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*Original article*

# Effects on skin by sub-aleurone layer residual rinse-free rice (Kinmemai rice): An open label test.

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## Abstract

***Purpose*:** In this study, we compared the subjective symptoms and changes in skin condition of university students that consumed sub-aleurone layer residual rinse-free rice (SARFR; Kinmemai rice) for one month, with polished rice free intake group.

***Method*:** The 59 subjects analyzed consisted of 37 in the SARFR group (24 males, 13 females 21.0 ± 1.5 years), and 22 in the control group (13 males, 9 females, 22.0 ± 1.2 years). In the SARFR group, 150 g or more of the test meal was ingested once a day for one month. In the control group, normal ingestion of polished rice was freely decided by participants. Before and after the test, the questionnaire, skin function by Clreo-Pro (Fujitex), and skin AGEs fluorescence by AGEs sensor (Sharp) were evaluated.

***Results*:** SARFR intake compliance was 84%, and no adverse events due to dyspepsia were observed. Skin age was significantly improved in the SARFR group compared to the control. This effect was remarkable for males and home students, and was not observed in boarding house students. There was no significant difference in skin AGEs fluorescence.

***Conclusion*:** It was suggested that SARFR contributes to health promotion, including skin condition, by reducing the indigestibility of brown rice and ensuring nutrition, which facilitates continuous intake.

***KEY WORDS*:** brown rice, sub-aleurone layer residual rinse-free rice (Kinmemai rice), skin condition, advanced glycation endproducts (AGEs)

## Introduction

One of the reasons why Japanese people have healthy longevity is because of their characteristic eating habits that differ from those of Western cultures. However, in recent years, diseases related to high glycative stress, *i.e.*, obesity, and type 2 diabetes mellitus (T2DM) have been increasing. Longitudinal medical surveys of Japanese Americans have shown that those who were originally obese are at increased risk of developing T2DM due to excessive fat intake [1)]. Even if the persons are lean, excessive carbohydrate intake increases the risk of obesity. To prevent obesity and T2DM, it is important to improve lifestyle habits such as diet "Shokuiku" and exercise "Taiiku". This study focused on the viewpoint of food education on rice, which is the main staple food of the Japanese.

It has been pointed out that rice-based food has advantages over wheat-based food, such as being gluten-free [2,3)] and having less fecal incontinence in the elderly [4)]. On the other hand, with regard to postprandial hyperglycemia (PPHG)

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by ingestion alone, cooked rice has some disadvantages compared to pasta[5]. This point can be improved by devising the order and combination of eating, *i.e.*, mabo-dofu with rice (mabo-don)[6], or beef bowl[7]. Although most of the rice food is polished rice, it is clear that the brown rice is rich in vitamins, minerals and dietary fiber and is nutritionally superior. However, there are many individuals who cannot eat brown rice for an extended period of time, and only a few people continue to eat it.

Regarding brown rice, it is known that there is a problem in compliance with continuous intake, and there are few reports of clinical trials so far[8]. Compliance means "observing the instructions", and in this study, it represents the rate at which brown rice can be continuously ingested as instructed. Various measures have been attempted to reduce the disadvantage of indigestion while utilizing the nutritional advantages of brown rice. Sub-aleurone layer residual rinse-free rice (SARFR), also known as Kinmemai rice, is a rice that has peeled the indigestible outer layer (*i.e.*, rind, pericarp), leaving the parts including a highly nutritive sub-aleurone layer, embryo base ("kinme")[9] and the boundary with endosperm, thus being tasty and looking the same as white polished rice. In this study, we examined the changes in the subjective symptoms, skin function, and the amount of accumulated advanced glycation endproducts (AGEs), which is an index of glycative stress, when the test product SARFR was ingested in young subjects for one month, and furthermore compared with a group that freely ingested purified rice.

## Methods

### Subjects

The subjects were men and women students from a university in Tokyo. This study was conducted with 61 subjects who agreed to participate in this trial in advance in writing, who met the selection criteria, did not conflict with the exclusion criteria, and were judged to be appropriate to participate by the principal investigator.

The selection criteria are shown below.

1) Men and women 18 to 60 years old at the time when the consent for participation in the study was obtained.
2) Persons in good health without chronic physical illness, including skin diseases.
3) Persons with the ability to give consent after receiving an adequate explanation of the purpose and content of the study, and who volunteer to participate at their own accord after proper understanding and provide a written consent to participate in this study.
4) Persons who can come on the designated examination date to undergo examination.
5) Persons determined to be suitable as a subject of this study by the principal investigator.

The exclusion criteria are shown below.

1) Persons who are currently receiving medication due to illness
2) Persons with a history of, or currently suffering from impaired glucose tolerance, mental illness, sleep disorders, hypertension, diabetes mellitus, dyslipidemia, or a serious illness.
3) Persons who have been taking drugs for the treatment of a disease for the past one month (excluding those with a history of taking temporary-relief medication for headaches, menstrual pain, and cold)
4) Persons with a history of, or currently suffering from a severe disease of the liver, kidney, heart, lungs, digestive organs, or a hematologic disease.
5) Persons with a history of, or currently suffering from a severe disease of the gastrointestinal tract, excluding appendicitis.
6) Persons with a body mass index (BMI) of more than 30 $kg/m^2$.
7) Those who may have allergic reactions to the test food, and those who may have serious allergic reactions to other foods or drugs.
8) Women pregnant, lactating or possibly pregnant.
9) Currently, and within the past 3 months, those who have a habit of continuously ingesting functional foods and health foods that claim to be related to skin quality improvement, and those who plan to take them during the test period (ingestion for the purpose of maintaining health was permitted).
10) Person with photosensitivity.
11) Persons who have been determined by the principal investigator as not suitable to be a subject of this study.

***Figure 1*** shows the transition of the number of test subjects. The breakdown of 59 subjects analyzed was 37 in the SARFR group (24 men and 13 women) and 22 in the control group (13 men and 9 women). The average age of each group was 21.0 ± 1.5 years in the SARFR group (men 21.4 ± 1.2 years, women 20.2 ± 1.7 years) and 22.0 ± 1.2 years in the control group (men 22.4 ± 1.2 years, women 21.4 ± 1.0 years).

### Exam design

This study was an open label study between parallel groups.

The SARFR group ingested SARFR, and the control group freely ingested normal polished rice without SARFR. The SARFR group ingested the test product once a day during the test period by any of the following methods.

- Cook the SARFR in the cafeteria, weigh it, and prepare at least 150 g or more for ingestion.
- Heat the packaged SARFR (160 g) in a microwave oven and ingest it.

