Effect of high-amylose rice "Hoshinishiki" on postprandial glucose levels measured by continuous glucose monitoring in patients with diabetes

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We examined the effect of consuming Hoshinishiki, a type of high-amylose rice, on postprandial glucose as measured by continuous glucose monitoring in diabetes patients. A single-blinded clinical trial involving 11 hospitalized patients diagnosed with type 1 or type 2 diabetes was performed. The patients consumed high-amylose rice for 2 days (days 2 and 4 of the study) and control rice for 2 days (days 1 and 3 of the study). Linear mixed models were used to test the effects on the 24-h mean glucose levels, time in range (TIR), incremental area under the curve of glucose levels at 2 h after meals, the average glucose levels at 1, 2, and 3 h after meals, and the maximum glucose levels within 3 h. The results showed that the consumption of high-amylose rice led to significantly lower 24-h mean glucose levels, levels at 2 and 3 h after a meal, and postprandial glucose peak levels within 3 h, as well as significantly higher TIR. A similar trend was observed when the analysis was restricted to patients with type 2 diabetes. These results suggest that high-amylose rice may be a more beneficial staple food for glycemic control than regular rice.

Key Words: **high-amylose rice, diabetes, glucose, continuous glucose monitoring**

Diabetes is a chronic disease posing a major threat to human health. As of 2019, there are 463 million patients with diabetes worldwide and this number continues to increase.[1] There are various risk factors for diabetes; a meta-analysis of cohort studies showed that high intake of white rice was associated with a higher risk of diabetes in Asian populations who consume rice as their staple diet vs Western populations.[2] Previous research has demonstrated that white rice is a type of food with high glycemic index.[3]

The exclusion of rice from diets is difficult due to the major role of this cereal in the diet of numerous populations, including the Japanese.[4] Therefore, a diet that includes rice but also exerts a lowering effect on glucose levels might be beneficial for patients with diabetes.

Rice is divided into rice bran, which has functional components, and endosperm, which is mainly consumed as a staple food. The endosperm also contains functional components such as amylose.[5,6]

High-amylose rice has been linked to a lower increase in postprandial glucose levels than has white rice.[7] Amylose has a linear structure that is not easily cleaved by α-amylase and decomposed; thus, it is classified as resistant starch type 2.[8] Owing to its molecular structure, amylose does not lead to major increases in blood glucose levels.[9] Therefore, higher amylose content of rice is associated with slower digestion and absorption of starch.[10] A previous study revealed that high-amylose rice may contribute to the correction of glucose levels compared with standard white rice.[11] High-amylose rice may thus be useful in the diet of patients with diabetes.

In recent years, the use of continuous glucose monitoring (CGM) has enabled the estimation of glucose level indices, such as time in range (TIR) and other indicators. This approach assists in the evaluation of the glycemic status, including the presence or absence of hypoglycemic risk, postprandial hyperglycemia, and glucose fluctuation range.[12] CGM is a useful tool for clarifying the role of high-amylose rice with respect to postprandial glucose levels. However, the effect of high-amylose rice intake on the continuous glucose levels has not been investigated thus far.

The purpose of this study was to examine the effect of high-amylose rice intake on continuous glucose levels measured by CGM in patients with diabetes.

Materials and Methods

Study design. This study was a single-blinded clinical trial conducted at Ehime University Hospital (Toon, Ehime, Japan) from November 2018 to August 2019. The study protocol was approved by Institutional Review Board, Ehime University Hospital During hospitalization, the research physicians explained in detail the purpose of this study to the subjects. All subjects provided written informed consent prior to their participation. This study was registered at the UMIN clinical trial registration system (identification number: UMIN000034675).

The subjects participated in this study for a maximum of 7 days. On alternate days, the subjects consumed high-amylose rice (every meal for 3 days) and white rice (control) (every meal for 4 days). A washout period was not included in this study (Fig. 1).

