



Effect of sorghum intake on postprandial blood glucose levels: A randomized, double-blind, crossover study

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Submission Date: December 7th, 2023; **Acceptance Date:** January 11th, 2024; **Publication Date:** January 16th, 2024

Please cite this article as: Miyazaki H., Nagae M., Uchida H., Shimizu K. Effect of Sorghum Intake on Postprandial Blood Glucose Levels - A Randomized, Double-Blind, Crossover Study. *Functional Foods in Health and Disease* 2024; 14(1): 87-95. DOI: <https://doi.org/10.31989/ffhd.v14i1.1266>

ABSTRACT

Background: Sorghum is consumed in Africa, North and South America, India, and other parts of the world, but it is one of several millets in Japan, and its physiological function for Japanese is not well known. In this study, we examined the effect of sorghum on postprandial blood glucose levels in healthy Japanese.

Objective: This study aims to investigate the effect of sorghum intake on postprandial blood glucose in healthy adults.

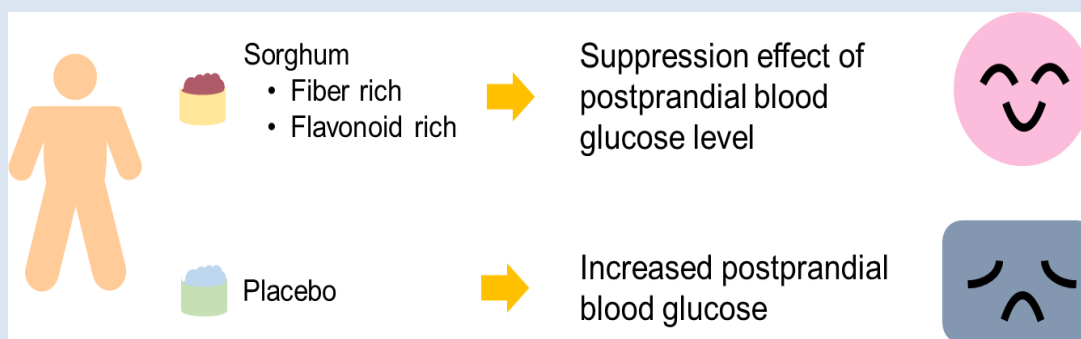
Methods: A double-blind crossover study was done on 17 healthy adult men and women recruited from the general population. After an early morning fasting blood glucose test, a placebo or sorghum porridge was administered and blood glucose levels were measured at 30, 60, and 120 minutes after the first washout period.

Result: At 60 and 120 minutes after intake, the blood glucose level of people who were administered sorghum porridge was significantly lower than that of those who were administered the placebo. The area under the blood glucose curve was also significantly lower for the test product than for the placebo.

Conclusion: Sorghum consumption can suppress the increase in postprandial blood glucose, suggesting that sorghum is useful in preventing the development of diabetes mellitus.

Keywords: Sorghum, blood glucose, postprandial blood glucose

Trial registration: UMIN-CTR: UMIN000046235



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INTRODUCTION

Diabetes is on the rise and is recognized as a major health issue worldwide, not only because of decreased life expectancy of individuals with diabetes, but also because of the cost of medical care for diabetes patients. According to the International Diabetes Federation (IDF) Diabetes Atlas 10th edition reports, 537 million adults (20–79 years old) are living with diabetes. This number is predicted to rise to 643 million by 2030 and 783 million by 2045 [1]. In Japan, there are an estimated 11 million people with diabetes, 45% of which are not yet diagnosed with the illness. People of Asian heritage tend to develop diabetes at a much lower body mass index (BMI) than people of a Caucasian ethnicity [2]. Along with this, insulin deficiency plays a greater role in type 2 diabetes in people of Asian descent than in people of Caucasian descent [3]. From these facts, it is considered that suppressing the postprandial blood glucose level is important in preventing the onset of diabetes in Japanese.

