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Hypoglycemic and Antioxidative Effects of Functional Rice Goami and Nokwon in High Fat-Fed Mice

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ABSTRACT Effects of newly developed functional rice grains Goami (high-amylose rice) and Nokwon (green-kerneled rice) on the glucose metabolism and antioxidative defense system in C57BL/6N mice under high fat diet condition were investigated. Animals were randomly divided into five groups (n = 8) and given experimental diets for eight weeks: normal control diet (NC), high fat diet (HF), and high fat diet supplemented with white rice (HF-WR), Goami rice (HF-GR), and Nokwon rice (HF-NR). At the end of the experimental period, the HF group exhibited markedly higher blood glucose level, insulin concentration, plasma lipid peroxidation and lower hepatic glycogen concentration than that exhibited by NC group. However, diet supplementation of Goami and Nokwon suppressed the high fat diet-induced hyperglycemia and oxidative stress through inhibition of the glucose-regulating enzymes and enhancement of the antioxidant enzymes activities. The results illustrate that the new functional rice Goami and Nokwon may be useful in the development of functional foods with preventive effect against high fat diet-induced hyperglycemia and oxidative stress.

Keywords : functional rice, glucose metabolism, antioxidant defense system, high fat diet, mice

Due to the rising trend in the global incidence of metabolic diseases and the increasing costs of medical service, functional foods have gained public interest in the recent years. Through fortification, enrichment, or genetic manipulation, traditional foods have been modified to contain added nutrients and functional components that provide health beneficial effects (Siro *et al*. 2008). Such foods lower cholesterol level and blood pressure, reduce the risk of diabetes and cardiovascular diseases, improve weight control, and enhance antioxidant defense status (Siro *et al*. 2008; Ejtahed *et al*. 2012; Mermel 2004).

Diabetes mellitus, a metabolic disease characterized by hyperglycemia, is a fast- growing health problem worldwide (Wild *et al*. 2004). Excessive intake of dietary fat has been associated with the development of glucose metabolism disorder and type 2 diabetes mellitus (Lichtenstein and Schwab 2000). Progression of hyperglycemia is related to oxidative stress that results from enhanced generation of free radicals and impaired antioxidant defense mechanism (West 2000). Although there are several oral medicines available for the treatment of diabetes, but various adverse side effects have been linked to these anti-diabetic drugs (Inzucchi 2002). Inclusion of functional foods with hypoglycemic activity and strong antioxidative property are therefore greatly needed.

Rice is one of the most important agricultural crops in the world and the staple food in many countries. With the increasing market demand for functional foods, rice scientists and plant breeders are continuously developing rice grains with enhanced functionality. Various functional rice grains, such as colored rice varieties with strong antioxidant activity, high-amylose cultivars that are rich in dietary fiber, beta-carotene-enriched golden rice, and giant embryo rice with high nutritional content, have been developed and produced (Beyer 2010; Min *et al*. 2012; Seo *et al*. 2011; Zhu *et al*. 2012). While a number of studies on the nutritional components of functional rice have been carried out in the past, knowledge on the physiological effects of different functional rice varieties, particularly the newly-developed ones, is still lacking. Thus, this study was conducted to determine the comparative effects of the traditional white rice and functional rice cultivars, such as high-amylose rice and green-kerneled rice, on the blood glucose level and antioxidant defense system in mice

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under high fat diet condition. The activities of antioxidant enzymes, as well as enzymes associated with glucose metabolism, were also determined.

MATERIALS AND METHODS

Rice cultivars and chemicals

The functional rice cultivars Goami (high-amylose rice) and Nokwon (green-kerneled rice) were provided by the Rural Development Administration (Suwon, Korea). The general white rice was obtained from a local market in Daegu, Korea. All rice grain samples were ground into powder prior to use and their proximate compositions (Table 1) were analyzed according to the methods of AOAC (AOAC 2003). Chemicals such as ethanol, potassium phosphate buffer, ketamine HCl, trichloroacetic acid, and thiobarbituric acid were obtained from Merck KGaA (Darnstadt, Germany). All other chemicals used were purchased from Sigma-Aldrich, Inc. (Steinhein, Germany).