CGM was performed during the course of this study. However, some data were missing due to various reasons, such as temporary discharge from the hospital, failure to wear the device, or not

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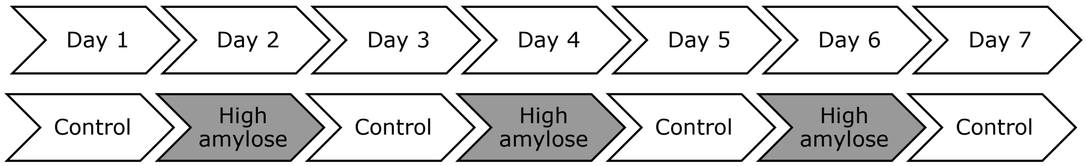

Fig. 1. Timeline of the study visits.

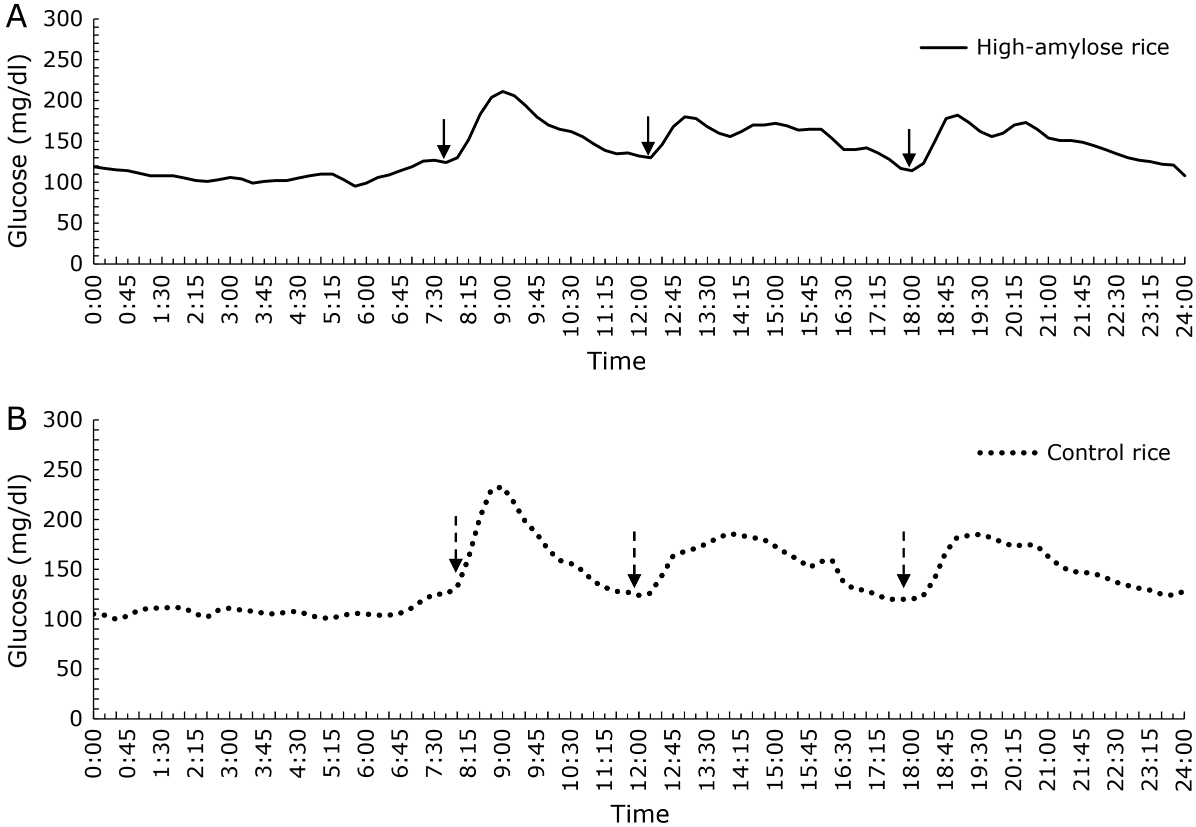

Fig. 2. Two typical examples of 24 h glucose from the continuous glucose monitoring system. (A) solid line represents one experimental day with high amylose rice consumption, while (B) dashed line represents one experimental day with consumption of control rice. The starts of meals are represented as arrows.

consuming the meals provided by the hospital. To ensure data consistency across participants (i.e., per person each rice at least 24-h continuous monitoring and consumption of both types of rice for 4 consecutive days), only a sub-period of 2 days of high amylose rice diet and of 2 days of control rice diet was selected and analyzed for each subject.

