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# Effects of Pre-Germinated Brown Rice on Blood Glucose and Lipid Levels in Free-Living Patients with Impaired Fasting Glucose or Type 2 Diabetes

Tzu-Fang HSU[1], Mitsuo KISE[2], Ming-Fu WANG[3], Yukihiko ITO[2], Mei-Due YANG[3], Hiromichi AOTO[2], Rie YOSHIHARA[4], Jyunichi YOKOYAMA[4], Daisuke KUNII[1] and Shigeru YAMAMOTO[1,5,*]

[1] *Institute of Health Biosciences, The University of Tokushima, Tokushima 770–8503, Japan*
[2] *FANCL Research Institute, FANCL Corporation, Yokohama 224–0806, Japan*
[3] *Department of Food and Nutrition, Providence University, Taichung 43301, Taiwan*
[4] *Jikei University School of Medicine, Tokyo 112–8610, Japan*
[5] *Ochanomizu University Graduate School of Humanities and Sciences, Tokyo, Japan.*

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***Summary*** White rice (WR) is made by polishing brown rice (BR) and has lost various nutrients; however, most people prefer it to BR, maybe because of the hardness of BR. Pre-germinated brown rice (PGBR) improves the problem of BR. It is made by soaking BR kernels in water to germinate and becomes softer than BR. In this study we compared the effects of WR and PGBR on blood glucose and lipid concentrations in the impaired fasting glucose (IFG) or type 2 diabetes patients. Six men and 5 women with impaired fasting glucose (IFG) or type 2 diabetes were randomly allocated to 6 wk on WR or PGBR diet separated by a 2 wk washout interval in a crossover design. Each subject was instructed to consume 3 packs of cooked WR or PGBR (180 g/pack) daily in each intervention phase. Blood samples were collected 4 times (in study weeks 0, 6, 8 and 14) for biochemical examination. Blood concentrations of fasting blood glucose, fructosamine, serum total cholesterol and triacylglycerol levels were favorably improved on the PGBR diet ($p<0.01$), but not on the WR diet. The present results suggest that diets including PGBR may be useful to control blood glucose level.

***Key Words*** white rice, pre-germinated brown rice, impaired fasting glucose (IFG), type 2 diabetes

The incidence of type 2 diabetes continues to rise in the world. Onset of type 2 diabetes closely involves genetics and environmental factors, and diet represents one of the important environmental factors. For example, a high-carbohydrate diet increases postprandial levels of blood glucose and insulin, and long-term consumption leads to insulin resistance (*1*). Furthermore, insulin resistance increases risk for diabetes, obesity and coronary artery disease (*2*, *3*). In diabetes, persistent hyperglycemia leads to various complications. Large-scale prospective cohort studies have shown that maintaining blood glucose level is important for the prevention of diabetes and its related complications (*4–6*). Several studies in recent years have documented relationships between ischemic heart diseases and postprandial high blood glucose concentration (*7–9*).

Different carbohydrates are digested differently, and digestibility directly affects blood glucose and insulin levels. Carbohydrates can be classified based on glycemic index (GI) (*10*), and the clinical usefulness of dietary guidance based on glycemic index (GI) appears promising (*11*). Rice is an important staple starchy food consumed by more than half of the global population; however, the glycemic index (GI) of it is high (*12*, *13*).

In recent years, a new type of rice has become available in Japan, called pre-germinated brown rice (PGBR). PGBR is made by soaking brown rice kernels in water to slightly germinate. PGBR is considered more healthful than WR, as it is richer in vitamins, minerals and dietary fiber. Regarding the effects of long-term consumption of PGBR, one study using streptozotocine-induced diabetic rats showed that compared to rats fed WR, levels of blood glucose and plasminogen activator inhibitor 1, which may increase the risk of diabetes and myocardial infarction (*14*), were significantly lower for rats fed PGBR, and blood lipid peroxide concentration tended to be lower (*15*). Our previous studies also showed that PGBR was better than WR to prevent the rapid increase of postprandial blood glucose concentration without increasing insulin secretion in humans (*16*, *17*). However, clinical evidence does not yet support the usefulness of long-term consumption of PGBR as a staple food.

