Glycative Stress Research

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Original article

Indigestible dextrin-containing drink and postprandial blood glucose.

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Abstract

***Purpose*:** It has been reported that indigestible dextrin has an effect of inhibiting the increase of postprandial blood glucose value. The purpose of this research was to verify an effect of inhibiting the increase of postprandial blood glucose value by the ingestion of indigestible dextrin-containing drink (test material).

***Method*:** Twenty-four subjects who had a high postprandial blood glucose value were selected out of 59 healthy males and females through screening, and 21 of them, excluding three who dropped out, were subjected to the experiment (eight males and 13 females, 42.0 ± 5.1 years). A randomized, double-blind, placebo-controlled using vinegar, crossover comparison test was conducted to verify its effect of inhibiting the increase of blood glucose value after the intake of white rice (200 g) by a single ingestion of test material. The values of blood glucose, insulin (IRI), glucagon, triglyceride (TG) and free fatty acid (FFA) were measured 0, 15, 30, 45, 60, 90 and 120 minutes after the intake of white rice. The values of calories included in the test material and control material were 37.5 kcal and 10.7 kcal, respectively, and those of carbohydrate substance included in them were 9.11 g and 2.58 g, respectively.

***Results*:** There was no significant difference in the change in blood glucose value after the intake of white rice between the test group, where the test material was ingested, and the control group in either the area under the curve (AUC) or the maximum blood glucose value. The value 15 minutes after the intake of food of the test group was significantly higher than that of the control group, and as a result, the effect of inhibiting the increase of blood glucose value by test material could not be verified. The initial value of glucagon was 136.6 ± 20.3 pg/mL in the case when the test material was ingested and that of the control group was 128.1 ± 17.5 pg/mL, and as a result, it was significantly higher in the case when the test material was ingested ($p < 0.01$).

***Conclusion*:** The effect of inhibiting the increase of postprandial blood glucose value by test material could not be verified under the test conditions in this research. It is considered to possibly be due to the amount of carbohydrate substance included in the test material and the value of glucagon during the test.

***KEY WORDS*:** Indigestible dextrin, vinegar, glucagon, triglyceride

Introduction

Diabetes is a common disease with strong glycation stress. As it is said that diabetes may lead to all kinds of diseases, it is important to pay attention not only to control the blood glucose value, but also improve lifestyle and control glycation stress completely in order to not cause complications in the treatment of diabetes.

Glucose is an example of the factors of evoking glycation stress. When excess glucose reacts with the proteins and amid acids in the body, it produces advanced glycation end products (AGEs) through various processes, such as the formation of Amadori compounds. AGEs accumulate in internal organs, tissues and cells and cause the dysfunctions by AGE functional proteins. Furthermore, they combine with RAGE (receptors for AGEs), specific receptors, and evoke the production of inflammatory cytokine.

There are various steps in the method of controlling glycation stress: first, control postprandial blood glucose value, second, control the production of AGEs, third, promote the dissolution and elimination of AGEs, and fourth, control the signaling system of AGEs/RAGE [1].

The functional foods and drinks on the market include several functional ingredients, and it is supposed that their anti-glycation activities act on various stages of glycation

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stress reaction. It is reported that indigestible dextrin has an effect of inhibiting the increase of postprandial blood glucose value, and the anti-glycation activity of mangosteen extract controls the production of AGEs [2]. In this research, the author et al. selected an indigestible dextrin-containing drink and conducted a randomized, double-blind, placebo-controlled crossover comparison test in order to verify its effect of inhibiting the increase of postprandial blood glucose value, the first stage of the process of glycation stress.

Method

Subjects

The subjects were 59 healthy persons (gender, age, body weight, body mass index [BMI]). The selection criteria was healthy persons 20 years old or more, and those who did not conflict the following exclusion criteria; for example, those who had a food or drug allergy, those who were in pregnancy or breastfeeding, those who were on medication or had disease followed up at that time, those who were diagnosed with diabetes, those who had significant heart failure, those who were taking antihypertensive drug, those who had had gastrointestinal surgery and those who were suspicious of infectious disease. Those whom the doctor supervising the experiment considered inappropriate were excluded as "Others."

In the pre-inspection (SCR) including the examination study after the intake of white rice, those who fell under the selection criteria, did not fall under the exclusion criteria and were considered appropriate to participate in the experiment were ranked based on the following criteria, and 24 higher ranked subjects were selected.

1) Ranked from the persons who had a higher value of the area under the curve (AUC) of blood glucose until 90 minutes after white rice load.
2) Ranked from persons who had less difference in blood glucose values between 60 minute and 90 minutes after white rice load.
3) Ranked from the persons whose maximum blood glucose value (Cmax) after white rice load were higher.

The subjects were randomly divided into two groups of 12 persons through the stratified block randomization where age, gender and blood glucose AUC, until 90 minutes after white rice load, were regarded as stratification factors. It was confirmed that there was no significant difference between group assignments.

After that, two persons who dropped out and one person who ate breakfast before the test were excluded, and 21 persons were regarded to be effective analysis subjects (42.0 ± 5.1 years; eight males: 42.1 ± 60 years, 13 females: 42.0 ± 4.8 years).

Test material

The subjects ingested indigestible dextrin-contained drink (test material) or placebo drink of vinegar 25 mL, four times diluted with water (100 mL in total; control material).

The ingredients included in the test material for one time ingestion were black vinegar (kurosu) 16.7 mL (750 mg as acetic acid), indigestible dextrin (Matsutani Chemical Industry Co., Ltd, Itami, Hyogo, Japan) 5 g, and mangosteen peel extract (Nippon Shinyaku, Kyoto, Japan) 100 mg and those included in the control material were black vinegar 0.167 mL, mangosteen peel extract 0 mg and indigestible dextrin 0 g. Each nutrient component is shown in ***Table 1***.

Blood glucose test protocol

The unified protocol of the Japanese Association for the Study of Glycemic Index (JASGI) was used as a reference [3,4]. The subjects complied with the following instructions on the previous day of the test: 1) refrain from strenuous exercise, 2) do not eat any food after 22:00, 3) avoid overeating and over-drinking and 4) do not stay up late.

On the day of the test, a resin catheter was placed into a vein and blood was collected at each measuring time. White rice, 200 g (*Sato-no-gohan*, Niigata product Koshihikari, Sato Foods Co., Ltd., Niigata, Japan), sprinkled with 2.5 g of *furikake* (dried food sprinkled over rice) (*noritama* (seaweed and egg), Marumiya Food Industry, Suginami-ku, Tokyo, Japan) was used as the reference diet. Water, 150 mL, was provided at the time of the test. The subjects digested the test material or control material 10 minutes before the white rice load.

