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A Study on Supplement Containing Taheebo Polyphenol of a Randomized Placebo-controlled Trial Part 2:

Analysis of Improvement in Bodily Vigor and Alleviation of Temporal Feeling of Fatigue

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● Abstract

Objectives: The objective of this research was to investigate the effectiveness of daily ingestion of a Taheebo tablet, which contains Taheebo polyphenol, for the effect on bodily vigor and alleviation of temporal feeling of fatigue. On this study, we re-analyzed the data of the previous study, focusing on the bodily vigor and alleviation of temporal feeling of fatigue.
Methods: A randomized, placebo-controlled, double-blind study was conducted to verify the vigor level of the overall body and the alleviation of temporal fatigue. The SEIV (total of 40 items) score (subjective reporting) was tested as primary outcomes. And also as a secondary endpoint, blood and urine tests were evaluated for the assessment of product safety.
Results: From all of 42 applicants, 14 were eliminated due to not meeting inclusion criteria. The 28 subjects were randomly assigned to intervention groups and made a start with ingestion. Among 28 subjects, 5 were withdrawn due to personal reasons (work commitment or bodily discomfort), and the remaining 23 subjects completed the study. In the intergroup comparison of SEIV, 9 items out of 22 illustrated a significant difference after 12-weeks of ingestion.
Conclusion: The present results suggest that daily ingestion of Taheebo tablets including Taheebo polyphenol can improve human bodily vigor and alleviation of temporal feeling of fatigue.

Key words: Taheebo, Taheebo polyphenol, bodily vigor, fatigue, SEIV

1. INTRODUCTION

The current Japanese society is often expressed as a "stress-sick" society, both young and old are suffering from chronic tiredness which lasts for more than six months. According to an epidemiological survey conducted by the Ministry of Education, Culture, Sports, Science and Technology in 2004, more than sixty (60) percent of people feel fatigued, and among them more than half feel a certain level of chronic tiredness and have difficulty working in full play due to the decreased work capacity [1]. The feeling of fatigue or malaise is sensations we experience in everyday life. Although they do not show any noticeable symptoms, they include the circumstances such as "lacking energy", "being low on energy" and/or "feeling unmotivated", which all greatly affect the amount of everyday activity. The constitution of WHO defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [2]. By this definition, although having a feeling of fatigue chronologically does not directly relate to diseases, it is far from "good shape" at the same time.

Since ancient times, many people have employed various means to pursue healthy life, and one of the major means is to find out the plants with health benefits and drink them as a decoction. Taheebo, which has been used as a form of tea after brewing the inner bark has been drunk by the Indians of Argentina or Paraguay since the era of ancient Inca Empire. It has been loved by them as "gift from God" or "light of God" for curing diseases or maintaining health. Since Taheebo contains a lot of ingredients such as vitamins, minerals, proteins, fibers and carbohydrates in a balanced manner, it is often said that there is no single alternative plant that contains so many types of ingredients. Also, Taheebo contains many types of polyphenols with an anti-oxidative effect. As explained so far, by ingesting Taheebo we can take in various kinds of valuable constituents all at once, and this characteristic closely relates to the fact that the researchers have reported a lot of efficacies such as an antitumor effect [3], anti-inflammatory effect [4],

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inhabitation of obesity and fat accumulation [5] and/or immunostimulatory activity [6].

