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Effect of low molecular weight rice bran derived arabinoxylan (Oryzaloze®) in improving physical condition through maintenance of homeostasis

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Key Words: Low molecular weight rice bran derived arabinoxylan, Maintenance of homeostasis, Immunity enhancing action, Stress resistance, Sleep, Improvement of body coldness

Abstract

Low molecular weight rice bran derived arabinoxylan (Oryzaloze®) was developed as a functional oligosaccharide with an immunity enhancing action whose main ingredient is the husks of purple-black rice. It has been acclaimed as a functional food that is effective in improving poor health and nutritional status that may cause immune deficiency. We examined the causal relationship between Oryzaloze® and the immunity enhancing action using an evaluation system based on stress resistance to 2-deoxy-D-glucose administration, and the action of inhibiting decline in immune function caused by stress, in other words, down-regulation of Th1 cell-mediated immunity was observed. From these results, we concluded that maintenance of homeostasis through stress resistance may affect activation of autonomic nerves, and we examined the effect in improving sleep and body coldness, which are typical of poor health, in adult women complaining of dissatisfaction with sleep and body coldness. In relation to sleep, we conducted an examination of activity of autonomic nerves through questionnaires and fluctuations in R waves according to records of heartrate during sleep, and improvement in sleep disorders and improvement in sleep quality were observed, suggesting activation of the autonomic nerves. In relation to bodily coldness, according to a questionnaire on bodily coldness, decreases in bodily coldness and sensations of coldness due to changes in the external temperature were found and an increase in core temperature was observed, and a study of temperature recovery after cold loading found that the temperature recovery rate increases, suggesting the action of promoting blood circulation in the capillary vessels. We examined Oryzaloze® mediated stress resistance based on the action of preventing decline in immune function and the action of strengthening the autonomic nervous system, and confirmed efficacy. It was inferred from these results that Oryzaloze® contributes to maintenance of homeostasis and acts to improve poor health and enhance QOL.

Introduction

Our health is maintained by complex factors and does not fail easily. This mechanism for maintaining homeostasis within an organism has been compared to a restoring force with the resilience of a sponge. However, infection or impairment of the lipid metabolism or carbohydrate metabolism as a result of chronic decline in biological functions due to aging or disruption in lifestyle habits can cause homeostasis to fail, resulting in illness and the need for treatment¹⁾. Usually, except in the case of infection, the failure in our health does not happen suddenly but progresses gradually. In many cases, during this process, people experience changes in their physical condition and are subjectively aware of a decline in their QOL. To recognize the change in this stage and restore homeostasis is a way to maintain health and will lead to reduction in healthcare costs. During our everyday lives, we are constantly exposed to psychological stress. It is also well-known that the autonomic nerves, which are closely related with our physical condition, are affected by stress²⁾. Oryzaloze® is recognized as an immunity enhancing food, but since immune functions are reported to be controlled by the autonomic nerves³⁾, we concluded that Oryzaloze® acts to strengthen the autonomic nervous system and examined the effect of Oryzaloze® in improving physical condition through stress resistance and strengthening of the autonomic nervous system.

1. Action of Oryzalose® in enhancing immunity against inhibition of metabolism caused by 2-deoxy D-glucose (2DG)

Purpose

Oryzalose® has been found to have the effect of enhancing immunity through activation of macrophages and NK cells. Since long-term intake of Oryzalose® has been observed to be effective in improving physical conditions which appear to be linked to autonomic failure, we examined the possibility of a biological defense mechanism achieved through stress resistance. Administration of 2-DG generates sugar utilization stress. This is known to cause down regulation of Th1 cell-mediated immunity similar to that caused by experiences of psychological and physical stress^{4, 5}. We examined whether Oryzalose® acts to defend the body against decline in immune function caused by the stress of 2-DG administration.

Experiment method

Experimental animals: We divided 15 Lewis albino rats weighing between 290g and 317g into 3 groups and used them in the experiment. (Table 1)

Table 1

Group#	Number of Animals	Treatment	Dose (mg/kg)
1	5	Vehicle PO / Vehicle SC	-
2	5	Vehicle PO / 2DG SC	0 / 500
3	5	Oryzalose® / 2DG SC	50 / 500

PO - oral SC - subcutaneous

Experiment method

Oryzalose® was dissolved in purified water and orally administered using a syringe. The dose was 50mg/kg, adjusted to 5ml/kg in each animal and was administered once daily for 4 consecutive days, and the control group was orally administered 5ml of purified water. 2-deoxy D-glucose 500mg/kg and saline as the control were administered subcutaneously 1 hour after administration of Oryzalose®. On the fifth day after initiation of the study, we collected peripheral blood from all rats under anesthesia, and analysed white blood cells, lymphocytes, T-cells (CD3), helper-T-cells (CD4), suppressor cytotoxic-T-cells (CD8), NK-cells and B-cells.