The intake of reference diet was performed in 10 minutes and the subjects chewed a bite of food 30 times. Following this, the following items were measured at 15 minutes (the second time), 30 minutes (the third time), 45 minutes (the fourth time), 60 minutes (the fifth time), 90 minutes (the sixth time) and 120 minutes (the seventh time) after the start of intake: blood glucose, immunoreactive insulin (IRI), glucagon, triglyceride (TG) and free fatty acid (FFA).

At the first time, the blood tests of blood urea nitrogen (BUN), creatinine, uric acid, aspartate transaminase (AST), alanine transaminase (ALT), γ-glutamyl transpeptidase (γ-GTP), total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and HbA1c (NGSP: National Glycohemoglobin Standardization Program) were conducted.

Insulin resistance index (homeostasis model assessment-insulin resistance (HOMA-IR) was calculated based upon the following formula: Fasting blood IRI concentration (μU/mL) × fasting blood glucose value (mg/dL)/405. The blood analysis was conducted in the Health Sciences Research Institute, Inc. (Yokohama, Japan) during June - September 2016.

Statistical analysis

The values of blood glucose in the lapse of time after the subjects' intake of food reduced by fasting blood glucose were regarded as variation (Δ) and the AUC from the start of intake to 120 minutes after the start was calculated. A paired t-test (IBM SPSS Statics24, IBM Japan, Minato-ku, Tokyo, Japan) was used for the statistical analysis.

Ethical standards

An Ethical Review Board concerning "the research targeting human" of the Society for Glycative Stress Research was held for this research and the ethicality and validity of the test were discussed. This research was conducted based on its approval (Approval Number: GSREC 2016-004) and a pre-registration of clinical trial was made (Registration number: UMIN000022817).

Results

Changes of values of postprandial blood glucose and insulin (IRI)

The value of the postprandial blood glucose (PBG) 15 minutes after the intake of food in the case where the test material was ingested was significantly higher than that of the control group; however, there was no significant difference in other time points (***Fig. 1***). The maximum blood glucose (Cmax) was 183.0 ± 24.7 mg/dL in the case when the test material was ingested, which was 178.8 ± 26.7 mg/dL in the control group; there was no significant difference between the groups. AUC was 18,178.9 ± 2,694.3 mg·min /dL in the case when the test material was ingested, which was 17,912.1 ± 2,426.3 mg·min /dL in the control group; there was no significant difference between the groups.

The values of IRI 15 minutes and 120 minutes after the intake of food in the case when the test material was ingested were significantly higher than those in the control group; however, there was no significant difference in other time points (***Fig. 2***). The AUC of IRI was 3,788.3 ± 1,555.8 μU·min /dL in the case when the test material was ingested, which was 3,392.7±1,471.6 μU·min/dL in the control group; there was no significant difference between the groups.

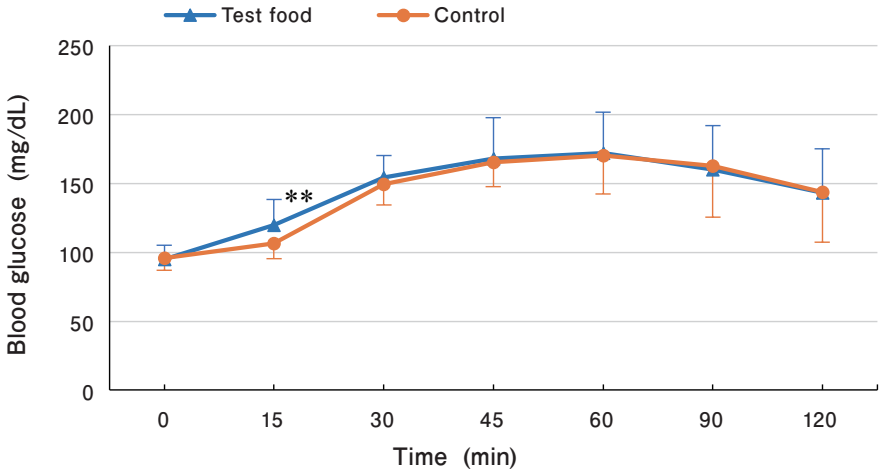

Fig. 1. **Comparison of blood glucose after steamed rice intake.**
Results are expressed as mean ± SD. **p < 0.01 vs control by Student's t test, n = 21.

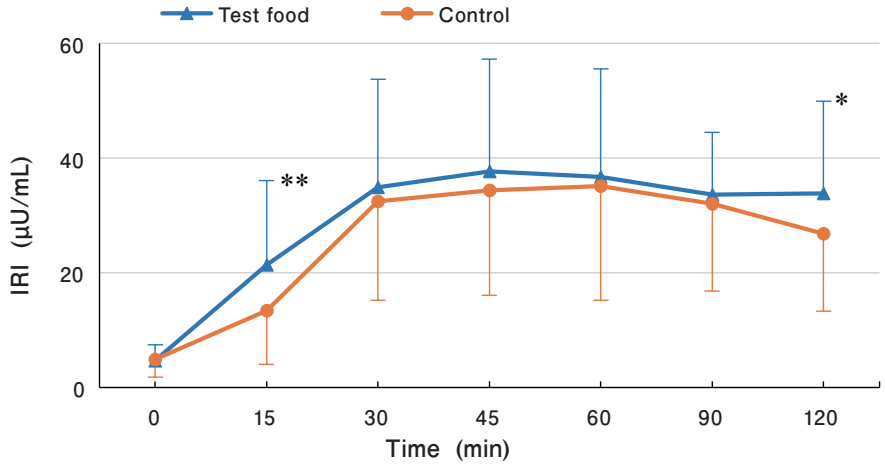

Fig. 2. **Comparison of serum IRI after steamed rice intake.**
Results are expressed as mean ± SD. *p < 0.05, **p < 0.01 vs control by Student's t test, n = 21. IRI, immunoreactive insulin.

Changes of glucagon value

The glucagon values 15 minutes before and after the intake of food in the case when the test material was ingested were significantly higher than those in the control group (***Fig. 3-a***). Although glucagon value significantly increased, transiently, 15 minutes after the intake of food by the test material being ingested, the values 30, 45, 60, 90 and 120 minutes after the intake of food significantly decreased compared with the value before the intake of food. The glucagon values 60 and 90 minutes after the intake of food significantly decreased compared with that before the intake of food in the control group; however, there was no significant difference between the value 120 minutes after the intake of food and that before the intake of food.