There are various views on the mechanism of fatigue, but it is basically believed that the feeling of fatigue occurs as a result of mixed factors. Now many people believe that it occurs when we lack the energy which is necessary for the recovery from oxidant stress [7]. Since Taheebo contains a lot of polyphenols with an anti-oxidative effect [8], it is speculated that Taheebo contributes to the prevention of oxidant stress and the alleviation of fatigue. However, there are not many reports which focus on anti-fatigue action of Taheebo. We previously reported the effectiveness of ingesting a Taheebo tablet on immunological function of healthy Japanese [9]. In the previous study, we set "the improvement of immune system" as a main outcome, and investigated the index of immune system called "SIV (Scoring of Immunological Vigor, which quantifies the immune strength using seven immune indexes)" and "SEIV (Self-Examination of Immunological Vigor, the subjective assessment of immunological vigor by Likert scale)". We concluded that the ingestion of the test product contributed to improving the immune strength. This study especially focuses on "the improvement of bodily vigor and alleviation of temporal feeling of fatigue", therefore extracted and studied the items directly related to the bodily vigor and feeling of fatigue, from the SEIV question items of the previous article. Since the items extracted from SEIV have similarities to those of POMS (Profile of mood states) which evaluates transient, yet definitive mood states from six criteria, we especially scrutinized the items related to "vigor" and "fatigue" among six criteria. Therefore, in this study, we reanalyzed the immunological test data, and illustrated the function of the test product for the improvement bodily vigor and alleviation of temporal feeling of fatigue using the immunological subjective assessment scales.

2. METHODS

2.1. Trial design

A randomized, placebo-controlled, double-blind study was conducted with the aid of a fund from TAHEEBO JAPAN CO., LTD. (Osaka) at two centers (OZ clinic, Tokyo, and JACTA, Tokyo). The study period was 12 weeks, from August 3rd to October 26th, 2015. This study was conducted in accordance with the ethical principles of the declaration of Helsinki. The study protocol was approved by the Institutional Review Board of Pharmaceutical Law Wisdoms (Tokyo). Written informed consent was obtained from all subjects.

The allocation of the test product to the subjects was carried out by the person in charge of allocation. The allocation list was sealed and strictly controlled in a safe deposit box of JACTA until the end of the study.

2.2. Subject

Healthy subjects participated in the present study. All of the subjects in this study were public volunteers who had enrolled in the monitor bank of CROee Inc. (Tokyo), recruited in July, 2015.

Table 1 Nutritional content of the sample per 100 g

Item	TNP	Placebo
Energy	404 kcal	321 kcal
Protein	1.3 g	0.8 g
Lipid	5.0 g	3.8 g
Ash	1.2 g	21.0 g
Carbohydrates	88.5 g	70.9 g
Salt equivalent	0.0605 mg	0.404 mg

2.2.1. Inclusion criteria

(1) Healthy Japanese men and women aged between 35 and 59 years with daily tiredness and fatigue;
(2) With relatively low self-examination of immunological vigor (SEIV, total of 40 items, not shown) [9] ≥ 90.

2.2.2. Exclusion criteria

(1) Previously suffered with malignant tumors, heat failure, or cardiac infarction;
(2) Under the care of a doctor for the treatment of chronic diseases such as atrial fibrillation, uneven heartbeat, rheumatism, diabetes, high blood pressure and diseases of the liver, kidney, cerebral system, circulatory system, and lipid metabolism;
(3) Taking medicines, including herbal medicines;
(4) Pregnant, nursing, or were likely to become pregnant during the trial;
(5) Judged to be unsuitable to participate in the test by the doctor responsible for the present study.

2.3. Randomization

Recruited subjects were 42 persons. Subjects who fulfilled eligibility criteria were 28 persons. The inclusion was judged by the principle investigator. All subjects were sequentially assigned based on a random number table to one of the masked products and randomized to group T (Test sample: 14) and group P (Placebo: 14). The allocation was pre-assigned on the basis of randomized numbers.

2.4. Description of test foods and blinding

The test food, "Taheebo NFD Premium" ("TNP") is a tablet containing Taheebo polyphenol. The amount of a daily intake is 6 tablets (1 tablet weighs 350 mg, therefore 6 tablets weigh 2.1 g). Placebo does not contain Taheebo polyphenol. **Table 1**. shows the nutritional content of the sample. Both tablets were indistinguishable in shape, color or taste. Tablets were managed by the identification symbol. All involved were blinded.

2.5. Experimental procedures

2.5.1. Experimental protocol

Subjects consumed 6 tablets of the supplement with hot or cold water every day for 12 weeks. Subjects were instructed as follows: to take the assigned foods as

Table 2　Schedule for the study.