Subjects. Patients eligible for inclusion in this study were inpatients aged 20–74 years and diagnosed with type 1 or type 2 diabetes according to the diagnostic criteria of the Japanese Diabetes Association.[13] Exclusion criteria were pregnancy and lactation, malignant neoplasms, ischemic heart disease, cerebrovascular disease, chronic kidney disease, dementia, and severe gastrointestinal diseases for which the patient was receiving treatment at the time of the study. Patients deemed unsuitable to participate by the physician were also excluded. At the start of hospitalization, the body mass index (BMI) of subjects ranged from 18.5 to 35.0 kg/m^2.

Finally, 11 patients (seven males and four females) aged 44–72 years with a BMI of 19.9–31.3 kg/m^2 participated in this study.

Glucose control index. A FreeStyle Libre Pro system (Abbott Diabetes Care Inc., Alameda, CA) and a special sensor were used to perform CGM. CGM involved the continuous recording of subcutaneous glucose concentration every 15 min. We calculated the time in range (TIR), time below range (TBR), and time above range (TAR). TIR is the percentage of time in a day when glucose levels range between 70 and 180 mg/dl, TBR is the percentage of time when glucose levels are lower than this range, and TAR is the percentage of time when glucose levels are above this range.[14]

As shown in the typical examples in Fig. 2, we measured a 24-h glucose levels recorded by the CGM. Through visual inspection, we observed differences in the postprandial glucose on different rice intake days. Therefore, we thought CGM-supported analyzing to illustrate different glucose variations after the consumption of different rice. To confirm the increase in postprandial glucose levels, based on the subjects' starts of meals, we calculated the incremental area under the curve (IAUC) of the glucose levels for 2 h after each meal, the average glucose levels every hour for 3 h after each meal, and the postprandial glucose peak levels within 3 h after each meal The postprandial glucose peak was defined as the highest glucose value recorded after a meal by the CGM system.

Test rice. The high-amylose rice used in this study was "Hoshinishiki". This rice was developed by the National Agriculture and Food Research Organization, and cultivated and harvested by the Ehime Prefectural Ministry of Agriculture, Forestry and Fisheries in 2018. For the control rice, we used ordinary rice that is usually served to inpatients in Ehime University Hospital. Table 1 shows the nutritional content of each type of rice analyzed at Japan Food Research Laboratories. The levels of amylose in Hoshinishiki were measured using a BL-TEC Auto Analyzer (B-L-Tech Co., Ltd., Osaka, Japan). According to the results, the percentage of amylose was 24.9 ± 0.6% (mean ± SD; $n = 3$).[15] The quantity provided to patients was based on the energy requirements indicated by the physicians, who ensured that the amount of carbohydrates was identical between groups.

Other measurements. Anthropometric measurements (i.e., height and weight) were recorded upon admission. Blood was drawn from the left elbow vein using a vacuum blood collection tube. The levels of glycated hemoglobin A1c and fasting glucose were also measured.

Statistical analysis. The average glucose levels every hour and the postprandial glucose peak levels within 3 h were not normally distributed. Therefore, natural logarithmic transformations were used for those variables. A linear mixed model was utilized to test the effect of high-amylose rice on the outcomes assessed by CGM. In addition, since insulin secretion differed between type 1 and type 2 diabetes, sensitivity analyses were conducted only for patients with type 2 diabetes ($n = 9$). Probability values for the statistical tests were two-tailed, and p values <0.05 denoted statistically significant difference. The SAS statistical package ver. 9.4 (Statistical Analysis System, Cary, NC) was used for the analyses.