The present study aimed to ascertain the clinical usefulness of a diet including PGBR on blood glucose management in patients with impaired fasting glucose (IFG) or type 2 diabetes.

*To whom correspondence should be addressed.
E-mail: yamamoto.shigeru@ocha.ac.jp

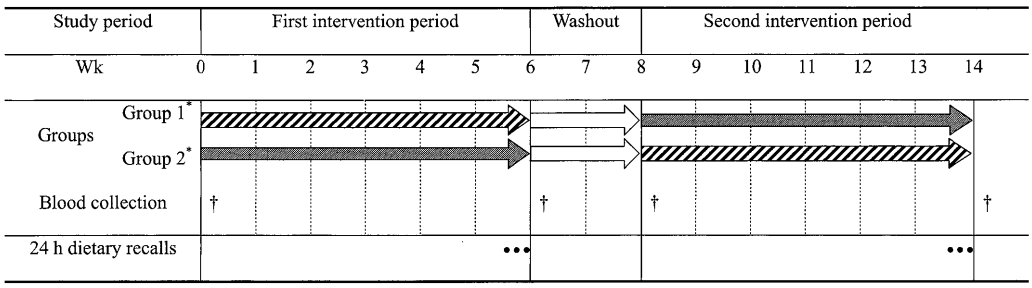


Fig. 1. Study design to observe the effect of WR and PGBR on blood glucose and lipid levels in free-living patients with type 2 diabetes. *Group 1, treatment from WR ($n$=6) to PGBR ($n$=5); Group 2, treatment from WR to PGBR. †Blood was collected in the mornings of weeks 0, 6, 8, and 14.

Table 1. Characteristics of test food (/100 g).

| | WR | PGBR |
|---|---|---|
| Dry matter (%) | 64.6 | 66.9 |
| Protein (g) | 2.8 | 3.2 |
| Fat (g) | 0.3 | 1.1 |
| Carbohydrate (g) | 32.2 | 28.3 |
| Total fiber (g) | 0.5 | 1.4 |
| Insoluble fiber (g) | 0.5 | 1.4 |
| Soluble fiber (g) | N.D. | N.D. |
| Resistant starch (g) | 0.5 | 0.4 |
| GABA (mg) | N.D. | 3.0 |
| γ-Oryzanol (mg) | N.D. | 7.9 |

Data are mean±SE. N.D., not detectable.

Table 2. Energy and nutrient intakes in the first and second intervention periods in Group 1 and 2.†

| | First intervention period | Second intervention period |
|---|---|---|
| Energy intake (kcal/d) | | |
| Group 1 | 1892.2±93.0 | 1891.9±88.2 |
| Group 2 | 1920.2±68.2 | 1961.4±73.2 |
| Protein (g/d) | | |
| Group 1 | 69.2±4.4 | 70.6±3.5 |
| Group 2 | 63.8±0.9 | 62.7±1.3 |
| Fat (g/d) | | |
| Group 1 | 64.8±3.3 | 61.0±2.7 |
| Group 2 | 70.7±3.2 | 71.7±2.6 |
| Carbohydrate (g/d) | | |
| Group 1 | 252.6±12.7 | 253.2±13.0 |
| Group 2 | 257.2±11.9 | 266.3±13.1 |
| Dark green vegetable (g/d) | | |
| Group 1 | 190.6±3.4 | 185.0±6.9 |
| Group 2 | 206.7±11.3 | 203.3±9.7 |
| Yellow vegetable (g/d) | | |
| Group 1 | 203.9±8.0 | 198.9±11.1 |
| Group 2 | 197.7±5.5 | 192.0±11.7 |
| Fruit (g/d) | | |
| Group 1 | 301.7±8.1 | 292.2±10.5 |
| Group 2 | 310.0±6.7 | 306.7±15.5 |
| Fiber (g/d) | | |
| Group 1 | 16.8±1.1 | 19.8±0.5 |
| Group 2 | 19.2±0.2 | 17.1±0.3* |

†Group 1 ($n$=6), treatment from WR to PGBR diet; Group 2 ($n$=5), treatment from PGBR to WR diet. Data are mean±SE.
*Significant difference from first intervention value by Wilcoxon's signed-rank test at $p<0.05$.