Sorghum is one of the world's major cereal grains and has been attracting attention as a sustainable grain that can be grown with less water and fertilizer than wheat [4]. The functionality of sorghum was reported

with a focus on its blood glucose reduction effect [5-6], body fat reduction effect [7], and antioxidant function [8-9]. In recent years, sorghum has attracted attention in Western countries because of its gluten-free properties. It is said to have come to Japan from China and has been cultivated as "Takakibi" or "Akakibi" since ancient times [10]. In recent years, the functionality of millet has attracted attention, and sorghum is one of them [11].

Most of the clinical trials on sorghum intake reported to date have been conducted in Africa [6,12,13], North, South America [5,7,9,14], Australia [8,16-17], and India [18-20]. In these studies, sorghum has been shown to be effective in reducing blood glucose levels. [5-6,14,16-17,20]. However, there have been few reports from Eastern Asian countries, including Japan. Research has proven that there are significant differences in glucose metabolism between people of different races [21-22]. The effect of food on postprandial blood glucose levels in healthy Japanese people has got attention in recent years, therefore there are several reports on this subject [23-25]. In this study, we investigated postprandial blood glucose levels in healthy Japanese men and women who consumed sorghum.

METHODS

Study design: Before participants started the study, study personnel provided study participants with a sufficient explanation of the purpose of the study, research content, ethical considerations, disadvantages of study participation, protection of personal information, and free will to participate as part of the informed consent process. After confirming a full understanding of the study, participants provided written consent to participate in the study. The principal investigator of this study was Kuniyoshi Shimizu (Professor, Faculty of Agriculture, Kyushu University), who had the final responsibility and authority to make all decisions.

This study was conducted in accordance with the intention of the Declaration of Helsinki (adopted in 1964, revised in 2013 by Fortaleza), in compliance with the Ethical Guidelines for Medical Research Involving Human Subjects (Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare, Notification No. 3, 2014, partially revised in 2017), and with the approval of the Bioethics Committee of the Kinki University Faculty of Industrial Science and Technology (approval number: 202102) and was registered in the clinical trial registration system UMIN Clinical Trial Registry (UMIN-CTR) (UMIN registration number: UMIN000046235).

Study participants: Subjects were selected to be generally healthy men and women between the ages of 20 and 70 years old. Exclusion criteria was as follows: (1) subjects who are continuously using healthy foods, quasi-drugs, or pharmaceuticals that claim or emphasize efficacy similar to or related to the efficacy being studied in this study, (2) subjects working night shifts or day and night shifts, (3) subjects who at the time of obtaining consent, were receiving treatment (hormone replacement therapy, drug therapy, exercise therapy, dietary therapy) at a medical institution for the treatment or prevention of diseases, or for whom

treatment is anticipated (4) subjects with a history of serious diseases involving glucose metabolism, lipid metabolism, liver function, renal function, heart, circulatory organs, respiratory organs, endocrine system, immune system, nervous system, or psychiatric diseases, (5) subjects with a history of alcohol or drug dependence, (6) subjects with possible allergy to food, (7) pregnant or lactating subjects at the time of consent, or aspired to become pregnant during the study period, (8) subjects determined to be inappropriate to participate in the study by the study director. As shown in Figure 1, among the 17 applicants, 4 subjects who violated the exclusion criteria were excluded, and 13 subjects (age: 50.3 ± 13.0 years, BMI: 21.1 ± 1.8 kg/m²) were included in the study.

Trial food and Trial methods: The test product was 360 g of sorghum porridge or 360 g of placebo porridge provided by BEST AMENITY Co., Ltd. (Table 1). Prepare the porridge by adding five times the amount of water as the grains and heat it for 30 minutes. The study design was a double-blind crossover study. Subjects were randomly divided into two groups: a test product-first group and a placebo-first group. The study was conducted with a one-week washout period. Subjects were told to fast from 9:00 p.m. on the day before the washout period and started consuming the test sample at 9:30 a.m. on the day of the study at the test site. Blood glucose levels were measured by the subjects themselves using a puncture device and a self-monitoring blood glucose meter. Blood glucose levels were measured before (0 minutes), 30 minutes, 60 minutes, and 120 minutes after the intake of the test sample. A blood glucose curve was generated from the measured blood glucose levels, and the incremental area under the curve (iAUC) was calculated using the trapezoidal formula.