Animals and diets

Forty 4-week-old male C57BL/6N mice, weighing 12 g, were obtained from Orient Inc. (Seoul, Korea). The animals obtained were individually housed in a stainless steel cage in a room maintained at 25℃ with 50% relative humidity and 12/12 h light/dark cycle. They were fed with pelletized chow diet for the first two weeks and then randomly divided into five dietary groups (n = 8). The first and second groups were fed with normal control (NC) and high fat (HF) diets, respectively. The other three groups were fed with a high fat diet supplemented with white rice (HF-WR), Goami rice (HF-GR), or Nokwon rice (HF-NR). The composition of the experimental diet (Table 2) was based on the AIN-76 semisynthetic diet (AIN 1977). The mice were fed for 8 weeks and allowed free access to food and water. At the end of the experimental period, the mice were anaesthetized with ketamine-HCl following a 12-h fast. The blood samples were drawn from the inferior vena cava into a heparin-coated tube and centrifuged at 1,000 rpm for 15 min at 4℃ to obtain the plasma and erythrocyte. After centrifugation, the plasma and buffy coat were removed and the erythrocytes were washed with physiological saline, followed by hemolysis with distilled water (McCord and Fridovich 1969). The hemoglobin concentration was measured using a commercial assay kit (Asan Pharmaceutical, Seoul, Korea). The liver was removed, rinsed with physiological saline, weighed, and stored at -70℃ until analysis. The current study protocol was approved by the Ethics Committee of Kyungpook National University for animal studies.

Table 1. General composition (g/100 g) of the rice samples.

Composition	White rice	Goami rice	Nokwon rice
Carbohydrate	79.76	72.01	69.74
Crude protein	6.11	8.17	6.89
Crude fat	0.33	3.64	2.40
Moisture	12.72	11.65	15.28
Ash	0.39	3.84	0.94
Dietary fiber	0.66	2.93	2.45

Table 2. Composition of experimental diets (%).

Component	Dietary group[1)]				
	NC	HF	HF-WR	HF-GR	HF-NR
Total Carbohydrate	65.0	50.0	50.0	50.0	50.0
Corn starch	15.0	-	-	-	-
sucrose	50.0	50.0	-	-	-
From rice source	-	-	50.0	50.0	50.0
Total Protein	20.0	20.0	20.0	20.0	20.0
Casein	20.0	20.0	16.2	14.1	15.2
From rice source	-	-	3.8	5.9	4.8
Total Fat	5.0	3.0	3.0	3.0	3.0
Corn oil	5.0	3.0	2.8	0.4	1.3
From rice source	-	-	0.2	2.6	1.7
Total Cellulose	5.0	5.0	5.0	5.0	5.0
Cellulose	5.0	5.0	4.6	2.9	3.3
From rice source	-	-	0.4	2.1	1.7
Vitamin mix[2)]	1.0	1.0	1.0	1.0	1.0
Mineral mix[3)]	3.5	3.5	3.5	3.5	3.5
DL-methionine	0.3	0.3	0.3	0.3	0.3
Lard	-	17.0	17.0	17.0	17.0
Choline chloride	0.2	0.2	0.2	0.2	0.2
Total (%)	100.0	100.0	100.0	100.0	100.0

[1)] NC, normal diet; HF, high fat diet; HF-WR, high fat diet + white rice; HF-GR, high fat diet + Goami rice; HF-NR, high fat diet + Nokwon rice.
[2)] AIN-76 vitamin mixture.
[3)] AIN-76 mineral mixture.

Measurement of blood glucose content

The blood glucose concentration was determined using Accu-Chek Active Blood Glucose Test Strips (Roche Diagnostics GmbH, Germany). Blood samples were drawn from the tail vein of the mice at 2-week intervals for 8 weeks.