Results

Characteristics of the subjects. Characteristics of the subjects are presented in Table 2. The mean age was 59.0 years and mean BMI was 26.0 kg/m^2. Seven participants (64%) were male. Nine participants (82%) were type 2 diabetes; in this subgroup, the mean age was 61.7 years and mean BMI was 26.3 kg/m^2.

Effects on glucose control index. The mean values and SD of glucose levels and glucose control indices for the high-amylose and control rice are shown in Table 3. The 24-h mean glucose levels were significantly lower in the high-amylose rice group (134.7 mg/dl) than in the control rice group (140.0 mg/dl) (p<0.01). There was no significant difference in TBR between high-amylose and control rice. The TIR associated with the high-amylose rice (81.72%) was significantly higher than that recorded for control rice (76.66%) ($p = 0.01$). High-amylose rice was linked to lower TAR values than control rice, but the difference was not significant (17.19% vs 21.83%; $p = 0.06$). Similar associations were observed when the analysis was limited to patients with type 2 diabetes. The differences in TAR (high-amylose rice: 11.52%, standard rice: 17.59%; $p = 0.02$) and TIR (high-amylose rice: 88.35%, standard rice: 81.77%; $p = 0.02$) were significant.

Effects on postprandial glucose responses. Table 4 shows the IAUC of 2-h postprandial glucose, the average glucose per hour for 3 h after meals, and the postprandial glucose peak levels within 3 h. There was no significant difference in IAUC between the two types of rice. However, the means of glucose level at 2 and 3 h after a meal, and the postprandial glucose peak levels within 3 h were significantly lower with the high-amylose rice than the control rice. (167.4, 141.4, and 197.2 mg/dl vs 188.0, 161.1, and 211.9 mg/dl, respectively). The similar effects on the postprandial glucose at 2 and 3 h was also observed when the analysis was limited to patients with type 2 diabetes.

Discussion

Consumption of high-amylose rice was associated with a higher TIR, and lower TAR compared with the consumption of

Table 1. Nutritional contents for each test rice (per 100 g)

	High-amylose rice	Control rice
Energy (kcal)	157	145
Carbohydrates (g)*	35.6	33
Dietary fiber (g)	0.8	0.5
Protein (g)	2.3	2.4
Fat (g)	0.4	0.4

*Exclude dietary fiber.

Table 2. Baseline characteristics of the subjects

	All	Type 2 diabetic patients
n	11	9
Male (%)	7 (64%)	5 (56%)
Age (years)	59.0 ± 9.9	61.7 ± 8.9
BMI (kg/m^2)	26.0 ± 3.9	26.3 ± 3.5
HbA1c (%)	8.8 ± 0.9	8.9 ± 1.0
Fasting plasma glucose (mg/dl)	160.2 ± 26.4	151.1 ± 20.0

Each value is expressed as the mean ± SD or number (%).

Table 3. Means and SD of glucose level and glucose control indices according to high-amylose and control rice

	High-amylose rice	Control rice	p value*
All (n = 11)			
Mean glucose level† (mg/dl)	134.7 (99.9, 181.6)	140.0 (102.2, 191.8)	<0.01
TBR (%)	1.09 ± 3.07	1.51 ± 4.49	0.99
TIR (%)	81.72 ± 20.03	76.66 ± 17.35	0.01
TAR (%)	17.19 ± 19.84	21.83 ± 17.26	0.06
Type 2 diabetic patients (n = 9)			
Mean glucose level† (mg/dl)	130.9 (103.1, 166.2)	136.6 (103.7, 179.9)	<0.01
TBR (%)	0.13 ± 0.52	0.64 ± 2.24	0.63
TIR (%)	88.35 ± 12.04	81.77 ± 13.94	0.02
TAR (%)	11.52 ± 12.16	17.59 ± 13.95	0.02

Each value was expressed as the mean ± SD. *Tested by linear mixed model. †Value was expressed as geometric mean (range of SD).