Statistical analysis: Correspondence t-tests were performed for differences between groups at each measurement time, and independent t-tests were performed to compare iAUCs between groups.

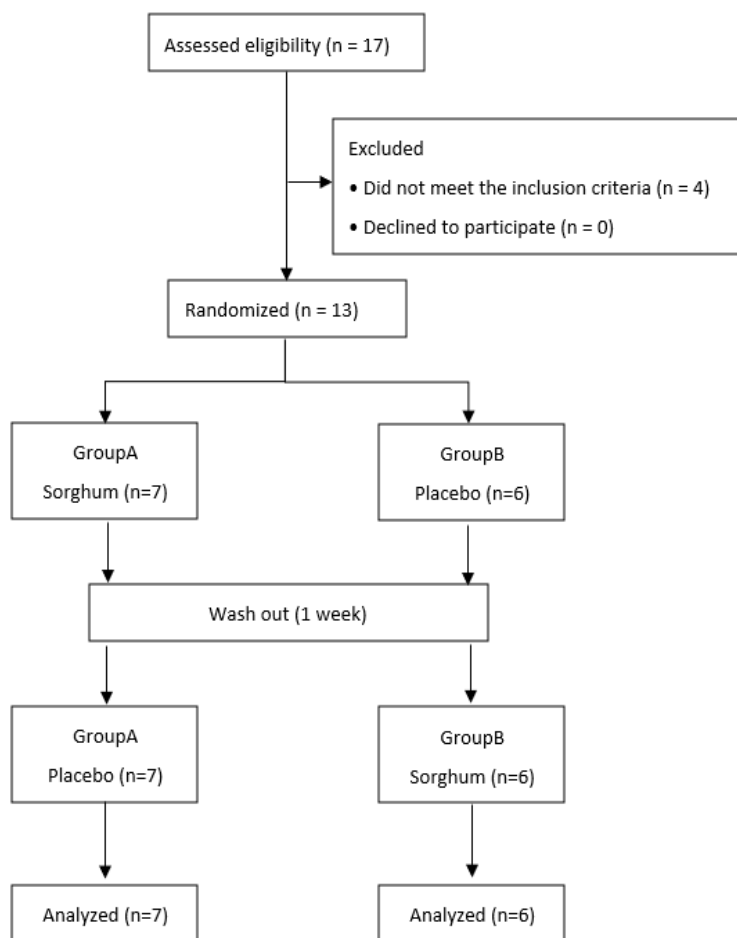


Figure 1. Flowchart of subjects in this study

Table 1. Nutritional values of the test products

	sorghum	placebo
Energy (kcal)	207	205
Carbohydrates (g)	45.5	46.6
Protein (g)	4.7	3.7
Fat (g)	1.1	0.5
Dietary fiber (g)	1.5	0.3

Table 2. Characteristics of the subjects

Sex (%)	
Female	11 (84.6)
male	2 (15.4)
Age	50.3 ± 13.0
BMI (kg/m ²)	21.2 ± 1.9
Fasting blood glucose (mg/dl)	100.5 ± 8.6

Mean ± SD

RESULTS

Table 2 shows the characteristics of the subjects. The mean fasting blood glucose level of the subjects was 100.5 ± 8.6 mg/dl. Figure 2 shows the blood glucose curve. There was no significant difference in blood glucose levels between the two groups before ingestion of the test substance (0 min). Although there was no difference in blood glucose levels between the groups at

30 minutes after intake of the sorghum, the blood glucose levels at 60 minutes ($p = 0.04$) and 120 minutes ($p = 0.021$) after intake of the sorghum were significantly lower than those who had the placebo. The AUC was also calculated and showed significantly lower values in the sorghum group compared to the placebo group ($p = 0.026$) as shown in Figure 3

