60 minutes prior to rice consumption controlled postprandial capillary blood glucose most effectively, significantly diminishing the postprandial increase in plasma glucose levels measured at 90 and 120 minutes after rice consumption (P < .05). The incremental area under the plasma glucose response curve for subjects who consumed both pinitol and rice was significantly lower than that for subjects who consumed only rice (P < .05), but pinitol had no apparent effect on postprandial insulin levels. Therefore, soybean-derived pinitol may be useful in controlling postprandial increases in blood glucose in patients with type 2 diabetes.

KEY WORDS: • diabetes • glucose • insulin • pinitol • soybean

INTRODUCTION

The prevalence of diabetes mellitus is increasing worldwide, and it will be a major health problem in the 21st century. The worldwide prevalence of diabetes mellitus was estimated to be 177 million cases in 2000 and is projected to increase to 366 million by 2030,1 largely owing to an aging population, increased urbanization, and more sedentary lifestyles.2 Diabetes is one of the five leading causes of death in most developed countries, and it is predicted to exceed both heart disease and cancer as the leading cause of death (through complications) by the year 2010.3

Type 2 diabetes mellitus, which accounts for more than 90% of diabetes cases, results from defects in insulin action.4 Cardiovascular disease (CVD), a major complication of diabetes, is the leading cause of premature death among patients with diabetes.5 In prospective randomized clinical trials, achieving near-normal glycemic control in patients with diabetes mellitus was associated with sustained, decreased rates of diabetic complications, including CVD.5,7 Avignon et al.8 have reported that in patients with type 2 diabetes postprandial glucose levels are a better marker of glycemic control than are fasting blood glucose levels. They found that postprandial plasma glucose levels, but not fasting blood glucose levels, correlated significantly with glycated hemoglobin levels. In addition, microvascular and macrovascular complications are associated with postprandial hyperglycemia but not with fasting blood glucose levels.9–12

3-O-Methyl-D-chiro-inositol (D-pinitol) appears to exert insulin-like effects.13–17 The administration of pinitol reduces blood glucose levels in streptozotocin-induced diabetic mice13 and in alloxan-induced diabetic rats.14 D-chiro-inositol, a metabolic product of pinitol, which improves glucose tolerance in normal rats,15 is a component of an inositol phosphoglycan16 that mediates insulin action.17 Soybeans are a good source of pinitol, and pinitol with high purity has been isolated from soybeans.18 If soybean-derived pinitol were to alleviate postprandial hyperglycemia, it could be useful in preventing complications of diabetes. In this study, we examined the effects of soy pinitol administration, at various dosages and lengths of time before cooked white rice consumption, on postprandial glucose and insulin responses in patients with type 2 diabetes.

MATERIALS AND METHODS

Materials

Soybean pinitol was a generous gift from Amicogen, Inc. (Jinju, Korea). Pinitol of 95% purity was prepared from soybeans by water extraction, chromatographic separation us-
The ingestion of 1.2 g of pinitol 60 minutes prior to rice consumption controlled postprandial capillary blood glucose the most effectively. Therefore, the effect of 1.2 g of pinitol on postprandial plasma glucose and insulin was also determined. Venous blood samples were collected at 0, 60, 90, 120, 180, and 240 minutes after the consumption of rice. Plasma glucose was measured using a glucose oxidase kit purchased from Sigma (St. Louis, MO), and insulin levels were measured using a radioimmunoassay kit from Linco (St. Charles, MO). The glucose and insulin response tests were administered on four separate occasions, with 2-week intervals. Capillary glucose and plasma glucose and insulin levels were expressed as increments from baseline. Incremental area under the response curve (AUC) values were calculated using the trapezoidal rule with fasting levels as the baseline. Results are expressed as the average of repeat measurements.

During the study, the patients were asked to avoid legumes and citrus fruits but not to otherwise change their usual medications, diets, or lifestyles. The study protocol was approved by the Institutional Review Board of Pusan Paik Hospital (Busan, Republic of Korea). Informed consent was obtained from all subjects prior to their entry into the study.