Results

As a result of sugar utilization stress caused by 2-DG administration, a significant increase in the proportion of lymphocytes due to a decrease in the total white blood cell count and an increase in lymphocytes and a significant decrease in NK-cells were observed. In the group administered Oryzalose®, no increase in the proportion of lymphocytes was observed because there was no decrease in the number of white blood cells and no increase in lymphocytes. Although Oryzalose® was not found to defend against a decrease in NK-cells, a tendency for reduction in CD8 was observed. (Table 2).

Table 2

Treatment mg/kg daily	N	Mean ± SEM													
		Lymphocytes	WBC	% ¹	Total T cells	% ¹	Helper T Cells	% ¹	Suppre s. cytotox T cells	% ¹	NK cells	% ¹	B cells	% ¹	
Vehicle PO + Vehicle SC	5	8856 ± 191	12500 ± 207	70.9 ± 1.4	5225 ± 228	58.9 ± 1.3	3188 ± 315	40.4 ± 1.0	1670 ± 74	18.8 ± 0.5	1290 ± 37	14.6 ± 0.6	1887 ± 63	21.3 ± 0.8	
Vehicle PO + 2-DG 300 SC	5	9112 ± 406	12200 ± 547	74.7 ± 1.0*	5475 ± 241	60.1 ± 1.0	3827 ± 157	42.1 ± 0.9	1709 ± 98	18.7 ± 0.3	1017 ± 93	11.1 ± 0.7*	2081 ± 94	22.9 ± 0.6	
Oryzalose® 50 PO + 2-DG 300 SC	5	8957 ± 406	12600 ± 769	71.5 ± 2.3	5359 ± 181	59.6 ± 1.4	3737 ± 120	41.9 ± 1.2	1596 ± 63	17.8 ± 0.2	959 ± 128	11.0 ± 0.8*	2117 ± 124	23.6 ± 0.9	

SEM : Standard error of the mean

* t test Veh + Veh p <0.05

Discussion

2-deoxy D-glucose (2-DG) is a glucose analog which lowers the glucose utilization efficiency of cells and causes sugar utilization stress. This gives rise to a decline in immune function in the form of down-regulation of TH1 cell-mediated immunity. The increase in the ratio of lymphocytes resulting from 2-DG administration signifies an increase in Th2 cells. It was observed that administration of Oryzalo[®] tends to enable prevention of a decrease in white blood cell count and variation in composition, which is characteristic immunosuppression of stress arising from inhibition of energy metabolism, and tends to result in a reduction in CD8. These results suggest that Oryzalo[®] acts to prevent decline in immune function caused by stress.

2. Effect of Oryzalo[®] in improving sleep and bodily coldness in adult women

Purpose

The intake of functional foods whose main ingredient is Oryzalo[®] is reported to improve quality of life or QOL of elderly people and enhance immune functions, and, in terms of QOL, its effect in improving sleep is particularly noticeable⁶. Consumers who have taken Oryzalo[®] products often report effectiveness in improving bodily coldness. Bodily coldness and sleep are deeply connected with the autonomic nerves and it is suggested that the severity of sleep disorders and bodily coldness is associated with poor health, and it does not only cause decline in QOL but is also accompanied by decline in immune function and metabolic function, and may lead to homeostatic failure. As for the persons complaining of such symptoms, such symptoms are reported to be seen frequently in healthy people, elderly people, cancer patients and others suffering from psychological or physical stress⁷. We conducted a study in healthy subjects believing that if the intake of functional foods whose main ingredient is Oryzalo[®] can improve such symptoms, then Oryzalo[®] could contribute to the promotion of health and prevention of illness.

Study method

Summary

We conducted a monitor study in women aged 20-59 years who were dissatisfied with sleep or bodily coldness to verify the effect of Oryzalo[®] on sleep and bodily coldness. We had 10 healthy women take a product containing Oryzalo[®] (1.3g/bag) after breakfast and two hours before going to sleep and continued this for 4 weeks. Before intake, and 2 and 4 weeks after intake, we conducted a Questionnaire about sleep and bodily coldness, body measurements and measurement of heart rate and R-R intervals during sleep, and study of temperature recovery after cold loading. We aggregated the measurement results, study results and questionnaire responses and compared before and after.