The test product was provided by Toyo Rice Co., Ltd. (Wakayama, Japan). The subjects participated in the pre-ingestion test for one day, the ingestion period for 33 days, and the post-intake test for one day.

Pre-intake tests for each group include a background survey by filling out a questionnaire, survey of lifestyle and skin condition by filling out a questionnaire, skin condition measurement by a device Clreo-Pro (Fujitex, Shinjuku-ku, Tokyo), skin AGEs score by an AGEs sensor device (RQ-

AG01J: Sharp Life Sciences, present Air Water Biodesign, Kobe, Hyogo, Japan). Post-ingestion tests included a survey of lifestyle-related and skin conditions, skin condition measurement, and AGEs score. In both the pre-ingestion test and the post-intake test, female subjects washed their face 20 minutes or more prior to the test to remove cosmetics, and performed skin diagnostic measurements after acclimation. The test period was from June 2019 to July 2019.

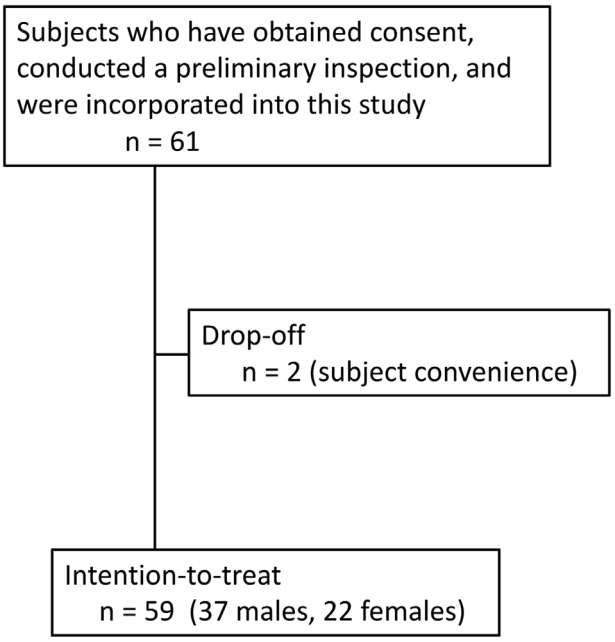


***Fig. 1.*** **Changes in the number of test subjects.**

### *Sub-aleurone layer residual rinse-free rice (SARFR)*

SARFR is the rice produced by the special rice processing as follows; the rice hulls (chaff), wax layer (rind), and bran layer, in order from the outside, were scraped off from the whole chaff, leaving the sub-aleurone layer, scutella of the germinal base (kinme) and the endosperm boundary to which the scutellum adheres (***Fig. 2***). Rice husk is inedible, the wax layer hinders water absorption and the bran layer is not tasty. The sub-aleurone layer is located between the starch layer and the bran layer, and is rich in the nutritional components of brown rice; it has a unique flavor and sweetness with a favorable taste. The nutritional components vary depending on the amount of soil microbes and the method of processing. In general, SARFR contains twice as much vitamin B1 and E as conventional polished rice, 1.5 times more dietary fiber, and more carbohydrate (probiotics) that adjusts the gastrointestinal environment by immersion in the cooking process or other factors; maltose reaches about 60 times, oligosaccharides 12 times, and lipopolysaccharide (LPS) reaches 6 times that of polished rice.

## *Evaluation item*

### *Skin index*

The skin indices includuded functions, skin age, overall skin health, pores, wrinkles, moisture, elasticity, skin tone, pigmentation (epidermis layer, dermis layer), oil content, and porphyrin, that were measured by Clreo-Pro.

### *AGEs measurement*

The AGEs score was measured using AGEs sensors [10, 11].

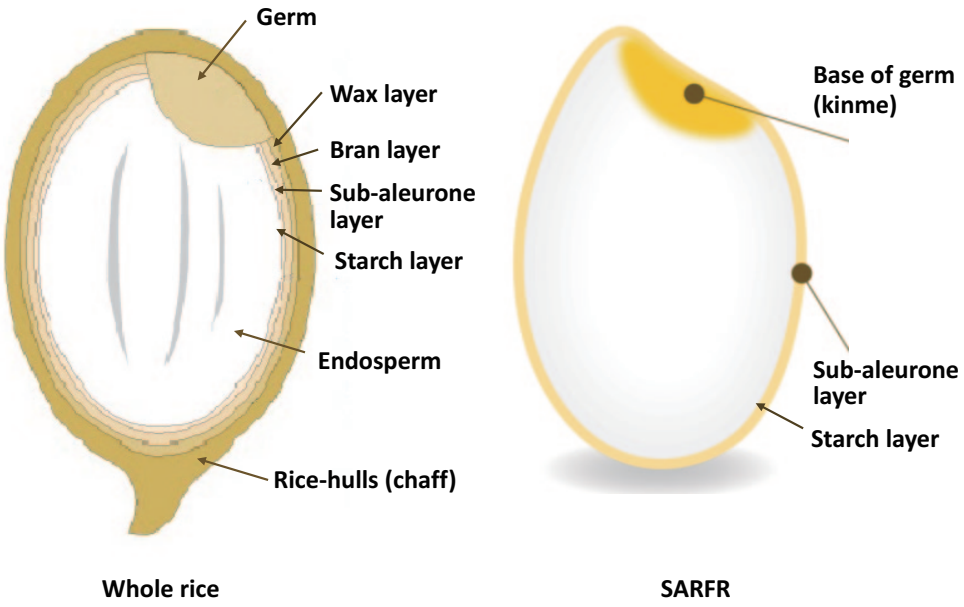


***Fig. 2.*** **Structure of rice and SARFR.**

SARFR, sub-aleurone layer residual rinse-free rice.

### *Subjective symptoms*

The contents of the questionnaire were questions about changes in eating habits, lifestyle habits (exercise, sleep, bowel movements, drinking, smoking, and mental stress), and skin conditions. The average value of compliance (the intake rate of the test product) was calculated based on the questionnaire.

### *Statistical analysis*

For analysis, a software SPSS (Statistics25: IBM Japan, Chuo-ku, Tokyo, Japan) was used to perform paired-t test or Wilcoxon signed rank test. A risk rate of less than 5% was defined as a significant difference.

### *Ethical standards*

This study was conducted in compliance with the Declaration of Helsinki (revised at the 2013 WMA Fortaleza General Assembly) and the ethical guidelines for human-based medical research (notification by Ministry of Education, Culture, Sports, Science and Technology [MEXT] and Ministry of Health, Labour and Welfare [MHLW]). This research obtained the approval of the Ethical Committee of the Society for Glycative Stress Research (GSE 2019-004), which has discussed the ethics and validity of the study. The clinical trial for this study was pre-registered (UMIN #000037017).