Determination of hepatic glycogen and plasma insulin levels

The hepatic glycogen concentration was measured based on the method of Seifter *et al*. (1950). Briefly, the liver (100 mg) was mixed with 30% KOH and heated at 100℃ for 30 min. The mixture was added with 1.5 mL ethanol (95%) and kept overnight at 4℃. The pellet was mixed with 4 mL distilled water and the mixture (500 μL) was then added with 0.2% anthrone (in 95% H_2SO_4). The absorbance was measured at 620 nm and the results were calculated based on a standard calibration curve of glucose. The plasma insulin concentration was determined using enzyme-linked immunosorbent assay (ELISA) kits (TMB Mouse Insulin ELISA kit, Sibayagi, Japan).

Lipid peroxidation analysis

The plasma thiobarbituric acid reactive substances (TBARS) were analyzed according to the method of Ohkawa *et al*. (1979). A 50 μL of plasma was added with trichloroacetic acid (5%, v/v) and 0.06 M thiobarbituric and incubated at 80℃ for 90 min. The mixtures were cooled at room temperature and centrifuged at 2,000 rpm for 25 min. The absorbance of the supernatant was measured at 535 nm. A malondialdehyde (MDA) solution was used as standard and the results were expressed in nmol/mL.

Determination of the activities of hepatic glucose-regulating and antioxidant enzymes

Hepatic enzyme source was prepared following the method Hulcher and Oleson (1973). The liver (0.3 g) was homogenized in buffer solution (0.1 M triethanolamine, 0.2 M EDTA, and 0.002 M dithiothreitol) and centrifuged at 1,000 rpm for 15 min at 4℃. The supernatant was further centrifuged at 10,000 rpm for 15 min at 4℃ and the resulting precipitate served as the mitochondrial fraction, while the resulting supernatant was centrifuged again at 105,000 rpm for 1 h at 4℃. The resulting supernatant and precipitate were the cytosol and microsome fractions, respectively.

For the analysis of glucose-regulating enzymes, the glucokinase (GK) activity was determined using the method of Davidson and Arion (1987) with slight modifications. The reaction mixture (0.98 mL), which consisted of 50 mM Hepes-NaOH (pH 7.4), 100 mM KCl, 7.5 mM $MgCl_2$, 2.5 mM dithioerythritol, 10 mg/mL albumin, 10 mM glucose, 4 units of glucose-6-phosphate dehydrogenase, 50 mM NAD^+, and 10 μL cytosol, was pre-incubated at 37℃ for 10 min. The reaction was initiated with the addition of 10 μL of 5 mM ATP and the mixture was incubated at 37℃ for 10 min. The change in absorbance at 340 nm was recorded. The glucose-6-phosphatase (G6pase) activity was determined according to the method of Alegre *et al*. (1988). The reaction mixture contained 765 μL of 131.58 mM Hepes-NaOH (pH 6.5), 100 μL of 18 mM EDTA (pH 6.5), 100 μL of 265 mM glucose-6-phosphate, 10 μL of 0.2 M $NADP^+$, 0.6 IU/ml mutarotase, and 0.6 IU/mL glucose dehydrogenase. After pre-incubation at 37℃ for 3 min, the mixture was added with 5 μL microsome and incubated at 37℃ for 4 min. The change in absorbance at 340 nm was measured. The phosphoenolpyruvate carboxykinase (PEPCK) activity was measured following the method of Bentle and Lardy (1976). The reaction mixture contained 72.92 mM sodium Hepes (pH 7.0), 10 mM dithiothreitol, 500 mM $NaHCO_3$, 10 mM $MnCl_2$, 25 mM NADH, 100 mM IDP, 200 mM PEP, 7.2 units of malic dehydrogenase, and 10 μL cytosol. The change in absorbance at 340 nm was recorded.