Verification conditions and methods

(1) Basic information

We measured body weight, body composition, blood pressure and core temperature using a body composition meter, blood pressure monitor and a basal thermometer respectively.

(2) Sleep-related

A. Questionnaire on sleep

1) Pittsburgh Sleep Quality Index (PSQI): Conducted before intake and 2 and 4 weeks after intake. Used as an indicator of the degree of sleep disorder. The score indicates the severity of the disorder.

2) Sleep Health Risk Index (SHRI): Conducted before intake and 2 and 4 weeks after intake.

Used as a measure for the assessment of sleep health. A score of 5.5 or higher is the yardstick for a pathological condition.

B. Records of heart rate during sleep

We measured and recorded heart rate from before going to sleep and after going to sleep before intake and 2 and 4 weeks after intake. We used the POLAR heartbeat measurement system for measurement. The heartbeats obtained (ECG) represent the activity of the right atrium, left atrium, right ventricle and left ventricle and can be categorized into P, Q, R, S and T waves. We are able to infer activity of the autonomic nerves including the sympathetic

nerves and parasympathetic nerves by observing fluctuations in R-R intervals. From the R-R intervals, we deduced LF, HF and LF/HF using MATLAB and through our own program.

(3) Bodily coldness-related

A. Questionnaire

Conducted before intake and 2 and 4 weeks after intake. The aim of the survey was to investigate general symptoms such as the degree and location of the bodily coldness and the frequency.

B. Temperature recovery study

Conducted before intake and 2 and 4 weeks after intake. We measured the process of recovery of the body temperature of the right hand after cold loading by thermography. After dipping the subject's right hand in cold water (12°C) for 1 minute, we measured the temperature of the back of the hand by thermography. We performed measurements at 1 minute intervals and observed the rise in temperature occurring in the 10 minutes afterwards.

Results

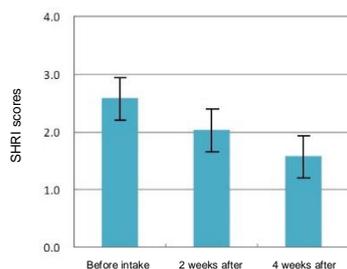
Sleep-related

PSQI: Table 3 shows fluctuation in the degree of sleep-related disorders according to the PSQI due to the intake of Oryzalose®. As the period of intake grows longer, a tendency for decrease in persons with severe symptoms for the items "sleep latency", "habitual sleep efficiency" and "daytime dysfunction" was seen. Changes in overall PSQI score show that, with each passage of time, persons with a score greater than 7 and persons with a score of 7 or less decreased while persons with a score of 3 or less increased. An analysis of changes after intake in persons with subjective symptoms for each of the disorder determining items revealed improvement in the scores of persons with subjective symptoms for all items. In particular, with respect to "sleep latency" and "habitual sleep efficiency," an improvement in scores was seen in more than 50% of participants. This suggests that the proportion of time in bed that was spent asleep (habitual sleep efficiency) increased due to shortening of the time between going to bed and falling asleep. This suggests, therefore, that, according to the PSQI, the intake of Oryzalose® results in overall improvement in sleep disorders.

Table 3 Changes in persons with subjective symptoms and improvers according to PSQI score

Question content	Persons with subjective symptoms (%)			Improvers (%)		Improvement rate (%)	
	Before intake	2 weeks after	4 weeks after	2 weeks after	4 weeks after	2 weeks after	4 weeks after
Sleep quality	100.0	33.3	33.3	66.7	66.7	66.7	66.7
Sleep latency	66.7	44.4	33.3	22.2	33.3	33.3	50.0
Sleep duration	66.7	44.4	33.3	22.2	33.3	33.3	50.0
Habitual sleep efficiency	55.6	11.1	11.1	44.4	44.4	80.0	80.0
Sleep disturbance	77.8	55.6	55.6	22.2	22.2	28.6	28.6
Use of sleeping medication	0.0	0.0	0.0	0.0	0.0	-	-
Daytime dysfunction	77.8	66.7	22.2	11.1	55.6	14.3	71.4
PSQI score	100.0	44.4	11.1	55.6	88.9	55.6	88.9

Figure 1 Changes in SHRI scores



SHRI: Figure 1 shows changes in scores. A score of 5.5 or higher is used as a pathologic yardstick for sleep. Although, from the outset before intake, the mean SHRI score was below 5.5, many of the participants had slightly high scores and had some kind of disorder. With progressive intake, SHRI scores fell and 4 weeks after intake the SHRI scores of all participants were lower than before intake. In the evaluation based on the SHRI, Oryzalose® was found to be generally effective for reducing the degree of sleep disorder.