### Statistical analysis

All data are shown as mean ± standard error of the mean. Differences among the incremental capillary glucose levels and AUC of the groups were assessed by analysis of variance using Duncan’s test as a follow-up test. Differences between incremental plasma glucose and insulin levels and AUC of the control and pinitol groups were assessed using a paired t test. Significance was defined as P < .05.

### RESULTS

All 15 patients completed the study. Pinitol was found to be generally well tolerated. The demographic and metabolic parameters of the patients at baseline are given in Table 1. The mean body mass index of the participants was 24.5 ± 0.7 kg/m². The mean fasting plasma glucose, insulin, and

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.3 ± 3.1</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>7.1 ± 1.4</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.5 ± 0.7</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>30.4 ± 1.4</td>
</tr>
<tr>
<td>Glycated hemoglobin (%)</td>
<td>8.9 ± 0.3</td>
</tr>
<tr>
<td>Plasma glucose (mg/dL)</td>
<td>144.9 ± 8.7</td>
</tr>
<tr>
<td>Plasma insulin (µU/mL)</td>
<td>16.0 ± 1.8</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>137.5 ± 7.1</td>
</tr>
<tr>
<td>Diastolic</td>
<td>89.3 ± 15.2</td>
</tr>
</tbody>
</table>

Data are mean ± standard error of the mean (SEM) values.

The principal contaminants were oligosaccharides and water.

### Subjects and methods

Fifteen Korean patients with uncomplicated type 2 diabetes mellitus (seven men, eight women; 60.3 ± 3.1 years old; duration of diabetes, 7.1 ± 1.4 years) participated in the study. After an overnight fast, patients ingested cooked white rice containing 50 g of available carbohydrate (64.2 g of rice) with or without prior ingestion of soy pinitol. Pinitol was given either as a 1.2 g dose at 0, 60, 120, or 180 minutes prior to rice ingestion or as a 0.6 g dose at 60 minutes prior to rice ingestion. The rice was ingested with 400 mL of lukewarm water and was consumed within 15 minutes. Finger-prick capillary blood glucose was measured at 0, 30, 60, 90, 120, 180, and 240 minutes after rice consumption, using an Accutrend-Glucose® Glucometer (Boehringer Mannheim, Mannheim, Germany). The tests were administered in a random order to each subject on 10 separate occasions, spaced at least 2 weeks apart.

The ingestion of 1.2 g of pinitol 60 minutes prior to rice consumption controlled postprandial capillary blood glucose

### Table 2. Incremental Capillary Glucose at Various Lengths of Time After Cooked White Rice Consumption in Patients with Type 2 Diabetes Mellitus Pretreated with Soy Pinitol

<table>
<thead>
<tr>
<th>Treatment (in g; minutes)</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
<th>180</th>
<th>240</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rice</td>
<td>65.5 ± 5.6</td>
<td>119.3 ± 6.7</td>
<td>122.5 ± 8.0</td>
<td>108.7 ± 8.0</td>
<td>65.7 ± 9.7</td>
<td>22.5 ± 9.4</td>
</tr>
<tr>
<td>Rice and pinitol (1.2; 0)</td>
<td>51.5 ± 5.3</td>
<td>116.0 ± 6.5</td>
<td>120.4 ± 7.9</td>
<td>96.4 ± 6.4</td>
<td>53.0 ± 10.3</td>
<td>18.2 ± 10.4</td>
</tr>
<tr>
<td>Rice and pinitol (1.2; 60)</td>
<td>55.5 ± 6.2</td>
<td>92.3 ± 6.3</td>
<td>92.9 ± 6.9b</td>
<td>73.6 ± 5.0b</td>
<td>32.8 ± 10.4</td>
<td>−5.0 ± 10.6</td>
</tr>
<tr>
<td>Rice and pinitol (1.2; 120)</td>
<td>61.8 ± 6.0</td>
<td>107.4 ± 7.0</td>
<td>117.7 ± 6.6</td>
<td>105.4 ± 8.3</td>
<td>63.6 ± 9.1</td>
<td>28.9 ± 11.0</td>
</tr>
<tr>
<td>Rice and pinitol (1.2; 180)</td>
<td>56.7 ± 5.3</td>
<td>112.2 ± 7.0</td>
<td>122.8 ± 7.6</td>
<td>110.6 ± 8.0</td>
<td>65.0 ± 10.0</td>
<td>26.2 ± 11.3</td>
</tr>
<tr>
<td>Rice and pinitol (0.6; 60)</td>
<td>58.4 ± 7.1</td>
<td>119.6 ± 8.6</td>
<td>125.4 ± 8.0</td>
<td>100.5 ± 6.8</td>
<td>52.6 ± 10.4</td>
<td>18.3 ± 7.9</td>
</tr>
</tbody>
</table>