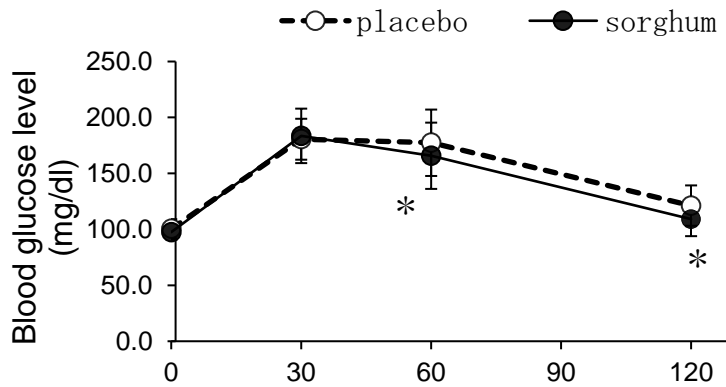


Figure 2. Blood glucose curves during ingestion of sorghum and placebo.

* $p < 0.05$ placebo vs sorghum.

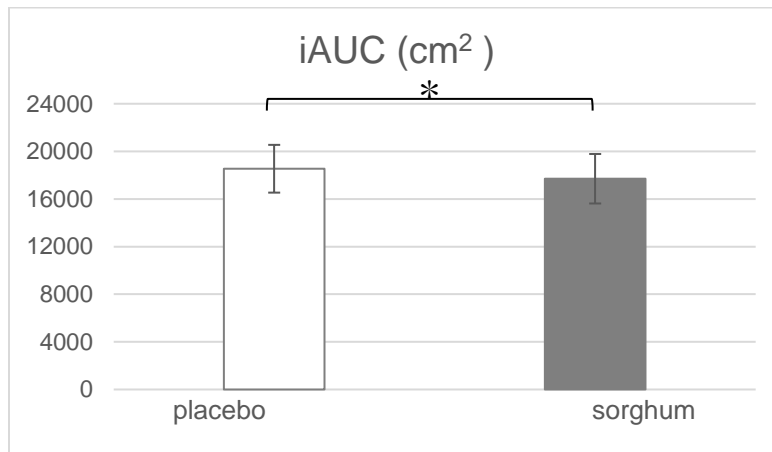


Figure 3. iAUC at intake of sorghum and placebo.

* $p < 0.05$ significance.

DISCUSSION

In this study, we investigated blood glucose levels in healthy subjects who consumed sorghum or a placebo and found that blood glucose levels were significantly lower at 60 minutes and 120 minutes after consumption

of sorghum compared with the placebo. Additionally, the iAUC was also significantly lower with sorghum consumption than with placebo consumption. One of the physiological functions of sorghum consumption has been reported to be its ability to lower postprandial

blood glucose; Poquette et al. [14] reported that muffin consumption with sorghum flour suppressed blood glucose and insulin secretion more than muffin consumption with wheat flour. In another report, consumption of sorghum drinks resulted in lower postprandial glycemic peaks compared to the non-sorghum drink [5]. Regarding the mechanism of action of sorghum on the blood glucose level suppression effect, the reduction of starch digestibility [15] and the influence of dietary fiber content [6,16-17] is considered, however, the involvement of flavonoid compounds contained in high concentrations of sorghum [26] is also attracting attention. It was reported that sorghum tannins reduce the activity of α -amylase [27-28] which breaks down starch contained in many foods humans consume. Taxifolin is one of the major polyphenolic compounds in sorghum [29].

It was demonstrated that taxifolin promotes glucose transporter 4 (GLUT4) translocation [30]. The transport of GLUT4 from the intracellular pool to the plasma membrane plays an important role in the glucose uptake mechanism of insulin into adipocytes and skeletal muscle cells [31-32]. Molecular mechanisms of GLUT4 transport by insulin are known to involve the activation of phosphatidylinositol-3-phosphate [33] and adenosine monophosphate-activated protein kinase (AMPK) [34]. It was reported that taxifolin activates both protein kinase B (Akt) and AMPK in a mouse model of type 2 diabetes and promotes GLUT4 translocation from the cytosol to the plasma membrane of L6 myotubular cells via both phosphoinositide-3-kinase (PI3K)/Akt and AMPK signaling pathways [30]. There are also reports that taxifolin has an inhibitory effect on α -glucosidase activity [35], however since the suppression of blood glucose levels in this study was observed after 60 minutes of intake, the mechanism of action is likely to be GLUT4-related.