## *Results*

### *Compliance*

Compliance in the SARFR group was 84%; 2 out of 39 dropped out (dropout rate 5%) and there was no dropout due to test product intake (***Fig. 1***). In the control group, 0 out of 61 dropped out. The reason for the dropout was due to personal circumstances.

### *Subjective symptoms*

There were no significant findings regarding lifestyle habits (*i.e.*, exercise, sleep, bowel movements, drinking, smoking, stress), and subjective symptoms regarding skin conditions.

### *Skin index*

***Table 1*** shows the results of the skin index. Regarding the skin age (variation), the value in the SARFR group was

***Table 1. Results of skin condition and AGEs fluorescence.***

| | | Before ingestion | One month after ingestion | Comparison between groups (by variation) |
|---|---|---|---|---|
| | | Mean SD | Mean SD | vs. control |
| Age (years) | SARFR | 21.0 ± 1.5 | | |
| | Control | 22.0 ± 1.2 | | |
| Pores (%) | SARFR | -0.9 ± 12.1 | -3.0 ± 12.2 | 0.589 |
| | Control | -2.0 ± 13.5 | -4.6 ± 11.3 | |
| Wrinkles (%) | SARFR | 2.8 ± 8.2 | 2.6 ± 8.5 | 0.558 |
| | Control | 0.5 ± 6.1 | -0.4 ± 4.9 | |
| Pigmentation (PL) stratum corneum (%) | SARFR | 2.9 ± 5.3 | 1.8 ± 5.7 | 0.942 |
| | Control | 1.9 ± 4.1 | 0.8 ± 3.7 | |
| Pigmentation (UV) stratum corneum (%) | SARFR | 6.3 ± 7.9 | 4.3 ± 8.3 | 0.419 |
| | Control | 3.9 ± 5.3 | 2.8 ± 5.0 | |
| Porphyrin | SARFR | 34.0 ± 8.5 | 32.1 ± 6.8 | 0.702 |
| | Control | 32.8 ± 9.9 | 30.1 ± 10.6 | |
| Skin tone | SARFR | 62.0 ± 5.5 | 62.8 ± 4.9 | 0.658 |
| | Control | 61.7 ± 4.7 | 62.8 ± 4.8 | |
| Elastisity (angle) | SARFR | 45.8 ± 5.6 | 44.4 ± 9.2 | 0.250 |
| | Control | 42.7 ± 7.7 | 43.6 ± 5.2 | |
| Skin health score | SARFR | 43.2 ± 10.8 | 49.2 ± 12.6 | 0.340 |
| | Control | 47.3 ± 9.6 | 50.9 ± 10.0 | |
| Skin age (year) | SARFR | 21.5 ± 1.9 | 21.1 ± 1.7 | **0.034** |
| | Control | 22.2 ± 1.6 | 22.0 ± 1.6 | |
| AGEs score | SARFR | 0.43 ± 0.07 | 0.44 ± 0.06 | 0.421 |
| | Control | 0.44 ± 0.21 | 0.46 ± 0.05 | |

SARFR, sub-aleurone layer residual rinse-free rice; AGEs, advanced glycation endproducts; PL, polarized right; UV, ultraviolet; SD, standard deviation; skin condition measured by Clreo-Pro (Fujitex); AGEs score measured by AGEs sensor (Sharp); SARFR group, n = 37; the control group, n = 22; Statistical analysis by Student's t test.

significantly larger than that in the control.

Regarding the skin age (variation), the SARFR group showed a significantly larger decrease than the control, being more improved ($p = 0.034$, ***Fig. 3-a***). There was no significant difference in women (***Fig. 3-c***).

There was a significant difference between the groups in the change of wrinkles, which was significantly improved in the SARFR group (***Fig. 4-a***). A significant difference was observed only in men (***Fig. 4-b***), but not in women (***Fig. 4-c***).

No significant changes were noted in other items.

### *Measurement of AGEs*

The intensity of skin AGEs fluorescence did not change significantly before and after the test in both groups, and there was no significant difference in the variation between groups (***Table 1***).

### *Subclass analysis*

Since there are differences in lifestyle habits between boarding house students and home students, subclass analysis was performed separately for both. The number of home students was 28 (20.9 ± 1.5 years) in the SARFR group and 12 (22.0 ± 1.1 years) in the control group. The boarding house students were 8 (21.0 ± 1.6 years old) in the SARFR group and 8 (22.3 ± 1.3 years old) in the control group.

In the home students, the SARFR group showed significant improvement in pores, pigmentation (polarized light), total skin health score, and skin age after ingestion (***Fig. 5***). In boarding house students, only ultraviolet (UV) pigmentation was significantly improved in the SARFR group (***Fig. 6***). Overall, the effect on skin quality was more pronounced in the home students.

### *Safety*

There were no adverse events attributable to the test product during the observation period.