## SUBJECTS AND METHODS

Eleven free-living subjects with type 2 diabetes (6 men and 5 women; 51.5±16.2 y of age [mean±SE, range 27–72 y]; body mass index (BMI) 25.1±3.4 kg/m$^2$ [mean±SE, range 18.9–31.2 kg/m$^2$]) were included in the study. Inclusion criteria were as follows: at the time of entry, fasting blood glucose (FBG)≥110 mg/dL. Throughout the study, the same drugs were administered without altering doses. One subject was administered insulin and 10 subjects were administered oral hypoglycemic agents (sulfonylurea $n$=8, biguanide $n$=9, thiazolidiones $n$=3 and alpha-glucosidase inhibitor $n$=2). This study was approved by the ethical review boards of both Providence University and Li Shin Hospital in Taiwan and was conducted in accordance with their rules and regulations. The protocol conformed to the Helsinki Declaration. Subjects were recruited through physicians at Li Shin Hospital (Pingjen, Taiwan). Informed consent was obtained from each participant.

The participants were randomly allocated to two experimental periods of 6 wk of WR or PGBR diet in a crossover design (first intervention period: 0 to 6 wk; second intervention period: 8 to 14 wk) (Fig. 1). During the 2 intervention periods, subjects were instructed to consume either WR or PGBR as the staple food. The washout period was set for 2 wk from weeks 6 to 8 of the study. Subjects were allowed to continue performing normal activities of daily living without restriction from entry to the start of the study.

In the present study, cooked rice packages were given to each subject. The rice samples were the same japonica rice variety (Hoshinoyume) and obtained from Hokkaido, Japan. The selected rice was a short grain variety with apparent amylose content of 18% determined on raw rice by the iodine blue colorimetric method. Characteristics of the cooked rice used in the present study are given in Table 1. During the study, each subject was instructed to eat 180 g of the cooked rice 3 times daily. Subjects were instructed to maintain similar activities

Table 3. Physical characteristics and biochemical parameters at weeks 0, 6, 8 and 14 in Group 1 and 2.†

| | First intervention period | | Second intervention period | |
|---|---|---|---|---|
| | week 0 | week 6 | week 8 | week 14 |
| Weight (kg) | | | | |
| Group 1 | 64.4±3.0 | 64.6±3.0 | 64.8±3.0 | 64.7±3.0 |
| Group 2 | 65.9±5.9 | 65.9±6.1 | 65.7±5.9 | 65.9±6.2 |
| Body fat (%) | | | | |
| Group 1 | 27.8±3.1 | 27.9±3.0 | 27.8±3.0 | 27.5±3.0 |
| Group 2 | 30.6±4.7 | 30.2±4.5 | 30.6±4.6 | 31.1±4.5 |
| BMI ($kg/m^2$) | | | | |
| Group 1 | 24.6±1.6 | 24.7±1.6 | 24.7±1.6 | 24.7±1.6 |
| Group 2 | 25.6±1.4 | 25.6±1.4 | 25.5±1.4 | 25.5±1.5 |
| W/H ratio | | | | |
| Group 1 | 0.9±0 | 0.9±0 | 0.9±0 | 0.9±0 |
| Group 2 | 0.9±0 | 0.9±0 | 0.9±0 | 0.9±0 |
| SBP (mmHg) | | | | |
| Group 1 | 120.3±5.7 | 118.3±7.0 | 119.7±7.1 | 121.7±6.2 |
| Group 2 | 119.4±5.1 | 125.6±8.5 | 125.4±7.7 | 122.4±6.3 |
| DBP (mmHg) | | | | |
| Group 1 | 70.0±4.9 | 69.0±3.8 | 67.7±4.2 | 71.3±4.2 |
| Group 2 | 71.4±3.4 | 75.2±3.0 | 75.2±3.3 | 70.4±2.3 |
| TP (g/dL) | | | | |
| Group 1 | 7.5±0.1 | 7.3±0.1 | 7.4±0.1 | 7.5±0.1 |
| Group 2 | 7.3±0.3 | 7.5±0.4 | 7.2±0.4 | 7.1±0.3 |
| Alb (g/dL) | | | | |
| Group 1 | 4.6±0.1 | 4.6±0.1 | 4.6±0.1 | 4.7±0.1 |
| Group 2 | 4.3±0.2 | 4.3±0.2 | 4.3±0.3 | 4.4±0.2 |
| Insulin ($\mu$U/mL) | | | | |
| Group 1 | 7.1±2.5 | 7.5±1.8 | 7.9±2.0 | 7.1±1.0 |
| Group 2 | 6.4±0.5 | 8.5±1.9 | 8.8±2.0 | 7.8±2.4 |
| TC (mg/dL) | | | | |
| Group 1 | 239.5±8.8 | 241.7±8.0 | 243.2±7.8 | 223.3±7.8* |
| Group 2 | 241.8±10.1 | 216.2±7.3* | 222.0±8.0 | 231.4±11.4 |
| TG (mg/dL) | | | | |
| Group 1 | 190.7±44.9 | 192.5±44.2 | 193.5±45.0 | 176.5±44.0* |
| Group 2 | 121.6±19.6 | 91.2±15.0* | 95.8±15.0 | 97.4±15.4 |
| HDL-C (mg/dL) | | | | |
| Group 1 | 48.0±4.4 | 46.7±3.8 | 47.5±3.8 | 53.3±4.6* |
| Group 2 | 52.0±3.5 | 63.2±4.2* | 59.6±3.7 | 57.4±4.4 |