Item \ Term	Screening	Pretrial test	Test period（12 w）
SEIV	●		●
Informed consent	●		
Selection and/or allocation	●		
Biochemical analysis of blood and urine		●	●
Ingestion of test foods			↔
Log			↔

● : Implementation
↔ : Daily practice during the test period

indicated; to maintain their usual lifestyles and habits; to avoid excessive amounts of food, drink, or alcohol; to maintain a daily record of lifestyle factors such as what they ate and a pedometer measurement during the test period; and to send the diary to the study coordinator every Friday by mobile email.

2.5.2. Outcome

The objective of this study was to verify immunological vigor of ingesting food containing Taheebo polyphenol. Bodily vigor and alleviation of temporal feeling of fatigue was set as the primary outcome. SEIV were used to evaluate that. SEIV is a self-examination of immunological vigor with Likert scales [10]. Blood biochemical and urine parameters were recorded to evaluate the safety of the test foods as the secondary outcome. These assessments were conducted upon entry into the study (pre-intervention) and after 12 weeks (post-intervention).

To evaluate the safety of the test foods, adverse events were collected by means of a written questionnaire during the study. According to the schedule shown in **Table 2**, we measured parameters on efficacy and safety.

2.6. Data analysis

The full analysis set principal was adopted in the present study and no sample size was used. All statistics were expressed as mean ± standard deviation (SD). For SEIV, intragroup comparisons were assessed using a Wilcoxon signed-rank test, and Mann-Whitney U test was used for intergroup of changes from the baseline. Regarding biochemical analyses of blood and urine, changes in the same group were assessed using paired t-test. Student's t-test was used for intergroup comparisons of changes from the baseline, and was used to compare subject's backgrounds between groups.

Multiplicity according to the occasions was not adjusted. Any subjects with missing values were eliminated from the analysis. Statistical analyses were performed using Statcel 4 (Yanai, 2015). The results were considered significant at the $< 5\%$ level in the two-sided test.

3. RESULTS

3.1. Participant demographics

From all of 42 applicants, 14 were eliminated according to the SEIV (total of 40 items) criteria (< 90). 28 subjects were randomly assigned to an intervention group and made a start with ingestion. 5 were withdrawn due to personal reasons and the remaining 23 subjects completed the study. These 5 subjects (all in the Placebo) were withdrawn for the following reasons: urgent work commitment (3 subjects); due to bodily discomfort (2 subjects). Thus, data obtained from the 23 subjects was used for the analysis of efficacy (**Figure 1**). There were no significant differences in the mean age, gender ratio or SEIV (total score of 21 items) between groups (**Table 3**).

3.2. SEIV

Table 4 shows the results of SEIV. After 12-weeks of ingestion, 8 items out of 23 illustrated a significant difference in intergroup comparison: 1, "Enjoyment of meal" ; 4," Wake up energetically without fatigue from the previous night" ; 5, "Feeling of fatigue is reduced by resting on weekends" ; 8, "Less frequency of stiff shoulder and lower back pain" ; 9, "Catching a cold" ; 11, "Less symptoms of stomatitis" ; 17, "Indifference to standing in the train" ; 21, "Want to be helpful to people and society." ; and 22, "Total score".

3.3. Blood and urine test

With respect to the blood test (data not shown), a significant difference was observed in Total Cholesterol, Potassium, Inorganic Phosphorus, Urea Nitrogen, Creatinine (Female) and Blood Sugar serum of TNP after 12-weeks of ingestion. The same difference was found in urinary specific gravity after 12-weeks of ingestion (data not shown). In either case, since the difference was minor one, the investigator judged it as the range of physiological variation (or clinically safe).

3.4. Adverse event

No adverse effects associated with the test product were observed in the course of the reporting.