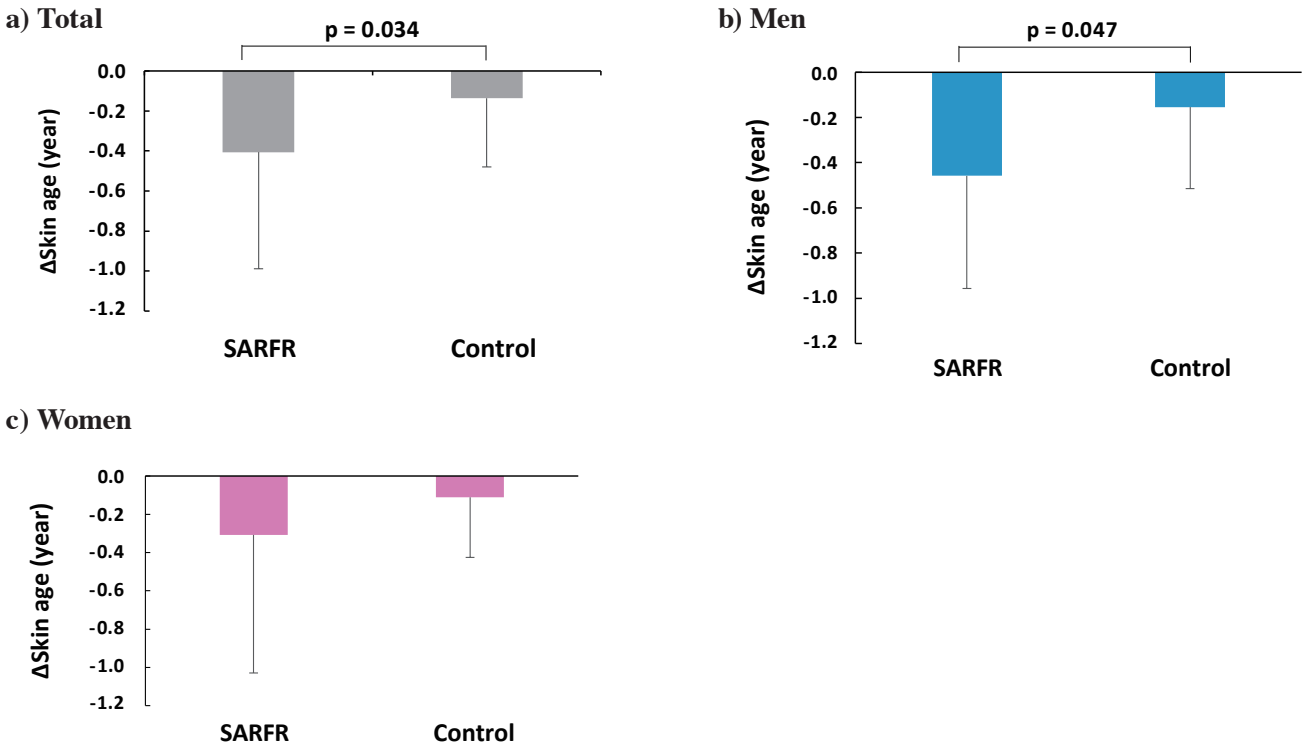


***Fig. 3.*** **Change of skin age.**

**a)** Total, SARFR group, n = 37; the control group, n = 22. **b)** Men, SARFR group, n = 24; the control group, n = 13. **c)** Women SARFR group, n = 13; the control group, n = 9. Skin age evaluated by Clreo-Pro (Fujitex). Results are expressed as mean ± SEM; Statistical analysis by Wilcoxon signed rank test. SARFR, sub-aleurone layer residual rinse-free rice; SEM, standard error mean.

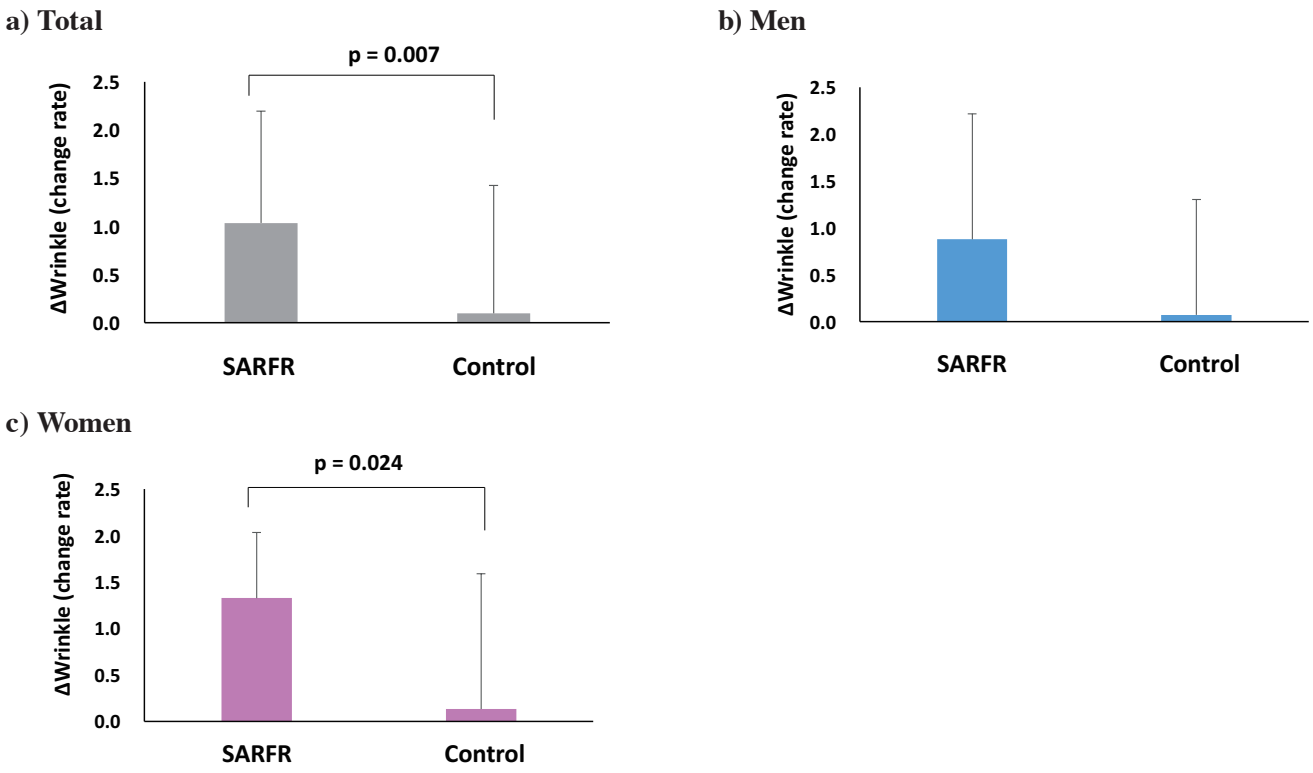


***Fig. 4.*** **Change of wirinkles.**

**a)** Total, SARFR group, n = 37; the control group, n = 22. **b)** Men, SARFR group, n = 24; the control group, n = 13. **c)** Women SARFR group, n = 13; the control group, n = 9. Winkles are evaluated by Clreo-Pro (Fujitex). Results are expressed as mean ± SEM; Statistical analysis by Wilcoxon signed rank test. SARFR, sub-aleurone layer residual rinse-free rice; SEM, standard error mean.