Data are mean ± standard error of the mean values.

aNumber in parentheses are (grams of soy pinitol ingested; minutes prior to ingestion of cooked rice that soy pinitol was administered).
bValues are significantly different at P < .05.
blood glycated hemoglobin levels were 144.9 ± 8.7 mg/dL, 16.0 ± 1.8 µU/mL, and 8.9 ± 0.3%, respectively.

Capillary glucose increases at 60, 90, 120, and 240 minutes after rice consumption were 119.3 ± 6.7, 122.5 ± 8.0, 108.7 ± 8.0, and 22.5 ± 9.5 mg/dL (Table 2). The ingestion of 1.2 g of pinitol 60 minutes before rice consumption significantly inhibited the increase in blood glucose levels measured at 90 minutes (17,884 ± 1,247 mg·min/dL) and 120 minutes (16,387 ± 1,247 mg·min/dL) compared with the increases in patients who consumed rice only, rice with 1.2 g of pinitol administered at 0, 120, or 180 minutes, or rice with 0.6 g of pinitol administered 60 minutes before rice consumption (P < .05). Patients who consumed 1.2 g of pinitol 60 minutes before consuming the rice had a capillary glucose incremental AUC of 12,326 ± 882 mg·min/dL. This response was significantly lower than that of the patients who consumed rice only (17,884 ± 1,247 mg·min/dL), the patients who ingested 1.2 g of pinitol at 0 minutes (16,387 ± 1,247 mg·min/dL), 120 minutes (17,209 ± 1,257 mg·min/dL), or 180 minutes (17,805 ± 1,078 mg·min/dL), or the patients who ingested 0.6 g of pinitol 60 minutes (16,741 ± 1,268 mg·min/dL) prior to consuming rice (Table 3, P < .05).

Since the ingestion of 1.2 g of pinitol 60 minutes prior to rice consumption controlled postprandial capillary blood glucose the most effectively, we measured its effect on postprandial plasma glucose and insulin responses. The ingestion of 1.2 g of pinitol 60 minutes prior to rice consumption significantly decreased postprandial plasma glucose increases at 60, 90, 120, and 180 minutes (P < .05) compared with the increases in patients who consumed only rice (Fig. 1). The ingestion of pinitol did not significantly affect postprandial plasma insulin levels (Fig. 2). As shown in Table 4, the plasma glucose incremental AUC for patients who

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### Table 3. Incremental AUC of Capillary Glucose After Consumption of Cooked White Rice and Soy Pinitol in Patients with Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Pinitol (g)</th>
<th>Minutes</th>
<th>AUC (mg·min/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rice</td>
<td>1.2</td>
<td>0</td>
<td>16,387 ± 1,247</td>
</tr>
<tr>
<td>Rice and pinitol</td>
<td>1.2</td>
<td>60</td>
<td>12,326 ± 882</td>
</tr>
<tr>
<td>Rice and pinitol</td>
<td>1.2</td>
<td>120</td>
<td>17,209 ± 1,257</td>
</tr>
<tr>
<td>Rice and pinitol</td>
<td>1.2</td>
<td>180</td>
<td>17,805 ± 1,078</td>
</tr>
<tr>
<td>Rice and pinitol</td>
<td>0.6</td>
<td>60</td>
<td>16,741 ± 1,268</td>
</tr>
</tbody>
</table>

Data are mean ± standard error of the mean values.

aGrams of soy pinitol ingested.

bMinutes prior to ingestion of cooked rice that soy pinitol was administered.

cValues are significantly different at P < .05.