The comparisons of amounts of change of glucagon showed that there was no difference in the values 15, 30, 45, 60 and 90 minutes after the intake of food between the groups; however, the value 120 minutes after the intake of food significantly decreased by the test material being ingested (***Fig. 3-b***).

Changes of fat profile

There was no significant difference between the changes of fat caused by the test material being ingested and those in the control group (***Fig. 4***).

As for the changes in FFA blood concentration, the value before the intake of food in the case when the test material was ingested was higher than that of the control group and there were no significant differences in the values during 15 minutes to 120 minutes after the intake of food between the groups (***Fig. 5-a***). The comparison of the FFA changes showed that all values from 15 minutes to 120 minutes after the intake of food in the case when the test material was ingested were significant lower than those of the control group (***Fig. 5-b***).

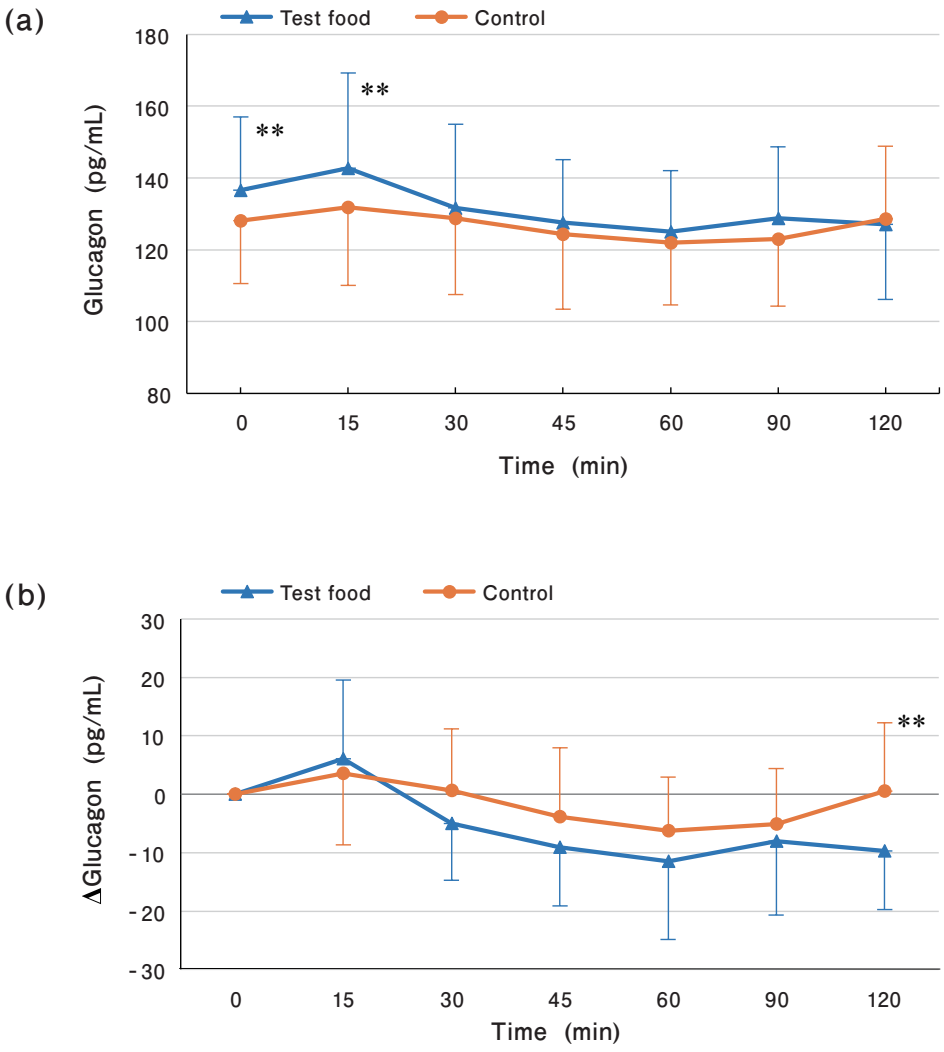

Fig. 3. **Comparison of serum glucagon values (a) and variation (b) after steamed rice intake.**

Results are expressed as mean ± standard error mean. **p < 0.01 vs control by Student's t test, n = 21.

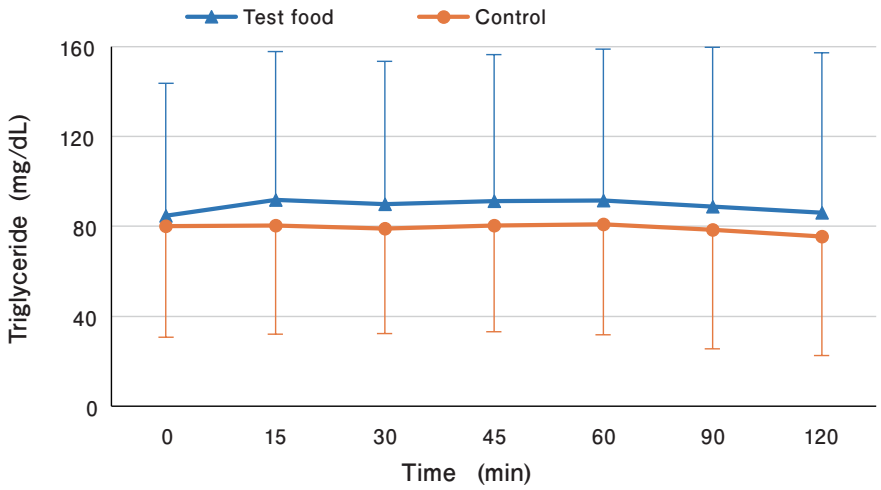

Fig. 4. **Comparison of serum triglyceride after steamed rice intake.**
Results are expressed as mean ± standard error mean, n = 21.