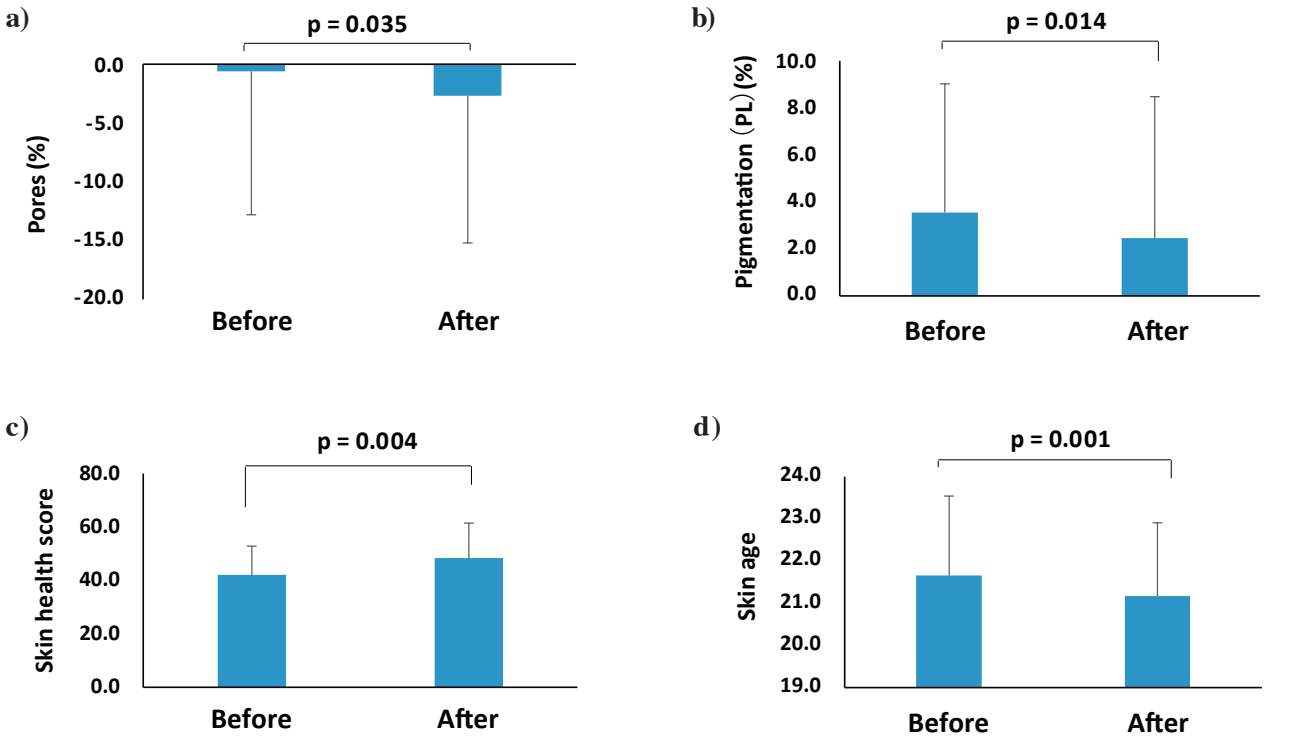


***Fig. 5.*** **Effects of SARFR on skin condition: Subclass analysis in home students.**

**a)** Pores. **b)** Pigmentation by PL. **c)** Total skin health score. **d)** Skin age. Skin condtions are evaluated by Clreo-Pro (Fujitex). Results are expressed as mean ± SEM; number of the home students, n = 12; Statistical analysis by paired-t test. SARFR, sub-aleurone layer residual rinse-free rice; PL, polished rice; SEM, standard error mean.

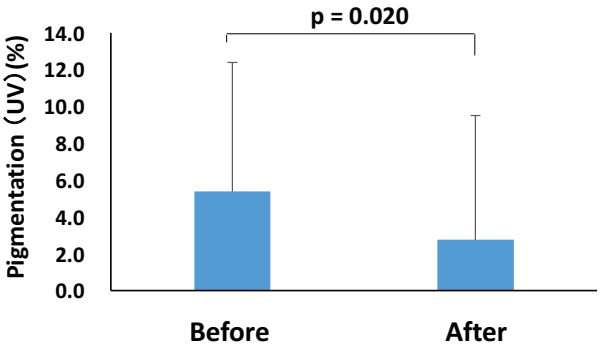


***Fig. 6.*** **Effects of SARFR on skin condition: Subclass analysis in the boarding house students.**

Skin condtions are evaluated by Clreo-Pro (Fujitex). Results are expressed as mean ± SEM; number of the boarding house students, n = 8; Statistical analysis by paired-t test. SARFR, sub-aleurone layer residual rinse-free rice; PL, polished rice; SEM, standard error mean.

## *Discussion*

This study compared the changes in skin condition and skin AGEs between two groups of students who took SARFR as a test product once a day for one month and ordinary polished rice. SARFR was processed so as to be easy to eat by removing only the epidermal wax layer and the outer layer containing a large amount of indigestible fiber from brown rice to leave the nutrients.

The reported effects of brown rice include suppression of elevated blood triglyceride/total cholesterol [8, 12], reduction of PPHG [13, 14], improvement of fasting blood glucose [15], reduction of HbA1c [16], prevention of bone density reduction in the elderly [17], visceral fat reduction in persons with metabolic syndrome [18], improved bowel movement [19], increased bone density [20], and improved vascular endothelial function [21]. It is not easy to prove because human intestinal flora varies greatly among individuals [22], however it has been pointed out that brown rice intake may have a positive effect on intestinal flora. When the effect of brown rice on human intestinal flora was examined, a significant increase in the number of *Bifidobacterium adolescentis* and *Enterococcus faecalis*, a significant decrease in the total number of bacteria, *Bacteroides*, *Eubacterium aerofaciens,* and *Escherichia coli* were observed by individuals ingesting brown rice [23]. Also, decreased detection rates of *Clostridium paraputrificum* and *Clostridium perfringens* were observed during brown rice intake. It has also been reported that brown rice eaters with a high subjective health have a high occupancy rate of butyric acid-producing bacteria, *i.e.*, *Faecalibacterium prausnitzii, Roseburia* genus, *Bilophila* genus [24].

Thus, it cannot be said that the brown rice diet is widely spread, although it is expected to be effective in preventing and improving lifestyle-related diseases. The reasons are that the taste and texture are different from that of polished rice, the cooking time is long, the digestion/absorption is poor due to the contained cellulose, digestion is poor, and it can cause abnormal intestinal fermentation. Anxiety about iron deficiency anemia due to the chelating effect of phytic acid has also been pointed out, but it is not a problem if we eat a normal amount of brown rice. It was also said that some people were worried about pesticide residue on brown rice. Although it was detected in some brands of brown rice in the past, there is almost no problem nowadays with domestic products.

The biggest problem among them might be the difficulty of digestion and absorption. To solve this problem, easy-to-eat processed products have been developed, including pre-germinated brown rice ("hatsuga genmai") [13, 14], surface-treated brown rice [25], ultra-high hydrostatic pressurizing brown rice [17], and use with a reduced mixing ratio (50% barley and brown rice) [18], as well as SARFR. As another method, brown rice extract is used as a supplement.