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Table 4. Means and SD of IAUC and postprandial glucose levels according to high-amylose and control rice

		High-amylose rice	Control rice	*p* value*
All (*n* = 11)				
IAUC values of 2 h postprandial glucose (min × mg/dl)		5,078.2 ± 2,290.1	5,159.4 ± 3,118.5	0.71
Mean value of postprandial glucose within 3 h (mg/dl)†	Fasting	124.9 (93.6, 166.7)	135.2 (99.8, 183.2)	0.34
	1 h	183.4 (139.8, 240.5)	191.7 (153.7, 239.0)	0.91
	2 h	167.4 (131.1, 213.6)	188.0 (150.5, 234.9)	0.03
	3 h	141.4 (103.9, 192.5)	161.1 (126.4, 205.4)	0.01
	The postprandial peak value for glucose	197.2 (159.0, 244.7)	211.9 (174.4, 257.3)	0.04
Type 2 diabetic patients (*n* = 9)				
IAUC values of 2 h postprandial glucose (min × g/dl)		5,075.0 ± 2,434.3	5,174.6 ± 2,696.6	0.62
Mean value of postprandial glucose within 3 h (mg/dl)†	Fasting	119.7 (99.2, 144.4)	127.8 (102.4, 159.4)	0.51
	1 h	179.4 (148.3, 217.1)	184.7 (154.9, 220.3)	1.00
	2 h	161.0 (133.4, 194.4)	180.6 (151.5, 215.2)	0.02
	3 h	141.4 (116.1, 172.1)	155.6 (127.6, 189.6)	0.08
	The postprandial peak value for glucose	189.1(160.3, 223.0)	202.6 (173.5, 236.5)	0.11

Each value is expressed as the mean ± SD. *Tested by linear mixed model. †Value is expressed as Geometric mean (range of SD).

control rice. Furthermore, there was no significant difference in the IAUC of 2 h postprandial glucose between the two types of rice. However, the 24-h mean glucose level, 2- and 3-h postprandial glucose levels, and the postprandial glucose peak levels within 3 h were significantly lower for high-amylose rice vs control rice.

The association of lower postprandial glucose levels with the intake of high-amylose rice vs control rice is consistent with the findings of previous studies.(16) However, in previous research involving healthy subjects high-amylose rice was associated with a significantly lower IAUC of glucose vs control rice,(17–19) which was not observed in the present study. In addition, a previous interventional study did not demonstrate significant difference in the area under the curve for 3-h postprandial glucose between high-amylose rice (23–25% amylose) and regular rice (14–17% amylose),(20) but found high amylose rice result in flatter glucose curve. The authors suggested that the lower initial glucose response and slower decline in glucose levels associated with the increasing levels of amylose may be related to differences in lipid–amylose complex content among different varieties of rice. A portion of the lipid content may affect the utilization rate of carbohydrates.(21) This is consistent with the results of the present study, which revealed significant differences with a higher TIR and lower TAR. It has been reported that amylose (a type of resistant starch) suppresses elevated blood glucose levels.(22) Research demonstrated that consumption of resistant starch prolongs the action duration of the glucose-dependent insulinotropic polypeptide,(23) a hormone that promotes insulin secretion.(24,25) This is consistent with the results of the present study, which revealed significant differences in postprandial glucose levels at later time points (i.e., 2 and 3 h). In addition, resistant starch may reduce the action of digestive enzymes on digestible starch, thereby reducing the rates of digestion and absorption in the small intestine. This effect moderates the glycemic response, resulting in lower glucose uptake into the blood.(26) This mechanism may underlie the better glycemic control associated with high-amylose rice vs regular rice.