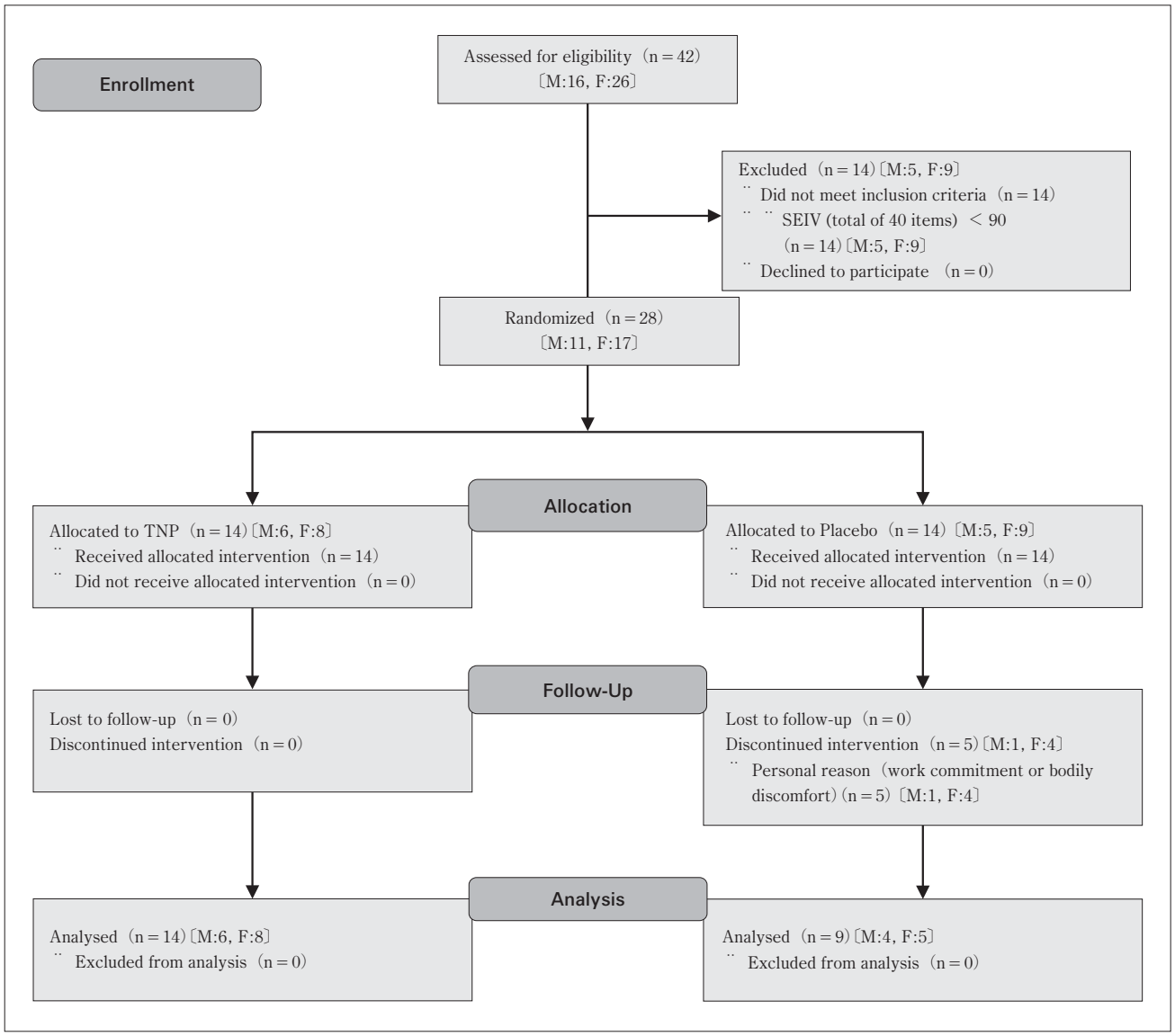

Figure 1 Flow diagram of subject disposition

Table 3 Subject demographics

Item	Unit	TNP	Placebo
Subjects	−	14	9
Male: female*	−	6 : 8	4 : 5
Age*	years	45.0 ± 4.6	47.8 ± 6.7
SEIV（total score of 21 items）*	score	63.6 ± 6.1	62.3 ± 3.8

mean ± SD

* No significant difference

4. DISCUSSION

We conducted a randomized, placebo-controlled, double-blind study to verify the effects of the test product containing Taheebo polyphenol among healthy Japanese. For this examination we used SEIV (Self-Examination of Immunological Vigor), which is an index for evaluating the bodily vigor and alleviation of temporal feeling of fatigue, in order to evaluate the vigor level of overall body and the alleviation of temporal fatigue. Since the items extracted from SEIV have similarities to those of POMS (Profile of Mood States), they should be suitable for the reasonably assessing the alleviation of fatigue. As the primary outcome, after 12-weeks of ingestion TNP showed a significant difference in 9 items and an improvement tendency in 3 items out of 22 items of