Heart rate records: LF (Low Frequency) indicates the activity level of the autonomic nervous system, HF (High Frequency) indicates the activity rate of the parasympathetic nerves and LF divided by HF, i.e. LF/HF indicates the activity rate of the sympathetic nerves. At 2 weeks after intake, LF increased in 4 out of 10 subjects, HF increased in 3 out of 10 subjects and LF/HF decreased in 2 out of 10 subjects. At 4 weeks after intake, LF increased in 4 out of 8 subjects, HF increased in 4 out of 8 subjects, and LF/HF decreased in 2 out of 8 subjects. (Figure 2 a, b and c) In the records of heartrate during sleep, the effect of Oryzalose® intake on the autonomic nerves was clearly evident. Since a tendency for activation of the autonomic nerves and increase in the degree of sympathetic nerve activity was observed, it is assumed that activity in the body that is controlled by the autonomic nerves is activated by Oryzalose® intake.

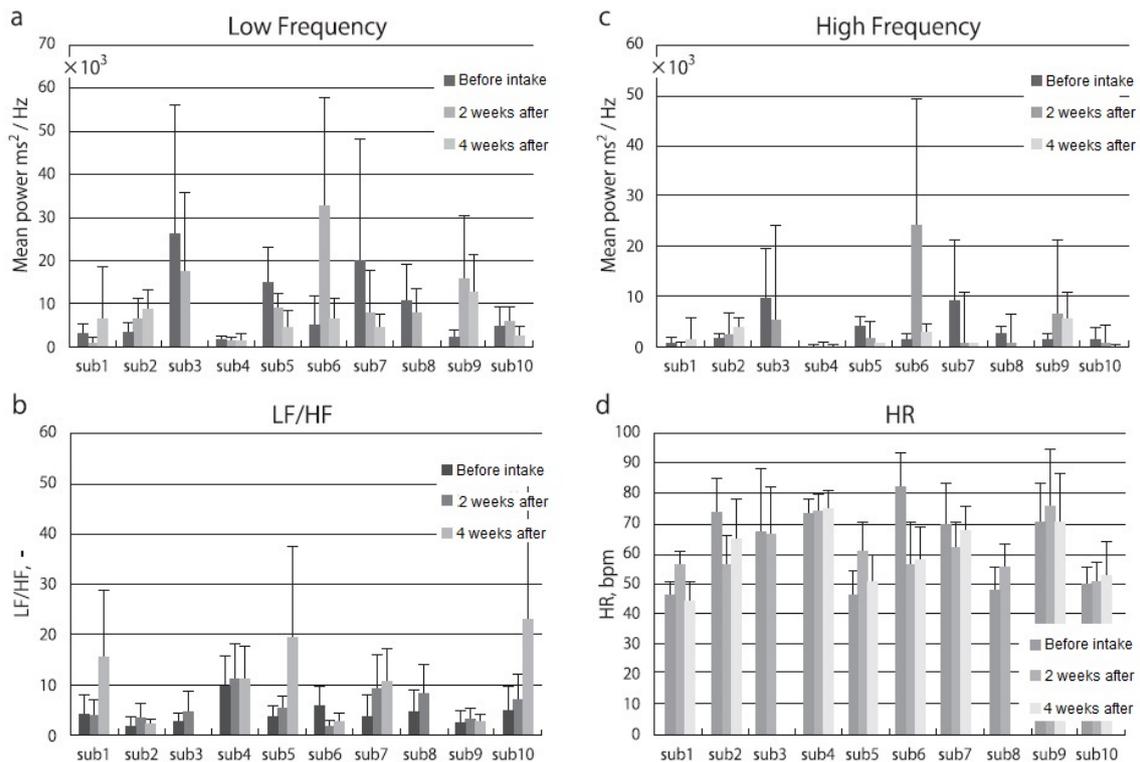


Figure 2 Heart rate records Analysis results
 (a: Autonomic nerves LF component, b: Sympathetic nerves LF/HF,
 c: Parasympathetic nerves HF component, d: Heart rate)
 Each value is based on the MEAN \pm SD. Subjects 3 and 9 at 4 weeks after intake were not measured due to the monitor.