Typical functional ingredients of brown rice are dietary fiber and lipophilic ingredients such as ferulic acid and γ-oryzanol. When γ-oryzanol is given to animal fat-fed mice, it has been shown to relieve endoplasmic reticulum stress in the hypothalamus and attenuate the animal fat preference [26]. Furthermore, by the epigenomic mechanism, γ-oryzanol acts to restore the decreased expression of dopamine receptors in the brain's reward system (ventral striatum) which recognizes the pleasure and satisfaction of eating mitigates, thus reducing the animal fat preference, followed by exhibiting the effect of transforming an "unsatisfied brain" into a "satisfied brain" [27]. As a result, it eliminates animal fat dependence, improves hyperglycemia, and ameliorates metabolic syndrome [28]. Furthermore, for the triterpene alcohol and sterol preparation (TASP) contained in the oil-soluble fraction in rice bran, there is evidence that TASP suppresses the increase in postprandial blood concentration of GIP (glucose-dependent insulinotropic polypeptide), a digestive tract hormone, and that it inhibits translocation of SGLT1 (glucose transporter sodium-dependent glucose transporter 1) to the cell membrane [29]. As a result of these overall actions, it is considered that glycative stress is reduced.

To date, there has been only one clinical trial report for SARFR. In that study, 25 people (6 men, 19 women) who stayed in an elderly facility participated and ingested rinse-free rice for two months every meal (control group), followed by intake of SARFR for 4 months (test group) in a non-crossing manner [9]. The results showed significant reduction of systolic blood pressure ($p = 0.008$) and a tendency to decrease diastolic blood pressure ($p = 0.079$), body fat percentage ($p = 0.064$), and HbA1c ($p = 0.050$) in the SARFR group.

There is a case report on the relationship between meal and mileage during the 118 days when Mr. Hazama Kanpei, a comedian, ran 50 km a day for 118 days [30]. The entire process consisted of 15 cycles, with a basic rule of running for five days and resting for one day. The breakfast on the day of running was 33 days of Japanese food and 66 days of Western food, and the dinner on the previous day was 30 days of Japanese food, 25 days of Western food, and 23 days of Chinese food. During the process, SARFR was served for Japanese food. The results of mileage and running time for each cycle show that the days when SARFR was ingested in the morning and afternoon, the running time was extended by 20 minutes, the mileage was 5.8 km longer,

and the average speed was 0.84 km/day faster than that of the Western food diet. On the day he consumed SARFR for breakfast, the running time and average speed were significantly longer, the mileage being 51.4 km for Japanese food and 45.6 km for Western food ($p < 0.05$).

There are several conference presentations on SARFR. It has been pointed out that the GI value of SARFR is lower than that of comon white rice [31], and this may be involved in the downward trend of HbA1c observed in the previous report of Kyo H et al. [9]. It is also reported that angiotensin intracellular signal transduction in the vascular smooth muscle was suppressed [32], and it may be involved in the hypotensive effect seen in the report of Kyo et al. [9]. In addition, the possibility of activation of immune function [33, 34], health promotion [35], and constipation amelioration [36] have been reported.

In young subjects in this study, some positive effects of SARFR intake were confirmed. First is the high level of compliance and no dropout due to the test food intake. If brown rice intake had been imposed on subjects, they usually would not provide such high compliance [37, 38]. This reflects that there is no problem in the taste and flavor of the test product, nor with digestive system symptoms due to indigestion and malabsorption. Rather, positive effects such as improved bowel movements were seen.

The second is the effect of improving skin function. In general, young subjects in their early twenties have a slight decrease in skin function and are better than middle-aged subjects. Nonetheless, it is significant that the test product intake showed a significant improvement effect on the skin age as compared with the control. In contrast, there was no significant change in skin AGEs fluorescence, its reason may be that the pre-value was close to the normal range and there was little room for improvement in young subjects.

Most skin function problems are said to be due to photoaging, which is caused by oxidative stress due to ultraviolet (UV) exposure. Next is the influence of glycative stress. This involves yellowing due to AGEs deposition on the skin and a decrease in skin elasticity due to the formation of glycated cross-links of collagen protein [39]. Also, it is associated with a decline in moisturizing function due to glycation and reduced production of filaggrin, a natural moisturizing factor (NMF) [40, 41]. Additionally AGEs act on pigment cells (melanocytes) to enhance melanin production, thus inducing spot formation [42]. It is speculated that these symptoms were alleviated as a result of reducing glycative stress by ingesting the test product (*Fig. 7*).

Regarding gender differences, almost no effect of SARFR was observed in women, but differences were observed in men. The reason may be that the skin of women in their early twenties was in almost normal health, thus being no room for further improvement.

Comparing boarders and home students, it has been reported that boarders have a lower nutritional satisfaction rate and especially a lower protein intake [43, 44]. Also, boarders

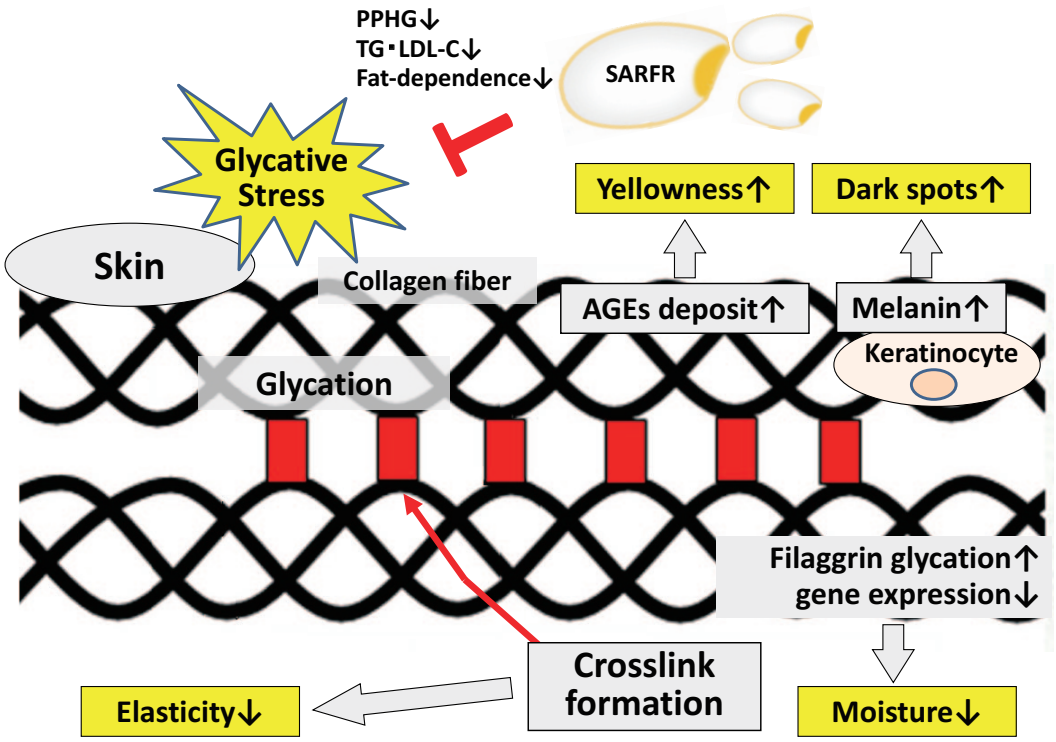


***Fig. 7.*** **Glycative stress-induced skin damges and the possible suppressive actions by SARFR.**

SARFR, sub-aleurone layer residual rinse-free rice; AGEs, advanced glycation endproducts; PPHG, post-prandial hyperglycemia: TG, triglycemide, LDL-C, low-desity lipoprotein-cholesterol.