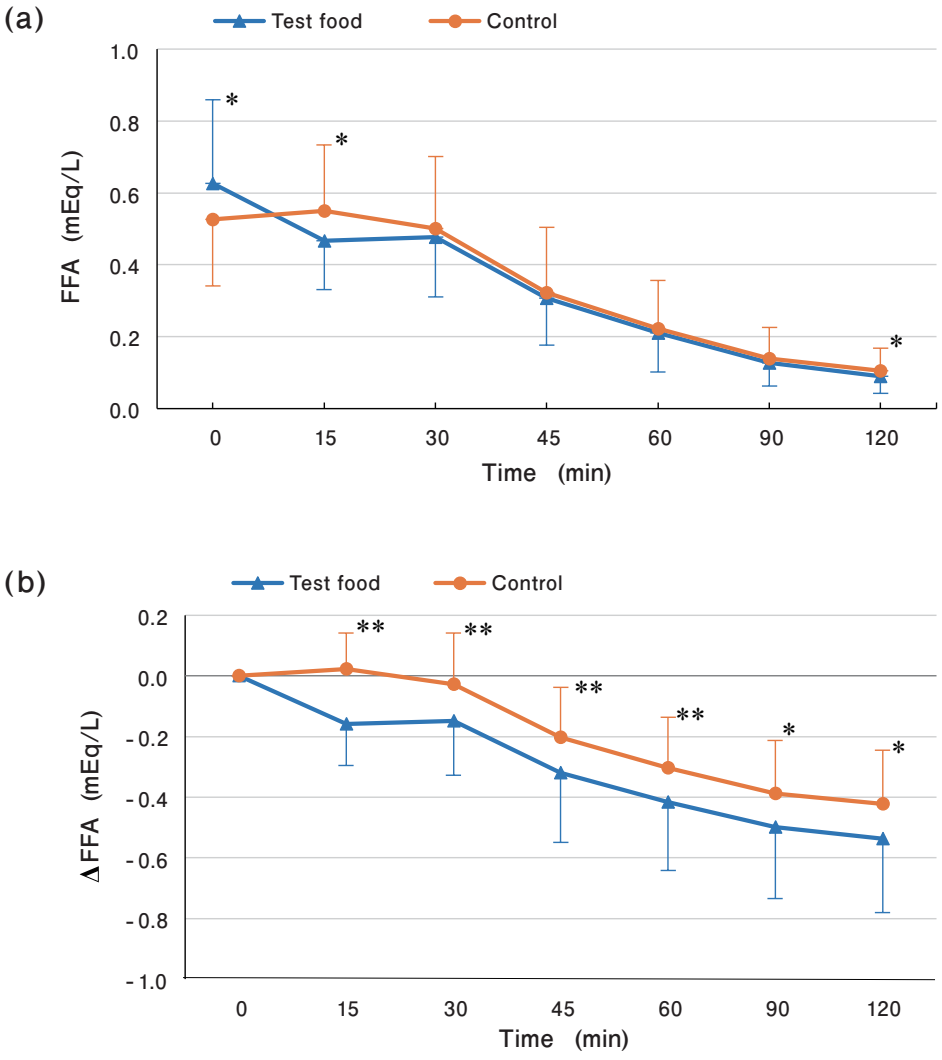

Fig. 5. **Comparison of plasma FFA (a) and variation (b) after steamed rice intake.**
Results are expressed as mean ± standard error mean. *p < 0.05, **p < 0.01 vs control by Student's t test, n = 21. FFA, free fatty acid.

Correlations with glucagon

The results of a correlative analysis of glucagon value with blood glucose values (fasting blood glucose value, Cmax and AUC), IRI, TG and FFA are shown in ***Fig. 6-a-f***. Among them, the items having weak correlation with glucagon were IRI ($r = 0.498$, $p < 0.05$) and TG ($r = 0.459$, $p < 0.05$). A weak correlation was also observed between glucagon, and HOMA-IR was observed ($r = 0.477$, $p < 0.05$, ***Fig. 7***).