Bodily coldness-related

Questionnaire: We conducted a questionnaire covering 9 items relating to bodily coldness. Table 4 shows the items and the results.

Persons with subjective symptoms relating to bodily coldness before intake was 63.3% on average and the rate of persons with subjective symptoms clearly dropped with the progression of Oryzalose® intake. At 2 weeks after intake, the rate of persons with subjective symptoms fell to 48.9%, dropping to 34.4% at 4 weeks after intake. The improvement rate at 4 weeks after intake was 52.1% on average, and Oryzalose® was clearly effective in improving bodily coldness. Efficacy is expected to increase further as a result of continued intake.

Study of temperature recovery after cold loading: We measured the process by which the base of the middle finger of the right hand recovers after cold loading in all monitors. From 0 to 3 minutes after cold loading, the gradient is steeper 2 and 4 weeks after intake than before intake, showing that rate of increase in the surface temperature of the hand is faster. A comparison based on mean values shows that temperatures were highest 2 weeks after intake, at around 1.7°C at 0 min, around 2.9°C at 2 min and around 2.8°C at 3 min (Figure 3). Figure 4 shows the

thermography of each monitor from 0 to 3 min after cold loading. It was confirmed from the images that, after intake, the temperature of the back of the hand, especially the finger tips, recovered to original temperature, turning red or white in 1 to 2 minutes and the rate of temperature recovery was quicker than before intake.

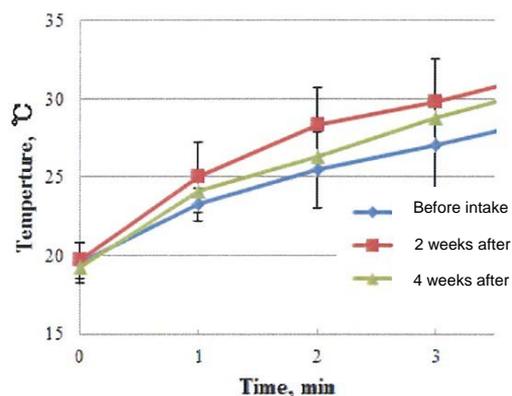
Table 4 Changes in persons with the subjective symptoms of bodily coldness and improvers

	Persons complaining of subjective symptoms (%)			Improvers (%)		Improvement rate (%)	
	Before intake	2 weeks after	4 weeks after	2 weeks after	4 weeks after	2 weeks after	4 weeks after
My hands, feet, shoulders, back and other parts of my body are painfully cold	80	50	40	30	40	37.5	50
My whole body is often painfully cold	80	30	50	50	30	62.5	37.5
People often say I have cold hands and feet	80	60	40	20	40	25	50
I wear more clothes than other people	50	40	20	10	30	20	60
I am sensitive to drops in temperature	70	40	40	30	30	42.9	42.9
My normal temperature is low	70	50	30	20	40	28.6	57.1
I wear socks to bed in the winter	70	60	30	10	40	14.3	57.1
In the winter, I need an electric blanket, a heater or a hot-water bottle when I sleep	70	60	20	10	50	14.3	71.4
In the winter I sometimes wake up because I feel cold	70	50	40	20	30	28.6	42.9

Conclusion

We examined the effect of Oryzalose® in maintaining homeostasis with respect to its effect in inhibiting decline in immunity caused by stress and its effect in improving sleep disorders and bodily coldness, which are typical of decline in QOL, and its efficacy was recognized. It is often reported that being under stress causes decline in the autonomic nerves and that continually being under stress leads to decline in QOL and to the failure of homeostasis or, in other words, illness^{8, 9)}. In the past, people have visited medical institutions saying they feel under the weather or are not feeling well and test results do not show anything unusual and they are not treated. However, subjectively these people are clearly not healthy suggesting that some kind of biological function is impaired. Subjective poor health is a sign of failure of homeostasis and by perceiving this as a danger signal and consciously improving lifestyle, good health can be restored. The results of this study are extremely interesting, suggesting that Oryzalose® functions effectively during such stages, promoting good health and demonstrating the effect of preventing illness. Since foods began being recognized as functional, the effect of intake of tertiary function components has often been reported^{10, 11)}. The results of this study suggest that the intake of not only nutrients but also tertiary function components that are largely non-nutrients is effective for promoting the health of the elderly and persons forced to live under constant psychological stress and for increasing the healing power of patients being treated for illness. In the future, I would like to examine the relationship between such actions of Oryzalose® and preventing illness and increasing healthy life expectancy.