have a larger amount of drinking [45], a higher rate of skipped breakfast [46], and more men with abnormal taste sense [47]. The elevated glycative stress due to disturbance of nutritional balance was more remarkable in male boarders, those who in this study might be in a similar situation.

### *Safety*

Brown rice, SARFR, and polished rice are basically staple foods that have been used in meals for many years, and can therefore be considered to have sufficient food safety. However, the problems of indigestion, abnormal intestinal fermentation, and residual pesticides have been pointed out regarding brown rice intake. The reason for this is based on the insufficient expansion due to hindered water absorption by the wax layer located on the surface of brown rice during steam cooking. SARFR is made by removing the wax layer and bran layer from brown rice by special processing, its color looks almost the same as that of polished rice (conventional white rice) and its taste reserved, resulting in the improvement of problems that are present in brown rice. Furthermore, it has been reported that SARFR contains almost no antimutagenic substance [48]. There are no reports of adverse events related to SARFR in this and past clinical trials. It was judged that there was no problem regarding the safety of SARFR.

## *Conclusion*

A test meal (SARFR) of 150 g or more once a day for university students was ingested for one month. Results indicate that indigestion was not observed, compliance was good, and a significant skin quality improving effect was observed. It was suggested that SARFR, by reducing indigestion of brown rice and securing nutritional value, may contribute to health promotion including improvement of skin quality.

## *Conflict of interest declaration*

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## *Reference*


1) Sugihiro T, Yoneda M, Ohno H, et al. Associations of nutrient intakes with obesity and diabetes mellitus in the longitudinal medical surveys of Japanese Americans. *J Diabetes Investig*. 2019; 10: 1229-1236.
2) Sato S, Koike Y, Ebisawa M. Natural history of immediate-type food allergy in childhood. *The Japanese Journal of Pediatric Allergy and Clinical Immunology*. 2019; 33: 41-46. (in Japanese)
3) Shibata-Ishiwata N. Breakthrough measures for food allergies based on menu analysis of school lunch. *The Allergy in Practice*. 2019; 39: 579-582. (in Japanese)
4) Nakano K, Takahashi T, Tsunoda A, et al. Dietary trends in patients with fecal incontinence compared with the National Health and Nutrition Survey. *J Anus Rectum Colon*. 2019; 3: 69-72.
5) 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.
6) 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.
7) Kawabata A, Yagi M, Ogura M, et al. Postprandial blood glucose level after intake of a bowl of rice topped with beef. *Glycative Stress Res*. 2015; 2: 67-71.
8) Yokoyama C, Maeda, Y, Ishikawa Y, et al. Verification of reducing effect on serum cholesterol level by the long-term consumption of the brown rice. *Journal for the Integrated Study of Dietary Habits*. 2017; 28: 2017. (in Japanese)
9) Kyo H, Suzuki N, Enomoto T, et al. Influence of the special processing rice on the factors of lifestyle related disease. *Japanese Journal of Complementary and Alternative Medicine*. 2018; 15: 103-108. (in Japanese)
10) Yamanaka M, Matsumura T, Ohno R, et al. Non-invasive measurement of skin autofluorescence to evaluate diabetic complications. *J Clin Biochem Nutr*. 2016; 58: 135-140.
11) Morita Y, Yagi M, Ishizaki K, et al. Evaluation of the glycative stress by non-invansive skin AGEs measurement devices. *Glycative Stress Res*. 2019; 6: 92-102.
12) Suzuki M. Repressive effect of dietary fiber fractions in unpolished rice on the increase in cholesterol and triglyceride. *Journal of Japanese Society of Food and Nutrition*. 1982; 35: 155-160. (in Japanese)
13) Ito Y, Mizukuchi A, Kise M, et al. Postprandial blood glucose and insulin responses to pre-germinated brown rice in healthy subjects. *J Med Invest*. 2005; 52: 159-164.
14) Ito Y. Postprandial blood glucose and insulin responses to breakfasts containing pre-germinated brown rice pr white rice in healthy subjects. *Yoboiryo Aggressive*. 2015; 2: 78-82. (in Japanese)
15) Hamano-Nagaoka M, Nishimura T, Matsuda R, et al. Evaluation of a nitric acid-based partial-digestion method for selective determination of inorganic arsenic in rice. *Shokuhin Eiseigaku Zasshi*. 2008; 49: 95-99.
16) Hayakawa T, Suzuki S, Kobayashi S, et al. Effect of pre-germianted brown rice on metabolism of glucose and lipid in patients with diabetes mellitus type 2. *Journal of the Japanese Association of Rural Medicine*. 2009; 58: 438-446. (in Japanese)
17) Hashimoto M, Matsuzaki K, Yano S, et al. Long-term oral intake of ultra-high hydrostatic pressurizing brown rice prevents bone mineral density decline in elderly people. *Pharmacometrics*. 2017; 92: 69-73. (in Japanese)
18) Maeda-Yamamoto M, Hirosawa T, Mihara Y, et al. Randomized, placebo-controlled, clinical study to investigate anti-metabolic syndrome effects of functional foods in humans. *Journal of the Japanese Society for Food Science and Technology*. 2017; 64: 23-33. (in Japanese)
19) Yoshihara E, Ishii M, Maruyama M, et al. Facts on bowel dysfunction in older people with dementia at group homes and the bowel management reviews. *Case Journal of Dementia Care*. 2017; 9: 371-379. (in Japanese)