†Group 1 ($n$=6), treatment from WR to PGBR diet; Group 2 ($n$=5), treatment from PGBR to WR diet. BMI: body mass index, W/H ratio: waist-hip ratio, SBP: systolic blood pressure, DBP: diastolic blood pressure, TP: total protein, Alb: serum albumin, TC: total cholesterol, TG: triglyceride, HDL-C: HDL-cholesterol.

*Significant difference between the week 0 and weeks 6, 8 and 14 within the same group was analyzed by Wilcoxon's signed-rank test at $p<0.05$. Data are mean±SE.

of daily living, including exercise.

Height was measured only at study week 0. Body weight and blood pressure were measured at study weeks 0, 6, 8, and 14. In each intervention period (WR and PGBR), dietary intakes were ascertained from 24 h dietary recalls conducted by national registered dietitians for 3 consecutive days in the last week of each intervention period (weeks 6 and 14). Using the Taiwan food composition table (*18*), energy consumption, nutrient consumption (proteins, lipids, carbohydrates and cholesterol), were calculated.

Blood samples were taken 4 times, in study weeks 0, 6, 8, and 14. After dividing samples into plasma and serum, serum samples were stored at −70°C until analyzing. Plasma glucose levels were measured using the glucose dehydrogenase method. Levels of serum fructosamine were measured by the colorimetric method. Levels of serum total cholesterol (TC), triacylglycerol (TG) and HDL-cholesterol (HDL-C) were measured using the enzymatic method, the selective inhibition method and the free glycerol diminishing method, respectively. Total protein (TP) and albumin (Alb) concentrations were measured by the timed endpoint method and nephelometry method, respectively (UM Clinical Laboratory, Taichung, Taiwan). Level of insulin was measured using the enzyme immunoassay (SRL, Tokyo, Japan). Laboratory technologists were blinded to the identity of subjects and intervention status, and the

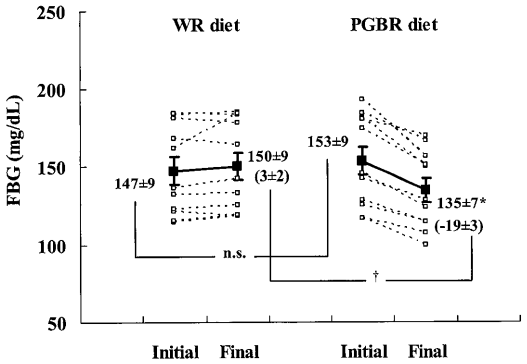


Fig. 2. Change in fasting blood glucose (FBG) concentration during WR diet or PGBR diet groups for 6 wk. Bold line: mean±SE; dotted fine line: individual data. Figure in parenthesis: mean±SE of "initial value−final value". *Significant difference from initial value by Wilcoxon's signed-rank test at $p<0.01$. †Significant difference between WR and PGBR diet groups including the figures in parenthesis ($p<0.01$), n.s.: not statistically significant ($p=0.053$).