For the antioxidant enzyme analysis, the superoxide dismutase (SOD) activity was spectrophotometrically measured using the method of Marklund and Marklund (1974). The reaction mixture containing 50 mM Tris-HCl buffer (pH 8.5), 10 mM EDTA, 0.1 mL cytosol or erythrocyte, and 7.2 mM pyrogallol was incubated at 25℃ for 10 min and added with 50 μL of 1 N HCl. The absorbance was measured at 420 nm and the activity was expressed as unit/mg protein, wherein one unit represents the amount of enzyme that inhibited the oxidation of pyrogallol by 50%. The amount of protein was determined using the Bradford protein assay (Bradford 1976). The glutathione peroxidase (GPx) activity was measured based on the method of Paglia and Valentine (1967) with slight modifications. A 0.1 mL of the cytosolic supernatant or erythrocyte was added to the reaction mixture (6 mM

glutathione, 1.2 mM NADPH, and 1.25 μM H_2O_2 in 20 mM Tris-HCl, pH 7.0) that was pre-incubated at 25℃ for 5 min. The mixture was further incubated at 25℃ for 5 min and its absorbance was measured at 340 nm. A molar extinction coefficient of 6.22/mM/cm was used to calculate the activity, which was expressed as nmol oxidized NADPH /min/mg protein. The catalase (CAT) activity was determined following the method of Aebi (1974). A mixture of 50 mM potassium phosphate buffer (pH 7.4) and 10 μL of mitochondrial fraction or erythrocyte was pre-incubated at 25℃ for 5 min and added with 0.1 mL of 30 mM H_2O_2. The disappearance of hydrogen peroxide was monitored spectrophotometrically at 240 nm for 5 min. A molar extinction coefficient of 0.041/mM/cm was used to calculate the CAT activity, which was expressed as the μmol decreased H_2O_2 /min/mg protein. The glutathione reductase (GR) activity was measured according to the method of Mize and Langdon (1952). A 10 μL of cytosol or erythrocyte was added to the reaction mixture (1 mM EDTA and 1 mM GSSG in a 0.1 M potassium phosphate buffer, pH 7.4) and the oxidation of NADPH was monitored at 340 nm. The activity was expressed as nmol oxidized NADPH/min/mg protein. The paraoxonase (PON) activity was determined using the method of Mackness *et al*. (1991). The microsome or erythrocyte (50 μL) was added to 1 ml Tris/HCl buffer (100 mM, pH 8.0) containing 2 mM $CaCl_2$ and 5.5 mM paraoxon. The absorbance of the mixture was measured at 412 nm at 25℃ to determine the generation rate of 4-nitrophenol. A molar extinction coefficient of 17100/M/cm was used in calculating the PON activity.

Statistical analysis

All data are presented as the mean ± S.E. The data was evaluated by one-way ANOVA using a Statistical Package for Social Sciences software program (SPSS Inc., Chicago, IL, USA) and the differences between the means were assessed using Duncan's multiple range test. Statistical significance was considered at $p<0.05$.

RESULTS

Body weight gain

All animals exhibited similar body weights prior to feeding with experimental diets. At the end of the experimental period, a marked increase in the final body weight was found in HF mice relative to that of the NC group (data not shown). On the other hand, the rice-fed groups, particularly HF-GR and HF-NR, showed significantly lower body weight gain and body fat than the HF group, indicating that the functional rice grains were able to suppress the weight gain in mice under high fat diet condition.

Blood glucose level

High fat feeding resulted in a substantial increase in the blood glucose level of mice (Fig. 1). All rice-fed groups showed significantly lower glucose level compared with that of the HF mice on the final day. In particular, the HF-GR mice exhibited a considerable decrease in the glucose level that was comparable with the control group.

Glycogen and insulin levels

The HF and HF-WR groups showed markedly lower glycogen level than the NC group (Table 3). Moreover, the HF mice exhibited significantly higher insulin level than the control group. On the other hand, diet supplementation with Goami