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### Table 4. Incremental AUC of Plasma Glucose and Insulin After Consumption of Cooked White Rice and Soy Pinitol

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Glucose (mg·min/dL)</th>
<th>Insulin (µU·min/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rice</td>
<td>17,327 ± 1,527</td>
<td>2,835 ± 608</td>
</tr>
<tr>
<td>Rice and pinitola</td>
<td>13,170 ± 1,050b</td>
<td>2,570 ± 418</td>
</tr>
</tbody>
</table>

Data are mean ± standard error of the mean values.

aSoy pinitol (1.2 g) was administered 60 minutes before rice consumption.

bValues are significantly different at P < .05.
consumed pinitol and rice (13.170 ± 1.050 mg · min/dL) was significantly lower (P < .05) than that for patients who consumed only rice (17.327 ± 1.527 mg · min/dL). The plasma insulin AUC for patients who consumed pinitol and rice (2.570 ± 418 μU · min/mL) was not significantly different from that for patients who consumed only rice (2.835 ± 608 μU · min/mL).

DISCUSSION

Patients with type 2 diabetes mellitus suffer a two- to fourfold increased risk of developing CVD, and approximately 80% of all patients with diabetes die of CVD. It is well documented that elevated 2-hour postprandial glucose excursions are associated with an increased risk of atherosclerosis and CVD. Therefore, interventions aimed at lowering the 2-hour postprandial blood glucose may be important in reducing diabetic complications and mortality.

In this study, we measured the effect of soy pinitol, administered at various dosages and lengths of time prior to cooked white rice consumption, on postprandial blood glucose in Korean patients with type 2 diabetes. Cooked white rice was used as a reference meal because white rice is a staple of the Korean diet. The ingestion of 1.2 g of pinitol at 60 minutes prior to the consumption of cooked rice was found to be more effective in controlling capillary blood glucose than was the consumption of rice alone, or rice with prior consumption of 1.2 g of pinitol at 0, 120, or 180 minutes or of 0.6 g of pinitol at 60 minutes. This treatment significantly decreased postprandial plasma glucose levels at 90 and 120 minutes. The ingestion of pinitol was associated with a statistically significant reduction (24.0%) in the plasma glucose incremental AUC, but had little influence on the insulin response AUC.

Bates et al. demonstrated that acute oral administration of D-pinitol to streptozotocin-induced diabetic mice produced a decrease in plasma glucose over 6 hours but not plasma insulin. In this study acute administration of soy pinitol was effective in controlling postprandial glucose level without a significant effect on plasma insulin levels in patients with type 2 diabetes. It was reported that D-pinitol increased glucose uptake by muscle cells. Thus it was suggested that D-pinitol could act via a post-receptor pathway of insulin action affecting glucose uptake.

Pinitol, a natural component of plants, is converted to D-chiro-inositol in the body, which may be a component of an inositol phosphoglycan. Inositol phosphoglycans are potentially important post-receptor mediators of insulin action. D-chiro-Inositol-containing phosphoglycan has been shown to activate both glycogen synthase phosphatase and pyruvate dehydrogenase phosphatase, which are involved in activating glucose metabolism. Thus, the soy pinitol administered in this study could interact with a pathway of insulin signaling resulting in flattening of the postprandial glucose response in patients with type 2 diabetes. Since cardiovascular complications are associated with postprandial hyperglycemia, chronic consumption of soy pinitol could be beneficial in preventing the cardiovascular complications of type 2 diabetes.

ACKNOWLEDGMENTS

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