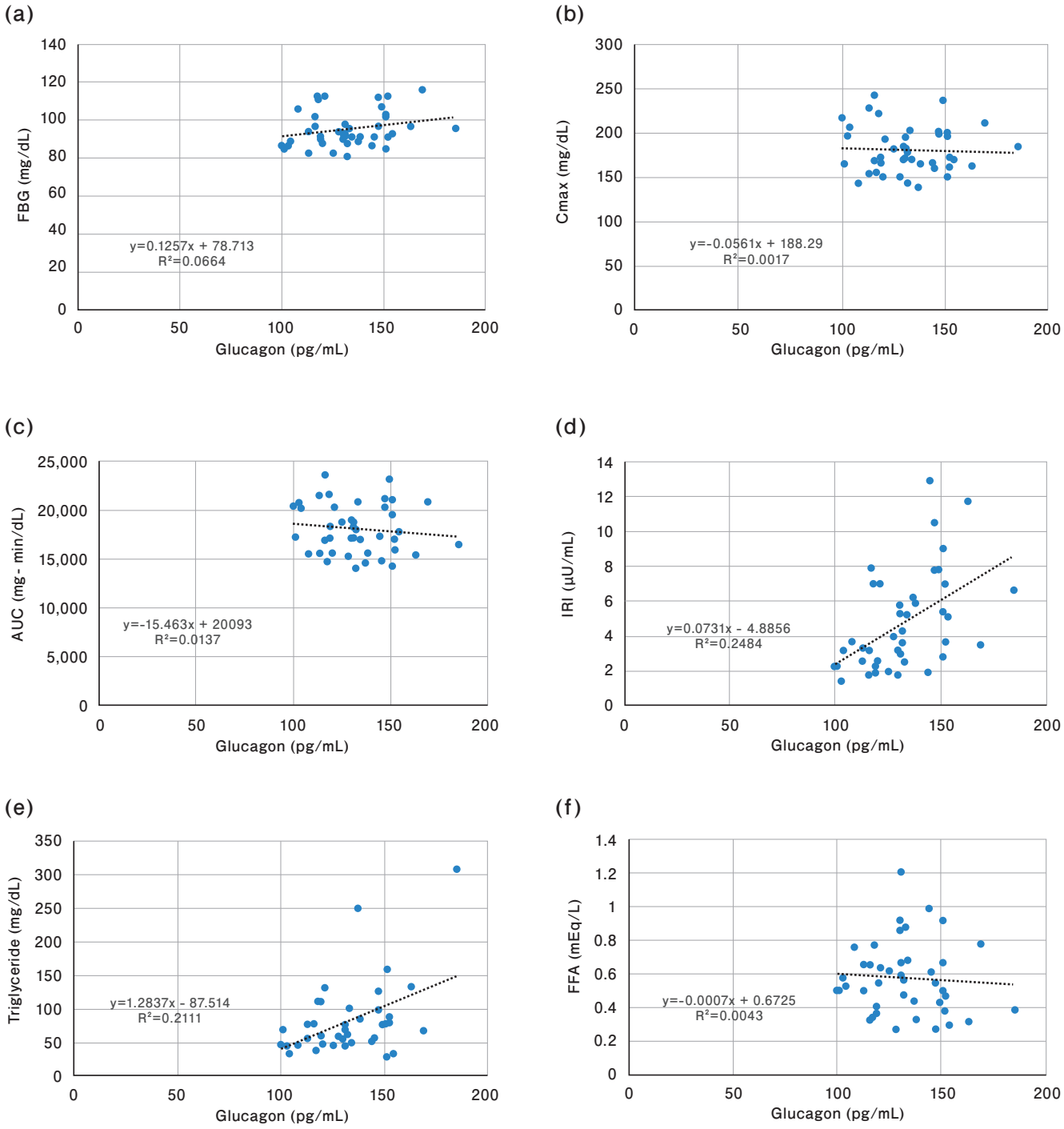

Fig. 6. **Correlation between glucagon and glucose/lipid metabolism markers.**

a: fasting blood glucose (FBG) at 0 min, b: Cmax, the maximum PBG values, c: AUC of PBG, d: IRI at 0 min, e: triglyceride (TG) at 0 min, f: free fatty acid (FFA) at 0 min, n = 42. Glucagon was measured at 0-min. PBG, postprandial blood glucose after steamed rice intake; AUC, area under curve of PBG; IRI, immunoreactive insulin.

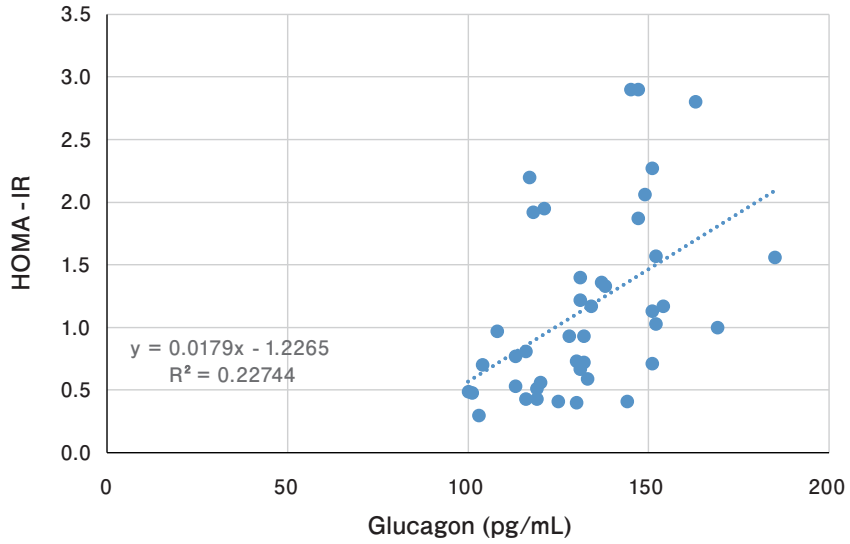

Fig. 7. **Correlation between glucagon and HOMA-IR.**
Glucagon, glucose and insulin (IRI) were measured at 0-min, n = 42. HOMA-IR, homeostasis model assessment-insulin resistance.

Discussion

The purpose of this research was to evaluate the effect of single ingestion of indigestible dextrin-containing drink (test material) or vinegar for placebo (control material) on inhibiting the increase of postprandial blood glucose value after the intake of white rice, targeting healthy males and females aged 20-50 years old by a randomized, double-blind crossover comparison test.

As a result, the value of blood glucose, shown as a difference in blood glucose change curve 15 minutes after the intake of food in the case when the test material was ingested, was significantly higher than that of the control group: however, there were no differences in Cmax and AUC between the groups. The values of IRI 15 minutes and 120 minutes after the intake of food in the case when the text material was ingested were significantly higher than those of the control group; however, there were no differences in Cmax and AUC between the groups. IRI (variation) and AUC were significantly higher in the case when the test material was ingested compared to those of the control group. In conclusion, even when rice was eaten after the test material was ingested, there was no improvement in the postprandial blood glucose increase.

The amounts of carbohydrate included in the drinks (per 25 mL) used in this test, which most easily affected blood glucose, were 9.11 g in the test material and 2.58 in the control material, and there was difference in calories (37.5 kcal in the test material and 10.7 kcal in the control material). It can be considered to be the reason why the blood glucose value 15 minutes after the intake of white rice in the case when the text material was ingested was significantly higher.

Glucagon

Regarding hormone dynamics, glucagon was also discussed in this research. Recently glucagon is paid attention to again in association with the clinical application of incretin-related drugs, such as DPP4 (dipeptidyl peptidase-4) inhibitory drug having glucagon inhibitory effect and GLP-1 (glucagon-like peptide-1) receptor agonist [5-9]. The fasting plasma glucagon concentration of diabetes patients increases more than that of healthy persons, and it causes high fasting blood glucose by the glucose output by the activated liver [10]. The volume of pancreatic β-cell, insulin-secreting cell, decreases at the formation of a morbid state of diabetes so that the secretion of insulin decreases, which is considered to be the main reason of high blood glucose value. Meanwhile, there is also a report that, despite a high blood glucose state, the volume of pancreatic α-cell, glucagon-secreting cell intrinsically having the effect of increasing blood glucose, increases [8].

In the experiment using receptor-deficient mice, it is said that the excess of glucagon is a more important factor of the elevation in blood glucose than the lack of insulin. In addition to the treatment of diabetes centering on insulin so far, new treatment strategies to redress the secretion of glucagon and inhibit its effect are paid attention [6,8]. Not only insulin secretory response but also the abnormality of the early reaction of glucagon secretion is involved in the abnormal glucose tolerance of gestational diabetes mellitus (GMD) at an early stage after childbirth [11].

Glucagon is secreted from pancreatic β-cells at the time of low blood glucose. It has an effect to breakdown glycogen, activates glyconeogenesis in the liver, and elevates blood glucose level and maintains it. In the case of diabetes patients, postprandial plasma glucagon concentration does not decrease enough, liver glycogen synthesis goes down and hepatic glucose production does not decline enough, thus often causing postprandial high blood glucose [12]. As the comparison of the test material and the control material, glucagon values before the intake of food and 15 minutes after the intake of food showed a significant difference between the groups, and the values were higher when the test material was ingested. In the case when the test material was ingested, the subjects ate white rice in the condition where blood glucagon value

was high, so that the test group possibly was in the condition where higher blood glucose tended to occurred more easily than the control group where the subjects ate white rice under the condition glucagon value was low.

The results of correlative analysis between glucagon level and glycolipid metabolism index are shown in ***Fig. 6***. The items that have weak positive correlation with glucagon were IRI (r = 0.498) and TG (r = 0.459). The weak positive correlation was observed between glucagon and HOMA-IR (r = 0.477), as shown in ***Fig. 7***, and suggests that the higher the glucagon level, the higher the insulin resistance becomes.