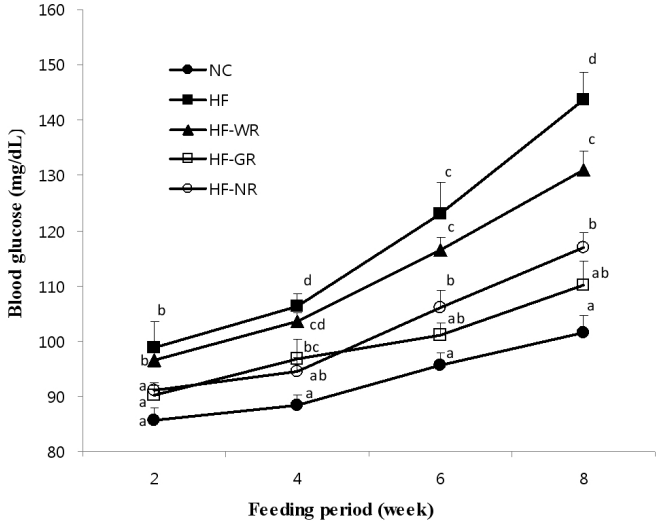

Fig. 1. Effect of diet supplementation of functional rice on the blood glucose level in high fat-fed mice. Means not sharing a common superscript are significantly different at $p<0.05$ (n = 8). NC, normal control diet; HF, high fat diet; HF-WR, high fat diet + white rice; HF-GR, high fat diet + Goami rice; HF-NR, high fat diet + Nokwon rice.

Table 3. Glycogen and insulin concentrations[1] in mice fed with high fat diet supplemented with functional rice.

Dietary group[2]	Glycogen (μg/g)	Insulin (ng/mL)
NC	101.49 ± 6.44^{c}	4.51 ± 0.07^{b}
HF	31.61 ± 3.77^{a}	5.79 ± 0.03^{c}
HF-WR	33.22 ± 4.93^{a}	4.41 ± 0.04^{b}
HF-GR	70.26 ± 8.56^{b}	4.25 ± 0.07^{a}
HF-NR	88.51 ± 1.77^{c}	4.37 ± 0.04^{ab}

[1] Values are means ± SE (n = 8). Means in the same column not sharing a common superscript are significantly different at $P < 0.05$.
[2] NC, normal diet; HF, high fat diet; HF-WR, high fat diet + white rice; HF-GR, high fat diet + Goami rice; HF-NR, high fat diet + Nokwon rice.

Table 4. Hepatic glucose-regulating enzyme activity in mice fed with high fat diet supplemented with functional rice.

Dietary group[1]	Enzyme activity (nmol/min/mg protein)[2]		
	GK	G6pase	PEPCK
NC	0.92 ± 0.13^{a}	122.03 ± 2.76^{a}	4.23 ± 0.10^{b}
HF	1.01 ± 0.11^{a}	145.96 ± 1.69^{c}	5.86 ± 0.30^{c}
HF-WR	0.95 ± 0.08^{a}	142.99 ± 2.04^{bc}	4.55 ± 0.27^{b}
HF-GR	1.11 ± 0.16^{a}	137.05 ± 2.02^{b}	2.34 ± 0.14^{a}
HF-NR	1.07 ± 0.10^{a}	155.81 ± 2.71^{d}	2.26 ± 0.20^{a}

[1] NC, normal diet; HF, high fat diet; HF-WR, high fat diet + white rice; HF-GR, high fat diet + Goami rice; HF-NR, high fat diet + Nokwon rice.
[2] Values are means ± SE (n = 8). Means in the same column not sharing a common superscript are significantly different at $P < 0.05$. GK, glucokinase; G6pase, glucse-6-phosphatase; PEPCK, phosphoenolpyruvate carboxykinase.

rice and Nokwon rice substantially increased and decreased the glycogen and insulin levels, respectively, in mice.

Hepatic glucose-regulating enzyme activities

The HF mice exhibited a significant increase in the activities of the G6pase and PECPCK enzymes relative to the control group (Table 4). However, supplementation of Goami rice in the high fat diet considerably reduced the activities of these enzymes. The HF-NR group also showed lower PEPCK activity, but higher G6pase enzyme activity. No significant change was found in the GK activity among the animal groups.

Plasma lipid peroxides

A marked increase in the plasma TBARS level was observed in HF mice relative to that of the NC group, but addition of rice in the diet significantly suppressed the elevation in the TBARS level (Table 5).

Table 5. Plasma TBARS level[1] in mice fed with high fat diet supplemented with functional rice.