In this study, insulin and other parameters related to glucose metabolism were not measured, and we were therefore unable to determine their roles in the investigated biological mechanism. However, a previous interventional study showed that all participants exhibited a significant decrease in the insulin response curve area after long-term consumption of foods with high amylose content.(27) Therefore, we presumed that a similar mechanism may be responsible for the findings of the present study. In addition, since high amylose rice is also high in dietary fiber, according to previous studies, intake of snacks high in dietary fiber can suppress postprandial blood glucose levels and the effect lasts until breakfast the next day.(28) This effect might also explain our findings. In this study, we cannot rule out the possibility of a carryover effect due to the small sample size and the fact that the high-amylose rice and control rice was consumed on alternate days. Furthermore, it is possible that the effect of high-amylose rice is also partly attributed to the treatment that inpatients were receiving at the time of the study.

Based on the results of the present study, high-amylose rice promotes faster reduction of elevated glucose levels after a meal in patients with diabetes compared with control rice. Hence, it may be a useful diet component for such patients. High-amylose rice is often considered undesirable by Japanese people because it is hard and has little stickiness. However, the Hoshinishiki rice used in this study has a relatively good eating quality. Moreover, in this study, there were no differences in the preference of patients for the consumption of high-amylose rice or control rice. Therefore, it is expected that high-amylose rice will be acceptable when offered as a staple food.

In this study, the high-amylose rice "Hoshinishiki" led to lower glucose levels at 3 h after consumption and higher overall levels of the glucose control index TIR, compared with control rice. These results suggest that high-amylose rice has the potential to become a staple food that is more useful for glucose control than regular rice.

Author Contributions

JL contributed to the study concept and design, performed statistical analysis, and drafted the manuscript. KM contributed to the study concept and design, analyzed and interpreted data, and critically revised the manuscript for important intellectual content. SM provided material support for the study. KT contributed to the acquisition of data. RK, YT, and HO contributed to the study concept and design, and provided study supervision.

Conflict of Interest

No potential conflicts of interest were disclosed.

References

1 IDF Diabetes Atlas 9th edition 2019. The International Diabetes Federation. https://www.diabetesatlas.org/en/sections/worldwide-toll-of-diabetes.html. Accessed 9 Dec 2019.

2 Hu EA, Pan A, Malik V, Sun Q. White rice consumption and risk of type 2 diabetes: meta-analysis and systematic review. *BMJ* 2012; **344**: e1454.

3 Miller JB, Pang E, Bramall L. Rice: a high or low glycemic index food? *Am J Clin Nutr* 1992; **56**: 1034–1036.

4 The National Health and Nutrition Survey in Japan, 2019. Ministry of Health, Labour and Welfare. https://www.mhlw.go.jp/content/001066903.pdf. Accessed 12 Jan 2021.

5 Tochitani S, Maehara Y, Kawase T, *et al*. Fermented rice bran supplementation ameliorates obesity via gut microbiota and metabolism modification in female mice. *J Clin Biochem Nutr* 2022; **70**: 160–174.

6 Choi JY, Paik DJ, Kwon DY, Park Y. Dietary supplementation with rice bran fermented with Lentinus edodes increases interferon-γ activity without causing adverse effects: a randomized, double-blind, placebo-controlled, parallel-group study. *Nutr J* 2014; **13**: 35.

7 Yamasaki M, Watanabe M, Yoneyama T, Nogi A, Wang L, Shiwaku K. Influence of rice with different amylose contents on postprandial glycemic response. *J Rural Med* 2007; **2**: 51–58.

8 Ebihara K. Nutritional and physiological functions of resistant starch. *J Cookery Sci Jpn* 2014; **47**: 49–52. (in Japanese)

9 Panlasigui LN, Thompson LU, Juliano BO, Perez CM, Yiu SH, Greenberg GR. Rice varieties with similar amylose content differ in starch digestibility and glycemic response in humans. *Am J Clin Nuir* 1991; **54**: 871–877.