This test was conducted presuming that the two tests started at a fixed time and the fasting time was also fixed. However, it should always be considered that the differences in glucagon values occur between the groups. It may be necessary to discuss the measures to correct the value of fasting glucagon value when glucose test is made.

Because there are significant differences in the values of glucagon before and 15 minutes after the intake of food between the groups, the change ratio was compared and it was found the value 120 minutes after the intake of food significantly decreased by the test material being ingested. Glucagon is secreted from pancreatic β-cells at the time of low blood glucose and has an effect to maintain blood glucose level. Given that high glucagon concentration easily leads to the postprandial high blood glucose and that the excess secretion of glucagon strains pancreatic α-cells, a low level of glucagon is desirable. In other words, it can be interpreted that it was a favorable effect of the test material.

Lipid metabolism

Postprandial lipid changes were also discussed in this test. Although there was no significant difference in the values of serum triglyceride between when the test material ingested and when the control material was ingested, the value 15 minutes after the intake of food was highest when the test material was ingested by the change with the passage of time of the change rate . Because there was significant difference in the value of FFA before the intake of food between the groups, the change ratios were compared, and as a result, all cases of 15, 30, 45, 60, 90 and 120 minutes after the intake of food showed low values by the test materials being ingested.

As the factor why the changing rate of TG was transiently high when the test material was ingested, a weak correlation was observed between glucagon and TG (***Fig. 6-e***), and therefore, it may be possible that because the test material significantly increased fasting glucagon compared with the control material, it increased TG. Its detailed mechanism was unable to be clarified in this research.

Generally speaking, in the cases of obesity and diabetes, the level of FFA becomes high caused by the increase of the FFA that is derived mainly from white adipose tissue and it invokes various cell damaging effects through the advancement of endoplasmic reticulum stress [13-15]. Nonalcoholic fatty liver disease (NAFLD) develops by the enhancement of biosynthesis of fatty acid in the liver and progresses to non-alcoholic steatohepatitis (NASH) [13]. If it causes damage in pancreatic β-cells, insulin production decreases further, and the formation of pathologic condition of diabetes advances [14]. In the case of obese persons, skeletal muscle intracellular fat accumulates in body because of the increase of FFA concentration in blood in addition to the decrease of adiponectin, lack of exercise and high-fat diet [15]. Judging from these reports, the decrease of FFA in this test was a positive effect of the test material.

However, there are many kinds of fatty acids, and each of them affects the body differently. The intake of saturated fatty acid and trans-fatty acid increases the risk of the onset of cardiovascular disease and the other hand omega-3 unsaturated fatty acids, including eicosapentaenoic acids (EPA), improve clinical conditions with their anti-atherosclerotic effect and inflammation-suppression effect [16]. It is required to establish the diagnostic method and evaluation method taking into consideration not only the measurement of FFA, but also the qualities of fats, in other words, the ratio of saturated fatty acid and unsaturated fatty acid, the ratio of omega-3 fatty acids and omega-6 fatty acids and the profile of fatty acids in blood, in the future.

Black vinegar (Kurosu)

Black vinegar is one of the functional ingredients of the test material. It is included in both the test material (16.7 mL) and the control material (0.167 mL), and its amount included in control material is very small at about 1%. The effect of acetic acid, a main ingredient of vinegar, on the postprandial blood glucose was discussed [17-20], and it was reported that when white rice mixed with rice vinegar was taken, AUC decreased more than when only rice was taken, [17,18], that the same effect as acetic acid was recognized in apple vinegar and tomato vinegar [19] and that the acetic acid has cholesterol-lowering effect [21,22]. In this test, the vinegar included in the test material possibly contributed to the lowing of AUC.

In our test of single intake of acetic acid drink, when vinegar drink including indigestible dextrin (2.5 g) and mixed herb extract (50 mg) was taken as test material before the intake of white rice, the elevation of blood glucose at an early stage was more gradual than when black vinegar drink or red vinegar drink was taken [23]. However, when the case of intake of test material and the case of intake of white rice only were compared, there was no significant difference in the changes of blood glucose, so that the effect of vinegar could not be confirmed [23]. Although it is expected that vinegar does not exacerbate glycation stress and rather it has positive impact on it. However, the effect of vinegar sometimes cannot be confirmed depending upon condition.

This test was conducted in the disadvantageous conditions where IRI value, insulin resistance (HOMA-IR) and TG tended to increase because the amount of carbohydrate (9.11 g) included in test material was three times higher than that of control material, and the level of glucagon was high at the time when test material was ingested. This also should be taken into consideration for the evaluation of test material.

In our past record, in a placebo-controlled randomized double-blind parallel-group comparison method with the continuous intake of vinegar drink (test material) including indigestible dextrin and mixed herb extract for eight weeks, the tendency to decrease carboxymethyl-lysine (CML) in stratum corneum, a glycation stress index, by the test material being ingested, was shown [24]. Mangosteen extract was used in the test material in this test as an anti-glycation material instead of mixed herb extract. It is expected that it can exert its effect of anti-glycation in clinical test.

Indigestible dextrin

Indigestible dextrin is added to various foods and

drinks, and there are many reports that it has a blood glucose elevation inhibitory effect and neutral fat-lowering effect [25-44]. In our laboratory as well, indigestible dextrin's blood glucose elevation inhibitory effect and neutral fat-lowering effect have been verified [23, 45].

The comparison of the changes of the values of postprandial blood glucose after the intake of noodles added with indigestible dextrin as a diet fiber, and those after the intake of noodles only (13 targeted examples) showed that there were no significant differences in glucose value, Cmax and AUC. Cmax was significantly lower after the intake of noodles added with indigestible dextrin than after the intake of noodles only, but there was no significant difference in AUC [45]. The comparisons of Max and AUC at the time when the indigestible-dextrin-containing soup and white rice were taken and when the white rice only was taken (14 targeted examples) showed that there were no significant differences in either Max or AUC.

In the test of a single intake of indigestible dextrin-containing vinegar drink (11 targeted examples), there were no significant differences in Cmax, blood glucose, AUC and the slope of blood glucose elevation caused by the presence or non-presence of indigestible dextrin [23]. In the test of a single intake of the same test material conducted for the confirmation (32 targeted examples) as well, there was no significant improvement in either Cmax or AUC after the intake of white rice, 300 g of the whole analysis [46].