Table 4　SEIV

	Item	Time points	Scores [1]		P-value [2]
			TNP（n = 14）	Placebo（n = 9）	
1	Enjoyment of meal	Baseline	1.6 ± 0.5	1.3 ± 0.5	
		Week 12	1.1 ± 0.4 *	2.1 ± 0.8 *	
		Change	− 0.4 ± 0.5	0.8 ± 0.7	0.001 ##
2	Meal is often 3 times per day.	Baseline	2.0 ± 1.4	2.0 ± 1.5	
		Week 12	1.9 ± 1.3	1.2 ± 0.4	
		Change	− 0.1 ± 0.7	− 0.8 ± 1.6	0.585
3	Nutritional balance of the meal is a considerable point.	Baseline	2.6 ± 1.2	2.3 ± 1.3	
		Week 12	2.3 ± 1.1	1.9 ± 0.6	
		Change	− 0.3 ± 1.0	− 0.4 ± 1.1	0.925
4	Wake up energetically without fatigue from the previous night.	Baseline	3.5 ± 1.5	3.2 ± 1.3	
		Week 12	2.3 ± 0.8 **	3.8 ± 1.0	
		Change	− 1.2 ± 1.1	0.6 ± 0.9	0.001 ##
5	Feeling of fatigue is reduced resting on weekends.	Baseline	4.3 ± 0.8	2.7 ± 1.1	
		Week 12	2.4 ± 1.0 **	3.6 ± 1.0 *	
		Change	− 1.9 ± 1.2	0.9 ± 0.6	<0.001 ##
6	Going to bed before 12 pm	Baseline	3.6 ± 1.5	3.1 ± 1.4	
		Week 12	3.3 ± 1.4	2.2 ± 1.0 †	
		Change	− 0.4 ± 0.9	− 0.9 ± 1.2	0.345
7	Getting sufficient quantity of sleep.	Baseline	3.6 ± 0.9	2.8 ± 1.5	
		Week 12	2.9 ± 0.9 *	2.1 ± 1.1 †	
		Change	− 0.7 ± 1.1	− 0.7 ± 0.9	0.825
8	Less frequency of stiff shoulder and lower back pain	Baseline	3.9 ± 1.3	3.6 ± 1.3	
		Week 12	2.9 ± 1.5 *	4.0 ± 0.9	
		Change	− 1.0 ± 1.2	0.4 ± 0.7	0.012 #
9	Catching a cold.	Baseline	2.6 ± 1.1	3.3 ± 1.5	
		Week 12	1.7 ± 1.1 *	3.4 ± 1.4	
		Change	− 0.9 ± 1.0	0.1 ± 0.3	0.015 #
10	Less symptoms of gastro-intestinal problem	Baseline	2.2 ± 1.1	3.0 ± 1.5	
		Week 12	1.9 ± 1.0	3.1 ± 1.6	
		Change	− 0.4 ± 0.9	0.1 ± 0.3	0.257
11	Less symptoms of stomatitis	Baseline	2.2 ± 1.1	2.6 ± 1.1	
		Week 12	1.6 ± 0.6 *	3.0 ± 1.2	
		Change	− 0.6 ± 0.7	0.4 ± 1.0	0.015 #
12	Normal bowel movement	Baseline	2.2 ± 1.1	2.9 ± 1.4	
		Week 12	2.1 ± 1.1	3.2 ± 1.2	
		Change	− 0.1 ± 0.9	0.3 ± 0.5	0.156
13	Try to take the stairs.	Baseline	3.5 ± 1.1	3.7 ± 1.2	
		Week 12	2.7 ± 1.1 †	3.9 ± 0.9	
		Change	− 0.8 ± 1.4	0.2 ± 0.7	0.055 ‡
14	Try to walk instead of vehicles.	Baseline	2.5 ± 1.3	3.0 ± 1.4	
		Week 12	1.7 ± 0.8 †	3.1 ± 1.3	
		Change	− 0.8 ± 1.5	0.1 ± 0.9	0.156
15	Fast pace walk	Baseline	2.9 ± 1.4	3.0 ± 1.3	
		Week 12	2.3 ± 1.0 †	2.1 ± 1.3 †	
		Change	− 0.6 ± 1.2	− 0.9 ± 1.4	0.875
16	Indifference to walking	Baseline	2.8 ± 1.3	2.9 ± 1.3	
		Week 12	1.8 ± 0.6 *	2.4 ± 1.1	
		Change	− 1.0 ± 1.2	− 0.4 ± 1.0	0.166
17	Indifference to standing in the train	Baseline	3.4 ± 1.6	3.7 ± 1.0	
		Week 12	2.3 ± 1.1 *	3.6 ± 0.9	
		Change	− 1.1 ± 1.4	− 0.1 ± 0.3	0.047 #
18	Indifference to running when needed	Baseline	3.5 ± 1.1	3.3 ± 1.2	
		Week 12	2.4 ± 1.2 *	1.7 ± 0.9 *	
		Change	− 1.1 ± 1.5	− 1.7 ± 1.1	0.378
19	Have a hobby containing physical exercise.	Baseline	3.9 ± 1.6	4.0 ± 1.6	
		Week 12	3.4 ± 1.5	3.0 ± 1.0 †	
		Change	− 0.6 ± 1.6	− 1.0 ± 1.6	0.450
20	Satisfied with your daily job.	Baseline	3.4 ± 1.3	3.4 ± 1.0	
		Week 12	2.8 ± 1.1 †	2.0 ± 0.9 *	
		Change	− 0.6 ± 1.2	− 1.4 ± 0.9	0.115
21	Want to be helpful to people and society.	Baseline	3.4 ± 1.2	2.6 ± 1.1	
		Week 12	2.6 ± 1.1 †	2.9 ± 1.1	
		Change	− 0.7 ± 1.2	0.3 ± 0.5	0.023 #
22	Total score	Baseline	63.6 ± 6.1	62.3 ± 3.8	
		Week 12	48.1 ± 11.0 **	58.3 ± 4.7	
		Change	− 15.6 ± 8.8	− 4.0 ± 7.7	0.006 ##