Sorghum contains about 20 times the dietary fiber than that of polished rice. Therefore, it is expected that more chewing is required when consuming sorghum than when consuming polished white rice. When comparing white rice and brown rice (richer in dietary fiber than white rice) it was reported that the number of times to chew brown rice is significantly higher than that of white rice [36]. Regarding the effect of chewing on blood glucose regulation, Takahara et al. [37] reported that mastication increases glucagon-like peptide 1 (GLP-1), which triggers insulin secretion and suppresses the increase in postprandial blood glucose levels. In this study, to lower the effect of mastication and to verify the effect of the ingredients in sorghum on blood glucose levels, porridge eaten softly in the same way both without almost chewing was used instead of rice with normal water content, and the mastication conditions were adjusted so that there was no difference between the placebo and chewing conditions. Under these conditions, sorghum intake showed a blood glucose suppression effect. It was established that a higher blood glucose suppression effect can be expected in the future by conducting similar tests using rice instead of porridge, due to the synergistic effects of mastication and the effect of rice porridge. It has been reported that the low-energy Japanese diet, which is rich in dietary fiber, can prevent obesity from enhancing of satiation by increased mastication required of the diet [38].

Sorghum is eaten as a staple food in Africa and Asia, but most studies have compared it to wheat [6,8,19]. Prasad et al. [18] reported that sorghum-based foods showed a significantly lower glycemic index than rice-based foods. However, the rice-based foods used in this trial were mixed with a variety of ingredients. In our study, we compared it to rice boiled with only water, a cooking method commonly used by Japanese people cook rice which is a staple food in the Asian diet. Our

study is the first report to compare rice alone with sorghum and to show that sorghum suppresses postprandial blood glucose levels.

The subjects in this study were generally healthy men and women. Those with mild hyperglycemia in the pre-test fasting blood glucose levels were not included. In the future, it is necessary to conduct a glucose tolerance test in the pretest to verify whether the same results in this study can be obtained in a population of subjects in the borderline diabetic range. One of the limitations of this study was that the excluded subjects were all male, which caused a gender bias among the subjects. It is reported that glucose absorption pattern is more influenced by body size, not by gender [39], so this is not a major problem. However, it is necessary to conduct clinical trials with several people who can be stratified by gender.

CONCLUSION

In this study, blood glucose levels at 60 and 120 minutes after a meal were significantly lower in healthy Japanese adult men and women who consumed sorghum porridge compared to white rice porridge, and the area under the blood glucose curve was also significantly lower. The results suggest that sorghum intake may contribute to the prevention of diabetes mellitus, a lifestyle-related disease that may be a risk factor for cardiovascular disease, cerebrovascular disease, and cancer, by suppressing postprandial hyperglycemia.

Abbreviations: UMIN: University Hospital Medical Information Network, BMI: body mass index, iAUC: area under the curve, GLUT4: glucose transporter 4, AMPK: AMP-activated protein kinase, PI3K: phosphoinositide-3-kinase, GLP-1: glucagon-like peptide 1,

Competing interests: The authors declare no conflict of interest. This study was funded by Kurume Research

Park, Fu-kuoka Prefecture. Hiroshi Uchida, the CEO of Best Amenity Co., Ltd was involved in providing test products, and is not involved in conducting the trial or analyzing data, and there is no commercial or financial relationship that could be construed as a potential conflict of interest.

Authors' contributions: Conceptualization, H.M. and M.N.; methodology, H.M. and M.N.; software, H.M.; validation, H.M., M.N. and K.S.; formal analysis, H.M.; investigation, H.M.; resources, H.M.; data curation, H.M.; writing---original draft preparation, H.M.; writing---review and editing, H.M.; visualization, H.M.; supervision, K.S.; project administration, K.S. and H.U.; funding acquisition, H.U. and K.S. All authors have read and agreed to the published version of the manuscript.

Acknowledgements: We would like to thank members of Onuki Laboratory, Faculty of Industrial Science and Technology, Kinki University.

Funding: This research was funded by Fukuoka Bioindustry R&D Initiatives 2021–2022.

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