In order to lower the value of glucose after the intake of white rice or noodles, the intake of the ingredients of Chinese chilli tofu (Mabo-tofu), Chinese chilli eggplant (Mabo-nasu) [47], beef bowl [48], salad noodles or soft-boiled egg noodles [48] as side dishes is more effective in lowering glucose value after the intake of white rice or noodles than that of indigestible dextrin.

If these reports are taken into consideration, the inhibiting effect of indigestible dextrin on postprandial blood glucose is not so large as the reason why skin fluorescent AGEs volume decreased, and the effect of vinegar cannot be confirmed depending on the conditions.

Conclusion

A randomized, double-blind crossover comparison test was conducted, targeting healthy male and female subjects aged from 20 to 50 years old. Before the test, subjects ingested indigestible dextrin-contained drink (test material) or placebo drink of vinegar (control material), and the inhibitory effects of the test material on the elevation of postprandial-blood glucose after the intake of white rice were evaluated. However, it could not be confirmed under the condition of this test, because of the following reasons: (1) the amount of carbohydrate (9.11 g) included in test material was three times higher than that of the control material, (2) the fasting glucagon value at the time when the test material was ingested was significantly higher than that of the control group and it possibly caused the increases of IRI, insulin resistance (HOMA-IR) and TG, and (3) it is possible that under these conditions, the functional ingredients included in the test material could not exert their effects enough. At present, the importance of glucagon in the pathological study of diabetes is paid attention. It is a new finding that the test material has the effect to decrease the glucagon, and therefore, further research on it is expected in the future.

Acknowledgements

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Conflict of interest

The authors claim no conflict of interest in this study.

Reference

1) Ichihashi M, Yagi M, Nomoto K, et al. Glycation stress and photo-aging in skin. Anti-Aging Med. 2011; 8: 23-29.
2) Ohno R, Moroishi N, Sugawa H, et al Mangosteen pericarp extract inhibits the formation of pentosidine and ameliorates skin elasticity. J Clin Biochem Nutr. 2015; 57: 27-32.
3) Japanese Association of the Study for Glycemic Index. Unified protocol (unified procedure). http://www.gikenkyukai.com/protocol.html (in Japanese)
4) Sugiyama M, Wakaki Y, Nakayama N, et al. Research on rice eating and glycemic index. Journal of Japanese Society on Nutrition Care and Management. 2003; 3: 1-15. (in Japanese)
5) Kawamori R. Incretins and glucagon secretion. The Journal of Adult Diseases. 2013; 43: 1449-1453. (in Japanese)
6) Kawamori D, Kulkarni RN. Insulin modulation of glucagon secretion: The role of insulin and other factors in the regulation of glucagon secretion. Islets. 2009; 1: 276-279.
7) Yamaguchi S, Otsuka Y, Ishihara H. Mechanism and regulation of glucagon secretion. Journal of Clinical and Experimental Medicine (Igaku No Ayumi). 2015; 252: 395-401. (in Japanese)
8) Miuchi M, Namba M. Diabetes mellitus and pancreatic α-cell dysfunction. Experimental Medicine (Jikken Igaku). 2015; 33: 903-907. (in Japanese)
9) Kitamura T. Glucagon: Recent findings. Diabetes Journal. 2016; 44: 41-48. (in Japanese)
10) Dunning BE, Gerich JE. The role of alpha-cell dysregulation in fasting and postprandial hyperglycemia in type 2 diabetes and therapeutic implications. Endocr Rev. 2007; 28: 253-283.