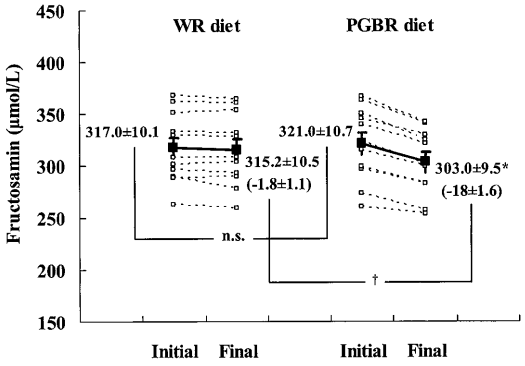


Fig. 3. Change in fructosamin level during WR diet or PGBR diet for 6 wk. Bold line: mean±SE; dotted fine line: individual data. Figure in parenthesis: mean±SE of "initial value−final value". *Significant difference from initial value by Wilcoxon's signed-rank test at $p<0.01$. †Significant difference between WR and PGBR diet groups including the figures in parenthesis ($p<0.01$), n.s.: not statistically significant ($p=0.396$).

person in charge of statistical analyses was blinded to the same information until the time of data analysis.

Numerical data were expressed as mean±SE. Blood glucose management markers, blood lipid-related markers, and dietary consumption were subjected to Wilcoxon's signed-rank tests in each experimental period. Values of $p<0.05$ were considered statistically significant. All statistical analyses were performed with the Stat View 5.0 (SAS Institute, Inc., USA).

## RESULTS

Subjects were examined by a physician in study weeks 0, 6, 8, and 14. Table 2 shows energy and nutrient intakes in the first and second intervention periods in Group 1 and 2. Between the WR and PGBR diets, no significant differences in dietary consumption were identified except dietary fiber content of Group 2 were significantly higher ($p<0.05$) after the PGBR diet consumption.

Table 3 shows physical characteristics and biochemical parameters at study weeks 0, 6, 8 and 12 in Group 1 and 2. Throughout the study, no marked shifts were displayed in physical characteristics such as body mass index (BMI) or percent body fat or serum biochemical parameters such as insulin, total protein (TP) or albumin (Alb). Levels of serum total cholesterol (TC), triacylglycerol (TG) and HDL-cholesterol (HDL-C) were significantly improved ($p<0.05$) after the PGBR diet consumption.

With the PGBR diet, fasting blood glucose (FBG) levels decreased significantly from the initial of 153±9 mg/dL to 135±7 mg/dL ($p<0.01$), but no marked changes were observed with the WR diet (147±9 mg/dL vs. 150±9 mg/dL, respectively) (Fig. 2). Means±SE of "Initial FBG value−final FBG value" in each dietary treatment were calculated (Fig. 2). They were 3±2 and −19±3 in the WR and PGBR groups, respectively. The FBG levels decreased more in the PGBR group than in the WR group ($p<0.01$).

In addition, in the PGBR diet, fructosamine levels decreased significantly from the initial of 321.0±10.7 μmol/L to 303.0±9.5 μmol/L ($p<0.01$), but in the WR diet, no marked changes were seen between initial and final intervention (317.0±10.1 μmol/L vs. 315.2±10.5 μmol/L, respectively) (Fig. 3). Means±SE of "Initial fructosamine value−final fructosamine value" in each dietary treatment are shown in Fig. 3. They were −1.8±1.1 and −18±1.6 in WR and PGBR groups, respectively. The decrease of the fructosamine level was greater in the PGBR group than in the WR group ($p<0.01$).

No significant difference in levels of fasting blood glucose (FBG) or fructosamine were noted before consumption of the WR diet or the PGBR diet. Furthermore, levels of fasting blood glucose (FBG) and fructosamine were significantly decreased after consuming the PGBR diet compared to the WR diet ($p<0.01$, each).