20) Matsuzaki K, Yano S, Sumiyoshi E, et al. Long-term ultra-high hydrostatic pressurized brown rice intake prevents bone mineral density decline in elderly Japanese individuals. *J Nutr Sci Vitaminol (Tokyo)*. 2019; 65: S88-S92.
21) Kondo K, Morino K, Nishio Y, et al. Fiber-rich diet with brown rice improves endothelial function in type 2 diabetes mellitus: A randomized controlled trial. *PLoS One*. 2017; 12: e0179869.
22) Nemoto H, Ikata K, Arimochi H, T, et al. Effects of fermented brown rice on the intestinal environments in healthy adult. *J Med Invest*. 2011; 58: 235-245.
23) Benno Y, Endo K, Miyoshi H, et al. Effect of rice fiber on human fecal microflora. *Microbiol Immunol*. 1989; 33: 435-440.
24) Fukushima-Hirakawa A. Study on relationship between self-rated health and intestinal microbiota. *Int J Hum Cult Stud*. 2019; 29: 101-111. (in Japanese)
25) Araki R, Matsuura A, Fujie K, et al. An exploratory randomized crossover trial to investigate the palatability of partially abraded brown rice. *Journal of Japanese Society of Nutrition and Food Science*. 2016; 69: 249-255. (in Japanese)
26) Kozuka C, Yabiku K, Sunagawa S, et al. Brown rice and its component, γ-oryzanol, attenuate the preference for high-fat diet by decreasing hypothalamic endoplasmic reticulum stress in mice. *Diabetes*. 2012; 61: 3084-3093.
27) Kozuka C, Kaname T, Shimizu-Okabe C, et al. Impact of brown rice-specific γ-oryzanol on epigenetic modulation of dopamine D2 receptors in brain striatum in high-fat-diet-induced obesity in mice. *Diabetologia*. 2017; 60: 1502-1511.
28) Masuzaki H, Kozuka C, Okamoto S, et al. Brown rice-specific γ-oryzanol as a promising prophylactic avenue to protect against diabetes mellitus and obesity in humans. *J Diabetes Investig*. 2019; 10: 18-25.
29) Shimotoyodome A, Okahara F. Anti-obese and anti-hyperglycemic effects of dietary triterpene alcohols and sterols from rice bran oil. *Oleoscience*. 2017; 17: 269-276. (in Japanese)
30) Hirakawa A, Miyachi M, Watanabe S. Effects of different meals for the around-the-world marathon-run. *Clinical and Functional Nutriology*. 2015; 7: 152-156. (in Japanese)
31) Uenobe M, Nakata K, Inagawa H. Benefits of subaleurone layer of milled rice (Kinmemai): Analysis of Kinmemai from the view point of glycemic index food. *ACN2015 Abstract Book*. 2015; 276. (abstract)
32) Utsunomiya H, Shirai H, Eguchi S, et al. Inhibitory effect of kinmemai (sub-aleurone layer residual rinse-free rice) on angiotensin intracellular signal transduction in vascular smooth muscle cells. *Proceedings of the Japanese Society of Pathology*. 2008; 97: 277. (abstract in Japanese)
33) Uenobe M, Nakata K, Inagawa H. A study of the immune effect of ingestion of kinmemai (sub-aleurone layer residual rinse-free rice) for one month in healthy adolescents. *Proceesings of Lectures of Japan Society of Nutrition and Food Science*. 2014; 68: 200. (abstract in Japanese)
34) Inagawa H, Kohchi C, Nakata K, et al. A study on the immune function of kinmemai (sub-aleurone layer residual rinse-free rice): Innate immunity activation ability of the sub-aleurone layer. *Proceesings of Lectures of Japan Society of Nutrition and Food Science*. 2013; 67: 121. (abstract in Japanese)
35) Okuda K. Positive effects on health due to continuous intake of kinmemai (sub-aleurone layer residual rinse-free rice). *Proceesings of Lectures of Japan Society of Nutrition and Food Science*. 2007; 61: 223. (abstract in Japanese)
36) Nishiyama N, Inejima T, Heya Y, et al. The ameliorating effect on bowel movements by sub-aleurone layer residual rinse-free rice. *The Japanese Journal of Nutrition and Dietetics*. 2018; 76(Suppl): 208. (abstract in Japanese)
37) Wedick NM, Sudha V, Spiegelman D, et al. Study design and methods for a randomized crossover trial substituting brown rice for white rice on diabetes risk factors in India. *Int J Food Sci Nutr*. 2015; 66: 797-804.
38) Zhang G, Malik VS, Pan A, et al. Substituting brown rice for white rice to lower diabetes risk: a focus-group study in Chinese adults J Am Diet Assoc. 2010; 110: 1216-1221.
39) Ichihashi M, Yagi M, Nomoto K, et al. Glycation stress and photo-aging in skin. *Anti-Aging Med*. 2011; 8: 23-29.
40) Cadau S, Leoty-Okombi S, Pain S, et al. *In vitro* glycation of an endothelialized and innervated tissue-engineered skin to screen anti-AGE molecules. *Biomaterials*. 2015; 51: 216-225.
41) Khmaladze I, Österlund C, Smiljanic S, et al. A novel multifunctional skin care formulation with a unique blend of antipollution, brightening and antiaging active complexes. *J Cosmet Dermatol*. 2020; 19: 1415-1425.
42) Abe Y, Takabe W, Yagi M, et al. Melanin synthesis induction by advanced glycation end-products (AGEs) without α- melanocyte stimulating hormone (α-MSH) or UV exposure. *Glycative Stress Res*. 2016; 3: 229-235.
43) Kaneko T, Sato M, Sasayama R, et al. Actual state of eating habits and Night-Eating Syndrome in medical students. *Bulletin of Yamanashi Medical College*. *Bulletin of Yamanashi Medical University*. 2001; 18: 7-10. (in Japanese)
44) Ohira M, Saegusa K, Sawai S, et al. A study on nourishment intake condition of nursing college students. *Journal of Mie Prefectural College of Nursing*. 2002; 6: 1-9. (in Japanese)
45) Iwamoto M. A study of awareness and behavior of nursing students regarding drinking, smoking and related factors. *Nursing Journal of Kagawa Medical University*. 2003; 7: 39-47. (in Japanese)
46) Nagahata T, Nakade M, Hasegawa J, et al. The relationship between skipping breakfast and the living arrangements of university students. *Jpn J Nutr Diet*. 2014; 72: 32-39. (in Japanese)
47) Kojima C, Susaki H, Ishida S, et al. The relationship between accurate conditions of taste and diet for the School of Nutritional Sciences' students. *Annual Report of Institute of Health and Nutrition Nagoya University of Arts and Sciences*. 2010; 4: 19-26.
48) Mori I, Natsui S, Takeda K, et al. Search for antimutagenic substances contained in kinmemai (sub-aleurone layer residual rinse-free rice). *Proceedings of the Japanese Society of Pathology*. 2008; 97: 1: 312. (abstract in Japanese)