11) Natsuda S, Horie I, Akeshima J, et al. Insufficient suppression of early-phase glucagon secretion after oral glucose load in women with impaired glucose tolerance at early postpartum after gestational diabetes. Diabetes & Pregnancy: The Journal of the Japanese Society of Diabetes and Pregnancy. 2016; 16: 180-187. (in Japanese)
12) Krssak M, Brehm A, Bernroider E, et al. Alterations in postprandial hepatic glycogen metabolism in type 2 diabetes. Diabetes. 2004; 53: 3048-3056.
13) Matsuzaka T, Shimano H. The pathogenesis of NAS and fatty acids. Cell (Saibo). 2014; 46: 358-361. (in Japanese)
14) Nagao Y, Tabe K, Tanizawa Y. Endoplasmic reticulum (ER) stress and diabetes. The Medical Frontline (Saishin Igaku). 2015; 70: 496-503. (in Japanese)
15) Tamura Y, Takeno K, Kakei S. The organ singularity: Lipid toxicity in the skeletal muscle. The Lipid. 2016; 27: 269-274. (in Japanese)
16) Matsuo Y, Asahara [Sato] T, Ogawa Y. Evaluation of the cardiovascular disease and biomarkers: Fatty acids and cardiovascular diseases. Vascular Biology & Medicine (Kekkan Igaku). 2014; 15: 169-177. (in Japanese)
17) Inage H, Sato Y, Sakakibara S, et al. The effect of vinegar intake on postprandial blood glucose level in healthy women. Journal of Japanese Society of Clinical Nutrition. 2006; 27: 321-325. (in Japanese)
18) Endo M, Matsuoka T. The efficacy of vinegar on the suppression of postprandial glucose elevation. Journal of the Japan Diabetes Society. 2011; 54: 192-199. (in Japanese)
19) Endo M, Matsuoka T, Nakanishi Y. Effect of vinegar on postprandial hyperglycemia: Kinds and intake methods of vinegar and vinegar-containing drinks. Bulletin of Notre Dame Seishin University. 2012; 36: 1-9. (in Japanese)
20) Sueda K, Okuda M, Yamada M. Effect of side dish on postprandial change in blood glucose in healthy female students: Dietary fiber, vinegar, butter, soybean products and dairy products. Journal of the Institute for Psychological and Physical Science (Shinshin Kagaku). 2009; 1: 23-30. (in Japanese)
21) Fushimi T, Oshima Y, Kishi M, et al. Influence of vinegar-containing beverage on serum total cholesterol and safety evaluation. Journal of Nutritional Food. 2005; 8: 13-26. (in Japanese)
22) Fushimi T, Kishi M, Oshima Y, et al. Influence of vinegar-containing beverage on subjects with hypercholesterolemia: (2) Seasonal effect on improvement of serum total cholesterol. Journal of Nutritional Food. 2007; 9: 9-23. (in Japanese)
23) Yagi M, Shimoide A, Yasui K, et al. Effect of a vinegar beverage containing indigestible dextrin and a mixed herbal extract on postprandial blood glucose levels: A single-dose study. Glycative Stress Res. 2014; 1: 8-13
24) Yagi M, Shimoide A, Hamada U, et al. Evaluation of the anti-glycation effect and the safety of a vinegar beverage containing indigestible dextrin and a mixed herbal extract: A placebo-controlled, double-blind study. Glycative Stress Res. 2014; 1: 14-24.
25) Matsuoka A, Saitou M, Nagano S. Continual medication tests of the dextrin that is difficult to digest: (1) The study of the improvement effect on lipid metabolism in normal subjects. Rinsho Eiyo. 1992; 80: 167-172. (in Japanese)
26) Fujiwara K, Matsuoka A. Continual medication tests of the dextrin that is difficult to digest: (2) The study of the improvement effect on lipid metabolism in patients with insulin-independent diabetes mellitus. Rinsho Eiyo. 1993; 83: 301-305. (in Japanese)
27) Tokunaga K, Matuoka A. Influence of "Food for specified health use" containing indigestible dextrin on glucose and lipid metabolism. Diabetes (Tonyobyo). 1999; 42: 61-65. (in Japanese)
28) Kajimoto O, Hirata H, Takahashi T, et al. Effect of indigestible dextrin-containing beverage on lipid metabolism and obesity-related biomarkers. Journal of Nutritional Food. 2000; 3: 47-58. (in Japanese)
29) Kajimoto O, Itsumi M, Sano A, et al. Influence of indigestible dextrin-containing tea beverage on mild hypertriglyceridemia. Journal of Nutritional Food. 2002; 5: 117-130. (in Japanese)
30) Yamamoto K, Kishimoto Y, Osumi K, et al. Long-term administration trial of reduced form indigestible dextrin: Influence on lipid metabolism and safety evaluation in the obesity patients. Journal of Japan Society for the Study of Obesity. 2006; 12: 35-39. (in Japanese)
31) Ono R, Takeshita M, Miyamoto K, et al. Influence of indigestible dextrin addition on constipation, glucose and lipid metabolism. Kidney (Jinzo). 2006; 28: 216-223. (in Japanese)
32) Hironaka T, Kishimoto Y, Matsubara K, et al. Inhibitory effect of tea containing resistant maltodextrin on the elevation of serum triglyceride after intake of lipid. Japanese Pharmacology & Therapeutics. 2008; 36: 445-451. (in Japanese)
33) Sato F, Saito A, Miyawaki H, et al. Effect of beverage containing resistant maltodextrin on postprandial serum triglyceride and the safety evaluation of long term or excessive intake of the beverage. Japanese Pharmacology & Therapeutics. 2009; 37: 857-866. (in Japanese)
34) Kishimoto Y, Hayashi N, Yamada T, et al. Favorable effect of resistant maltodextrin on postprandial blood glucose, insulin and triglyceride levels. Japanese Pharmacology & Therapeutics. 2009; 37: 277-283. (in Japanese)
35) Tanaka T, Nakamura J, Kitagawa Y, et al. Effect of carbonated beverage containing resistant maltodextrin on postprandial serum triglyceride: A randomized, double-blind, placebo-controlled, crossover study. Japanese Pharmacology & Therapeutics. 2011; 39: 813-821. (in Japanese)
36) Takahashi T, Fujiwara K, Ito S, et al. Effect of carbonated beverage containing resistant maltodextrin on postprandial serum triglyceride: A randomized double-blind placebo-controlled crossover study. Japanese Pharmacology & Therapeutics. 2013; 41: 1061-1068. (in Japanese)
37) Kobayashi Y, Kaneko Y, Katayama M, et al. Effect of carbonated beverage containing resistant maltodextrin on postprandial serum triglyceride and the safety evaluation of long-term or excessive intake of the beverage. Japanese Pharmacology & Therapeutics. 2013; 41: 863-875. (in Japanese)
38) Kanehira T, Kondo S, Sato N, et al. Suppression of postprandial increase in serum triglyceride by the intake of indigestible dextrin-containing carbonated beverage. Japanese Pharmacology & Therapeutics. 2014; 42: 985-993. (in Japanese)

39) Ashigai H, Kobayashi Y, Kaneko Y, et al. Effect of carbonated beverage containing resistant maltodextrin on postprandial serum triglyceride levels: Randomized double-blinded placebo-controlling crossover study. Japanese Pharmacology & Therapeutics. 2014; 42: 661-669. (in Japanese)
40) Kishinaga Y, Yamada F, Nambu S. Safety evaluation in long-term or excessive intake of coffee containing resistant maltodextrin. Japanese Pharmacology & Therapeutics. 2014; 42: 353-358. (in Japanese)
41) Shinoda Y, Kametani N, Uno T, et al. Effects of carbonated beverage containing resistant maltodextrin on postprandial serum triglyceride and safety evaluation of long-term or excessive consumption of the beverage. Japanese Pharmacology & Therapeutics. 2014; 42: 265-279. (in Japanese)
42) Kanehira T, Fukagawa M, Matsumoto D. Effects of indigestible dextrin-containing carbonated beverage on the postprandial increase in serum triglyceride. Japanese Pharmacology & Therapeutics. 2014; 42: 115-121. (in Japanese)
43) Shinoda Y, Kametani N, Uno T, et al. Effects of carbonated beverage containing resistant maltodextrin on postprandial serum triglyceride: A randomized double-blind placebo-controlled crossover study. Japanese Pharmacology & Therapeutics. 2015; 43: 1031-1038. (in Japanese)
44) Kaneko K, Kondo S, Ito K, et al. Suppression of postprandial increase in serum triglyceride by the intake of indigestible dextrin-containing tea beverage: A randomized, placebo-controlled, double-blind, crossover study. Pharmacology & Therapeutics. 2016; 44: 263-270. (in Japanese)
45) Matsushima M, Yagi M, Hamada U, et al. Effects of choice of staple food and the addition of dietary fiber on changes in postprandial blood glucose level. Glycative Stress Res. 2014; 1: 46-52.
46) Suzuki K, Kowatari Y, Shimada H, et al. Effect of vinegar drink containing indigestible dextrin and mixed herbal extract on postprandial blood glucose level: A randomized double blind cross-over study. Japanese Pharmacology & Therapeutics. 2013; 41: 911-917. (in Japanese)
47) Matsushima M, Yagi M, Hamada U,et al. Prevention of postprandial hyperglycemia by the combination of a staple food and a side dish. Glycative Stress Res. 2014; 1: 53-59.
48) Ogura M, Kubo R, Kobayashi T, et al. Influence of beef bowl (gyudon) materials on postprandial blood glucose. Glycative Stress Res. 2016; 3: 210-221.