Effects of pre-germinated brown rice (PGBR) on streptozotocin-induced diabetic rats were studied. The feeding of a PGBR diet to diabetic rats ameliorated the elevation of blood glucose and PAI-1 concentrations significantly, and tended to decrease the plasma lipid peroxide concentrations in comparison with rats fed a white rice diet. These results suggest that intake of PGBR instead of white rice is effective for the prevention of diabetic vascular complications.

Key words: pre-germinated brown rice; white rice; type-1 plasminogen activator inhibitor (PAI-1); diabetes

Diabetic macrovascular complications associated with hyperglycemia and hyperlipidemia have been demonstrated to be linked with the mortality among diabetic patients. An increased plasma concentration of type-1 plasminogen activator inhibitor (PAI-1) has been observed in type 2 diabetic patients with vascular diseases. PAI-1 is the major physiological inhibitor of tissue-type PA (tPA) and urokinase-type PA (uPA). Both tPA and uPA convert a zymogen plasminogen into an active enzyme, plasmin. Impaired fibrinolytic potential due to the increased level of plasma PAI-1 has been shown to be a major risk factor for myocardial infarction in diabetes mellitus. Increased oxidative stress in the hyperglycemia has also been recognized as a causative factor of vascular damage. Thus the hyperglycemia is thought to be one of the important risk factors for vascular complications in diabetes mellitus.

Pre-germinated brown rice (PGBR) has recently been widely served in Japan. PGBR had been developed industrially in order to improve the nutritional functions of its source material, brown rice. PGBR can be produced by soaking brown rice in water for slight germination. Amounts of some constituents including γ-aminobutyric acid (GABA) are greatly increased in PGBR. It has been reported that GABA and its related enzymes are located in pancreatic beta cells and that GABA stimulates insulin secretion from the pancreas. Thus PGBR or its ingredient is thought to ameliorate the disorders such as diabetes, although there is little scientific evidence regarding nutritional function.

In this study the effects of long-term intake of PGBR on the diabetic parameters was examined in comparison with the intake of white rice. We have especially focused on the effects of PGBR on plasma PAI-1 concentration which contributes to increase the mortality rate of diabetic patients, and found the facts that as compared to white rice, PGBR intake could ameliorate hyperglycemia and concomitant increase of plasma PAI-1 concentrations in the experimentally-induced diabetic rats.

All animal experiments were done in accordance with institutional guidelines established by the Laboratory Animal Care and Use Committee of Nihon University College of Bioresource Sciences. Male Wistar strain rats (Nippon Bio-Suppl., Tokyo, Japan), weighing 100 g, received intraperitoneal injection of streptozotocin (65 mg/kg, dissolved in 100 mmol/l sodium citrate buffer, pH 4.5; Wako Pure Chemical Inc. Ltd., Osaka, Japan). Control rats received only the same volume of sodium citrate buffer. The rats were kept on a standard diet (CE-2, CLEA JAPAN Inc., Tokyo, Japan) for 13 days after the streptozotocin injection, and then divided into four groups: Non-diabetic rats fed white rice diet (NW), non-diabetic rats fed PGBR diet (NB), diabetic rats fed white rice diet (DW), diabetic rats fed PGBR diet (DB). These rats were allowed free access to the experimental diets and water for 7 weeks. AIN-93G (Oriental Yeast Co., Ltd., Tokyo, Japan) containing 53% corn-starch was used as basic diet. Corn-starch of AIN-93G was replaced with white rice powder for the “white rice diet” or replaced with PGBR powder (FANCL Co., Kanagawa, Japan) for the “PGBR diet”. White rice powder contained (per 100 g of powder) water, 15.8 g; protein, 5.7 g; fat, 1.7 g; carbohydrate, 75.7 g; dietary

Note

The Effect of Pre-germinated Brown Rice Intake on Blood Glucose and PAI-1 Levels in Streptozotocin-induced Diabetic Rats

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Abbreviations: PGBR, pre-germinated brown rice; PAI-1, type-1 plasminogen activator inhibitor; tPA, tissue-type plasminogen activator; uPA, urokinase-type plasminogen activator; TBA, thiobarbituric acid; LDL, low density lipoprotein


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fiber, 0.6 g; Ca, 4.7 mg; Mg, 32.2 mg; thiamine, 0.11 mg; total tocopherols, 0.3 mg; and free γ-aminobutyric acid, 3 mg. PGBR powder contained (per 100 g of powder) water, 14.7 g; protein, 6.9 g; fat, 2.5 g; carbohydrate, 72 g; dietary fiber, 2.7 g; Ca, 8.8 mg; Mg, 117 mg; thiamine, 0.37 mg; total tocopherols, 1.3 mg; free γ-aminobutyric acid, 15 mg. Amounts of food intake and body weight were measured every day, and blood glucose was measured by DEXTER-Z II (Bayer Medical Co., Ltd., Leverkusen, Germany) once a week using blood obtained from the tail vein. The rats were starved for 18 hours before the measurement of blood glucose concentration. Serum triglyceride concentration was measured by using a commercial kit (Wako Pure Chemical Inc., Ltd.). Plasma PAI-1 concentration was measured by an ELISA system using anti-rat PAI-1 rabbit IgG (American Diagnostica Inc., CT, USA) and recombinant rat PAI-1 (American Diagnostica Inc.) as standards. The plasma lipid peroxide concentration was measured by SRL Inc. (Tokyo, Japan) using thiobarbituric acid (TBA) method. Serum insulin concentration was measured by a commercial ELISA kit (LBIS™, Shibayagi Co., Ltd., Gunma, Japan).