Dietary group[2]	Plasma TBARS (nmol/mL)
NC	7.37 ± 0.84^{a}
HF	12.15 ± 1.16^{b}
HF-WR	7.68 ± 0.95^{a}
HF-GR	6.24 ± 0.31^{a}
HF-NR	7.71 ± 1.04^{a}

[1] Values are means ± SE (n = 8). Means in the same column not sharing a common superscript are significantly different at $P < 0.05$. TBARS, thiobarbituric acid reactive substances.
[2] NC, normal diet; HF, high fat diet; HF-WR, high fat diet + white rice; HF-GR, high fat diet + Goami rice; HF-NR, high fat diet + Nokwon rice.

Antioxidant enzyme activities

High fat feeding resulted in a significant decrease in the activities of GPx and hepatic GR and PON enzymes in mice (Table 6). However, supplementation of Goami and Nokwon

Table 6. Antioxidant enzyme activity in mice fed with high fat diet supplemented with functional rice.

	NC[1)]	HF	HF-WR	HF-GR	HF-NR
Hepatic enzymes[2)]					
SOD (unit/mg protein)	1.88 ± 0.10^{ab}	1.26 ± 0.08^{a}	1.79 ± 0.16^{ab}	2.23 ± 0.22^{b}	1.71 ± 0.23^{ab}
GPx (nmol/min/mg protein)	7.34 ± 0.07^{d}	2.77 ± 0.15^{a}	3.37 ± 0.15^{a}	5.80 ± 0.20^{b}	6.56 ± 0.33^{c}
CAT (μmol/min/mg protein)	1.23 ± 0.02^{a}	1.17 ± 0.04^{a}	1.25 ± 0.03^{a}	1.28 ± 0.02^{a}	1.29 ± 0.02^{a}
GR (nmol/min/mg protein)	8.77 ± 0.41^{bc}	4.15 ± 0.31^{a}	4.60 ± 0.47^{a}	9.92 ± 0.95^{c}	7.03 ± 0.60^{b}
PON (nmol/min/mg protein)	0.61 ± 0.03^{c}	0.47 ± 0.02^{a}	0.50 ± 0.02^{ab}	0.56 ± 0.02^{bc}	0.52 ± 0.02^{b}
Erythrocyte enzymes					
SOD (unit/mg protein)	4.65 ± 0.15^{ab}	4.08 ± 0.10^{a}	5.30 ± 0.12^{bc}	5.78 ± 0.22^{c}	5.71 ± 0.32^{c}
GPx (nmol/min/mg protein)	0.32 ± 0.05^{c}	0.16 ± 0.01^{a}	0.17 ± 0.03^{a}	0.21 ± 0.01^{ab}	0.25 ± 0.02^{bc}
CAT (μmol/min/mg protein)	0.30 ± 0.03^{a}	0.30 ± 0.02^{a}	0.34 ± 0.01^{ab}	0.34 ± 0.01^{ab}	0.37 ± 0.01^{b}
GR (nmol/min/mg protein)	0.62 ± 0.06^{ab}	0.32 ± 0.02^{a}	0.28 ± 0.03^{a}	0.62 ± 0.02^{ab}	1.33 ± 0.05^{b}

[1)] NC, normal diet; HF, high fat diet; HF-WR, high fat diet + white rice; HF-GR, high fat diet + Goami rice; HF-NR, high fat diet + Nokwon rice.
[2)] Values are means ± SE (n = 8). Means in the same column not sharing a common superscript are significantly different at $P < 0.05$. SOD, superoxide dismutase; GPx, glutathione peroxidase; CAT, catalase; GR, glutathione reductase; PON, paraoxonase.

in the high fat diet markedly increased the enzyme activities. Moreover, the HF-NR group exhibited significantly higher activities of erythrocyte SOD, CAT, and GR enzymes compared with the HF group. Likewise, the HF-GR group showed considerably higher SOD activity than the HF mice. No significant changes were found in the activity of hepatic CAT in all animal groups.