## DISCUSSION

It has been known the fasting blood glucose (FBG) level represents current blood glucose status; the fructosamine levels represents the history of blood glucose status during the previous 1–2 wk. The present results show that, unlike WR, consuming PGBR as a staple food significantly decreases fasting blood glucose (FBG) and fructosamine in patients with type 2 diabetes ($p<0.01$). Hence, these results suggest that blood glucose levels were maintained favorably during the intervention period. Serum levels of total cholesterol (TC) and triglyceride (TG) significantly improved after consuming the PGBR diet ($p<0.01$). Conversely, no significant changes in blood glucose management or lipid-related markers were noted between initial or final values when taking the WR diet.

Dietary and exercise habits markedly affect levels of blood glucose and lipids (3–5). Subjects in the present study were instructed to avoid changes in dietary and

exercise habits as much as possible to minimize confounding factors. During the 2 study periods, dietary intake was measured by using 24 h dietary recalls in each subject during 3 consecutive days of the two intervention periods. No marked differences in energy or nutrition intakes (Table 2) and no changes in body mass index (BMI) or body fat were observed between the two groups (Table 3). These findings suggest that energy consumption and physical activity were maintained during the study; and dietary and exercise habits did not markedly affect blood glucose or lipid levels. As hypoglycemic agents, 9 subjects were taking sulfonylurea and biguanide drugs, and 1 subject was taking only an insulin preparation. Throughout the study, the same drugs and doses were administered without change. Therefore, the effects from medicine on blood glucose management and lipid-related parameters may be eliminated.

The reason for the improved blood glucose management markers with the PGBR diet is suggested to be that the physical shape of grains delays digestion and absorption of carbohydrates. PGBR comprises endosperm, aleurone layer, bran layer and germ. As the endosperm is covered by the bran layer, starches do not come into contact with digestive enzymes as often as they do with WR. In a study in which humans were instructed to eat either BR or WR, blood glucose and insulin reaction were lower with BR when compared to WR (*19*). An in vitro study showed that the rate of starch hydrolysis was markedly lower for BR than for WR (*20*). Past studies have shown that dietary fibers lower the risk for diabetes (*21*), suggesting that the dietary fibers included in bran suppress the absorption of saccharides broken down by digestive enzymes, ultimately suppressing increases in postprandial blood glucose levels. In the rodent, it has been reported that the blood glucose-lowering effect of PGBR may be derived from the higher dietary fiber of PGBR than WR (*22*).

Consumption of PGBR significantly improved levels of blood lipids. Regarding the mechanisms of improved blood lipid levels, increased fiber intake may be suggested. As the other possible factor, we may be able to suggest the reduced postprandial secretion of insulin, which induces the synthesis of total cholesterol (TC) (*23*) and triacylglycerol (TG) (*24*). Rice bran from PGBR contains γ-oryzanols (ferulate ester of triterpene alcohols) which are effective in improving hyperlipidemia (*25–27*). Furthermore, in vitro studies have shown high adsorption of bile acid by rice bran (*28, 29*). In a recent study, a PGBR diet suppressed hypercholesterolemia, and enhanced fecal bile acid excretion without affecting cholesterol synthesis in the host liver of hepatoma-bearing rats (*30*). With regard to nutritional guidelines for diabetes management, the accuracy of conventional guidance based on high carbohydrate consumption is being questioned. The reason for this is that a high-carbohydrate diet can increase levels of blood glucose, insulin and triacylglycerol (TG) (*31*). The glycemic index (GI) of WR is substantially higher than that of BR, which is less refined. As a result, from the perspective of blood glucose management, consumption of WR should be minimized. At present, insufficient data is available to support the idea that long-term consumption of WR may increase the risk of diabetes or heart disease. In the present study, patients with type 2 diabetes were instructed to consume 180 g of rice 3 times a day for 6 wk, and no changes in blood glucose management or lipid-related markers occurred with the WR diet. Long-term large-scale intervention studies are thus warranted to clarify relationships between WR consumption and diseases such as diabetes and heart disease. The present results show that, in type 2 diabetes patients with favorable blood glucose levels controlled by drug and dietary therapy, consumption of PGBR, which is less refined than WR, significantly improves levels of blood glucose, fructosamine (blood glucose management markers), total cholesterol (TC), triglyceride (TG) and HDL-cholesterol (HDL-C) (lipid-related markers).

While the present study was only a small-scale study lasting 6 wk, the results suggest that consumption of PGBR as a staple food in patients with type 2 diabetes is useful in improving blood glucose and lipid levels.

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