Total amounts of food intake during the 7-weeks experimental period were not significantly different between the white rice group and the PGBR group in both normal and diabetic rats, however, the rats tended to prefer the PGBR diet rather than white rice diet (Table 1). The modest body weight gain which would be due to the metabolic disorder with diabetes was observed in the diabetic group, but there was no significant difference between white rice and PGBR diet groups in both normal and diabetic groups (Table 1). The serum triglyceride level of the diabetic group was increased as compared to that of normal group, although there was no significant difference among the groups (Table 1).

Blood glucose concentrations were mostly equal between normal rat groups, NW and NB, throughout the experimental period. Whereas in the diabetic group, blood glucose concentration was lower in the rat fed PGBR (DB) than that in white rice fed rats (DW) (Fig. 1). These results are very similar to those obtained from a human study; the glycemic index obtained from volunteers taking PGBR was significantly lower than that of those who were taking the white rice (unpublished data). The blood glucose-lowering effect of PGBR may be derived from the properties of PGBR involving substantially higher content of dietary fiber than white rice (about 5-fold, as described before), and PGBR exhibits the lower postprandial glycemic response. Intake of barley containing high dietary fiber is known to reduce the fasting plasma glucose, plasma cholesterol, and triglyceride levels in spontaneous diabetic rat. Therefore, the tendency to lower the serum triglyceride elevation in DB group may also be derived from dietary fiber in PGBR.

**Table 1.** Total Amount of Food Intake, Body Weights and Serum Triglyceride of Rats Fed Either White Rice or Pre-germinated Brown Rice.

<table>
<thead>
<tr>
<th></th>
<th>Total amount of food intake (g)</th>
<th>Body weight (g)</th>
<th>Triglyceride (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 time 7 weeks</td>
<td>7 weeks</td>
<td></td>
</tr>
<tr>
<td>NW</td>
<td>1387±34</td>
<td>178.0±3.2</td>
<td>532.4±14.5</td>
</tr>
<tr>
<td>NB</td>
<td>1422±46</td>
<td>179.4±2.5</td>
<td>530.3±15.3</td>
</tr>
<tr>
<td>DW</td>
<td>1496±63</td>
<td>123.0±7.0</td>
<td>156.5±16.7</td>
</tr>
<tr>
<td>DB</td>
<td>1546±30</td>
<td>119.5±6.1</td>
<td>167.7±13.5</td>
</tr>
</tbody>
</table>

NW, normal rats fed white rice diet (n=8); NB, normal rats fed PGBR diet (n=7); DW, diabetic rats fed white rice diet (n=4); DB, diabetic rats fed PGBR diet (n=5). Triglyceride concentration was measured by a commercial kit as described in the text. Each value represents the mean±S.E.

![Fig. 1. Blood Glucose Concentration of Rats Fed Either White Rice or PGBR.](image-url)

NW, normal rats fed white rice diet (n=8); NB, normal rats fed PGBR diet (n=7); DW, diabetic rats fed white rice diet (n=4); DB, diabetic rats fed PGBR diet (n=5). Blood glucose concentrations were measured as described in the text. Each value represents the mean±S.E. Absence of error bars for a given data point indicated that S.E. is smaller than the size of symbol. The statistical analysis was done by the Student’s t-test. *P < 0.05 vs. DW.
concentration was also measured in this study: NW, 1.51±0.53; NB, 1.04±0.35; DW, 0.29±0.07; DB, 0.62±0.15 ng/ml. In the diabetic rats, the plasma insulin concentration was correlated with plasma PAI-1 and glucose concentrations.

Oxidative stress occurring as a consequence of hyperglycemia is known to play a central role in the pathogenesis and progression of diabetes and its complication. In this study, the plasma lipid peroxide concentration was significantly increased in the diabetic rats fed white rice (DW) in comparison with normal rats fed either white rice or PGBR. In the diabetic rats, feeding of PGBR tended to decrease the plasma lipid peroxide concentration in comparison with the feeding of white rice, although there was no statistic significance between both groups (DW vs. DB). This peroxide-lowering effect is considered to be derived from not only antioxidative vitamin (tocopherol) which is contained highly in PGBR but also other factors effective in preventing the increase in blood glucose concentration. Moreover, it has been reported that the oxidized LDL induces PAI-1 production in vascular endothelial cells. Therefore, the antioxidative effect of PGBR would be one of the factors in preventing the elevation of plasma PAI-1 concentration in DB group. Taken together, the findings obtained from this study indicate that there is potential benefit from the intake of PGBR instead of white rice in the prevention of diabetic vascular complications such as ischemic heart disease.

In summary, PGBR ameliorated the blood glucose, plasma PAI-1, and lipid peroxide concentrations in diabetic rats in comparison with these parameters of diabetic rats fed white rice. These effects might be derived from the properties of PGBR that include substantially higher contents of functional components such as tocopherols, dietary fiber, GABA and other unknown factor(s), and from the property to exhibit the lower postprandial glycemic response.

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