10 Ohtsubo K. Characteristics and selection of suitable rice cultivars depending on utilizations (2). *J Cookery Sci Jpn* 2018; **51**: 290–296. (in Japanese)

11 Unno R, Hayashi Y, Takagi R, Takano K, Kawamori R. Effect of long-term consumption of high-amylose rice "Yuki no Ho" on blood glucose profile in glucose intolerant subjects. *J Metab Clin Nutr Jpn* 2015; **18**: 375–385. (in Japanese)

12 Sato A. The usefulness of continuous glucose monitoring systems (CGMS). *Shinshu Med J* 2018; **66**: 17–27. (in Japanese)

13 Araki E, Goto A, Kondo T, *et al*. Japanese Clinical Practice Guideline for Diabetes 2019. *Diabetol Int* 2020; **11**: 165–223.

14 Battelino T, Danne T, Bergenstal RM, *et al*. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. *Diabetes Care* 2019; **42**: 1593–1603.

15 Maruyama K, Minakuchi S, Tomooka K, Tanigawa T. Examination of the glycemic index for the high-amylose rice variety "Hoshinishiki" grown in Ehime prefecture. *J Nutr Sci Vitaminol* 2019; **72**: 85–89. (in Japanese)

16 Unno R, Hayashi Y, Takaki R, *et al*. Effects of high amylose rice "Yuki no Ho" rice on postprandial blood glucose and insulin secretion in type 2 diabetes patients on medication. *J Metab Clin Nutr Jpn* 2016; **19**: 111–120. (in Japanese)

17 Zenel AM, Stewart ML. High amylose white rice reduces post-prandial glycemic response but not appetite in humans. *Nutrients* 2015; **7**: 5362–5374.

18 Unno R, Hayashi Y, Takagi R, Takano K, Kawamori R. Effects of high amylose rice "Yuki no Ho" on postprandial blood glucose and insulin secretion in healthy adults. *J Metab Clin Nutr Jpn* 2012; **15**: 167–173. (in Japanese)

19 Yamaguchi T, Enoki Y, Sasagawa K, Fujimura S. Evaluation of postprandial glycemic response and physical properties of high-amylose rice "Koshinokaori". *J Nutr Sci Vitaminol* 2019; **65**: S117–S121.

20 Goddard MS, Young G; Marcus R. The effect of amylose content on insulin and glucose responses to ingested rice. *Am J Clin Nutr* 1984; **39**: 388–392.

21 Collier G, O'Dea K. The effect of coingestion of fat on the glucose, insulin, and gastric inhibitory polypeptide responses to carbohydrate and protein. *Am J Clin Nutr* 1983; **37**: 941–944.

22 EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA).. Scientific opinion on the substantiation of health claims related to resistant starch and reduction of post-prandial glycaemic responses (ID 681), "digestive health benefits" (ID 682) and "favours a normal colon metabolism" (ID 783) pursuant to Article 13(1) of regulation (EC) No 1924/2006. *EFSA Journal* 2011; **9**: 2024.

23 Masako D, Yamada H, Kitagawa N, *et al*. New therapeutics for diabetes mellitus - Incretin related drugs. *Med J Kyoto Second Red Cross Hospital* 2011; **32**: 19–27. (in Japanese)

24 MacNeil S, Rebry RM, Tetlow IJ, Emes MJ, McKeown B, Graham TE. Resistant starch intake at breakfast affects postprandial responses in type 2 diabetics and enhances the glucose-dependent insulinotropic polypeptide-insulin relationship following a second meal. *Appl Physiol Nutr Metab* 2013; **38**: 1187–1195.

25 Weickert MO, Mohlig M, Koebnick C, *et al*. Impact of cereal fibre on glucose-regulating factors. *Diabetologia* 2005; **48**: 2343–2353.

26 Hayakawa T, Tsuge H. Starch intake and health-physiological effects of resistant starch. *J Jpn Assoc Dietary Fiber Res* 1999; **3**: 55–64. (in Japanese)

27 Behall KM, Howe JC. Effect of long-term consumption of amylose vs amylopectin starch on metabolic variables in human subjects. *Am J Clin Nutr* 1995; **61**: 334–340.

28 Kim HK, Nanba T, Ozaki M, *et al*. Effect of the intake of a snack containing dietary fiber on postprandial glucose levels. *Foods* 2020; **9**: 1500.

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