DISCUSSION

In recent years, a number of rice varieties have been developed with enhanced functional quality and health beneficial properties. The present study investigated the hypoglycemic and antioxidative effects of new functional rice cultivars Goami, a high-amylose rice, and Nokwon, a green-kerneled rice. Results showed that while the high fat diet markedly increased the blood glucose level in mice, the addition of functional rice grains in the diet significantly suppressed this high fat-induced hyperglycemia. Moreover, the increase in the glycogen concentration and decrease in the insulin level in mice fed with functional rice grains indicated a marked improvement in the glycemic control in these animals. Dietary feeding of white rice, on the other hand, showed marginal effect on the glucose metabolism in high fat-fed mice. The hypoglycemic effect of Goami and Nokwon rice may probably be attributed to their high dietary fiber content. Scientific studies have shown that dietary fibers could modulate the glucose and lipid metabolisms, thereby reducing the risk for type 2 diabetes mellitus (Lattimer and Haub 2010; Madar 1983). Ingested dietary fibers form a viscous gel matrix in the gastrointestinal tract which delays gastric emptying and decreases the diffusion of nutrient for absorption, resulting in the reduction of glucose transport to absorptive surfaces (Viuda-Martos *et al* 2010). The hypoglycemic action of functional rice is perhaps associated with the inhibition of G6pase and PEPCK activities. These hepatic enzymes are involved in the regulation of gluconeogenesis and hepatic glucose output, and their increased activities have been associated with enhanced glucose production (Friedman *et al*. 1997; She *et al*. 2000; Van Schaftingen and Gerin 2002). The significant increase in the G6pase activity in the HF-NR mice was unexpected since there was a considerable decrease in the glucose concentration in these animals. Nevertheless, this enhanced enzyme activity did not cause a negative effect on the glucose level in mice, indicating that other factors may be involved in the glucose-lowering effect of Nokwon rice. The underlying mechanism by which functional rice alters the enzyme activities warrants further investigation.

The progression of hyperglycemia is associated with oxidative stress, which results from increased free radical generation

and impaired antioxidant defense system (Maritim *et al* 2003). To analyze the lipid peroxidation and oxidative stress in laboratory animals, the TBARS assay is commonly employed. In the present study, a marked reduction in the plasma TBARS was observed in rice-fed groups compared with that of the high fat-fed mice, suggesting a decreased rate of lipid peroxidation. A highly complex antioxidant protection system has been developed by the cells in order to control oxidative stress and regulate the destructive potential of free radicals. This includes antioxidant enzymes, such as SOD, GPx, CAT, GR and PON, which catalyze free radicals-quenching reactions. The significant decrease in the plasma TBARS and enhancement in the activities of GPx, GR, PON, SOD and erythrocyte CAT enzymes in HF-GR and HF-NR groups relative to HF mice suggest a marked enhancement in the antioxidative system of the mice, making them less susceptible to peroxidative damage under high fat diet condition. The SOD enzyme protect the cells from oxidative damage by converting superoxide radicals into hydrogen peroxides, which are then utilized and degraded by CAT and GPx enzymes into non-toxic products (Reiter *et al*. 2002). On the other hand, the GR enzyme converts oxidized glutathione to antioxidant reduced glutathione (Mullineaux and Creissen 1997) and the PON enzyme hydrolyzes biologically active oxidized phospholipids and destroys lipid hydroperoxides (Ng *et al* 2005). Diabetes is a free radical-mediated disease, hence, functional foods that have strong antioxidative property could reduce glucose levels by protecting the cells against free radicals under hyperglycemic condition. The enhancement of glucose metabolism observed in mice fed with Goami and Nokwon is probably partly due to the *in vivo* antioxidative status-improving effect of these functional rice grains.

In conclusion, the results demonstrate that functional rice Goami and Nokwon could improve the glucose metabolism and suppress oxidative stress in mice under high fat diet condition through the inhibition of G6pase and PEPCK activities and enhancement of the antioxidant enzyme activities. This study provides the first evidence of the hypoglycemic and antioxidative effects of these new functional rice cultivars, indicating that they may be beneficial in the development of functional food for the prevention and treatment of high fat diet-induced hyperglycemia and oxidative stress.

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