(0 to 3 min after cold loading)



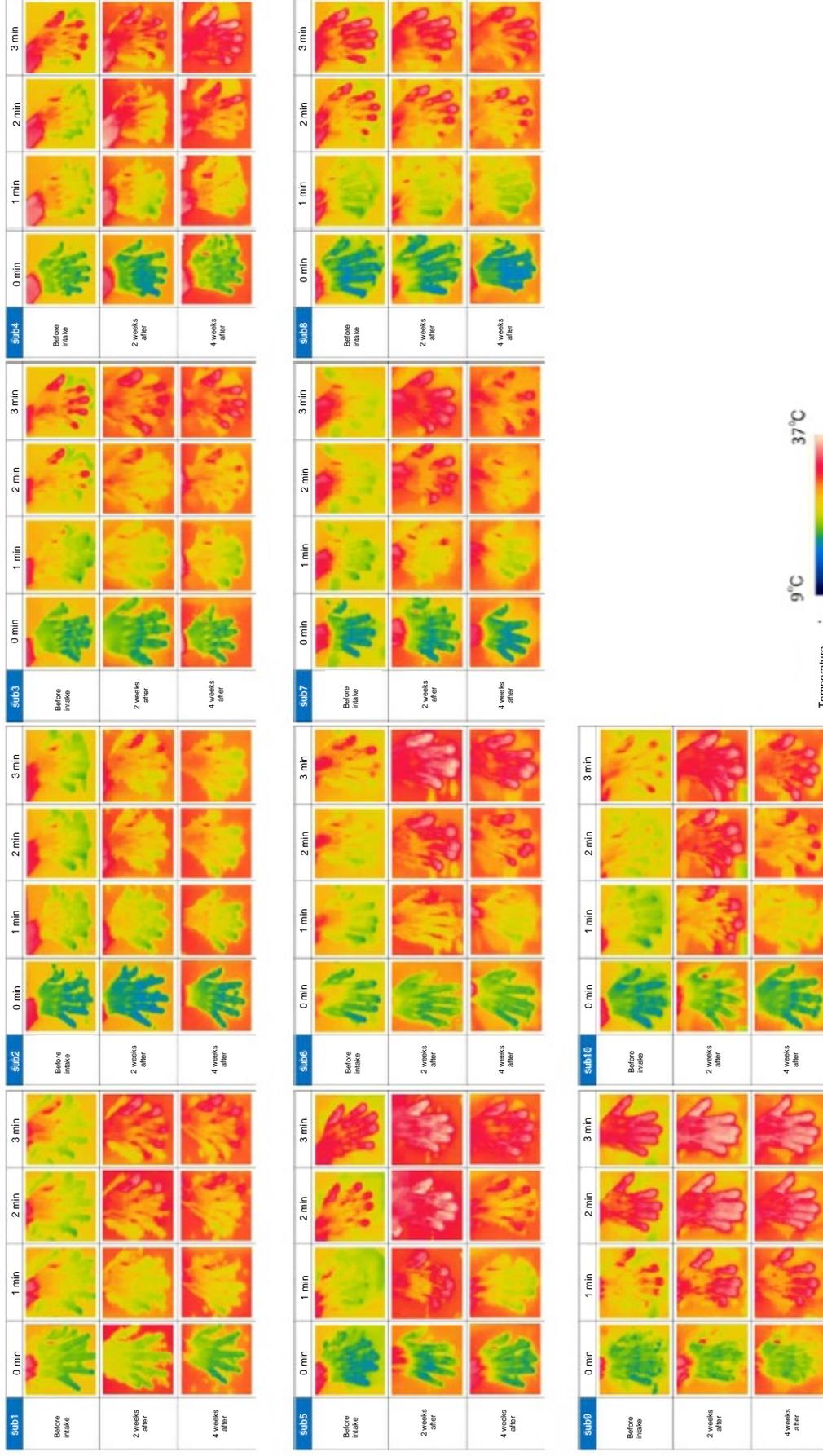


Figure 4. Changes in skin temperature of each monitor from 0 to 3 min before and after intake (thermography). Figure shows process of recovery in body temperature after cold loading (horizontal axis: time elapsed, vertical axis: intake period). The longer the intake period, the quicker the rise in body temperature. This finding is particularly noticeable at the finger tips.

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