Scores are expressed as the mean ± SD.
1) † $p < 0.1$, * $p < 0.05$, ** $p < 0.01$ against baseline.
2) ‡ $p < 0.1$, # $p < 0.05$, ## $p < 0.01$ between-group difference in change from baseline.

SEIV, compared to Placebo. At the same time, as the secondary outcome the observation of clinical findings such as medical interview, blood and urine test revealed no abnormal change had been triggered by the ingestion of test product.

Main findings

In this study, we evaluated the effect of the tablet containing Taheebo polyphenol for the bodily vigor and alleviation of temporal feeling of fatigue, by comparing scores of SEIV which enables us to assess the scores from a standpoint of immunology. SEIV is an indicator for evaluating the symptoms subjectively. In this study, a significant difference was observed in several items such as "Wake up energetically without fatigue from the previous night." (#4), "Feeling of fatigue is reduced resting on weekends." (#5), "Indifference to standing in the train" (#17), "Less frequency of stiff shoulder and lower back pain" (#8), "Less symptoms of stomatitis" (#11), "Catching a cold." (#9), "Want to be helpful to people and society." (#21), and "Enjoyment of meal" (#1). In addition, the total score (#22) of TNP showed a significant difference compared to the Placebo.

In this study we used the modified version of SEIV in which the investigator customized the test items of SEIV to meet the test objectives of evaluating the bodily vigor alleviation of temporal feeling of fatigue. In addition, many test items of SEIV resemble those of POMS (The Profile of Mood States) which is a relatively new psychological rating scale used to assess transient, distinct mood states; for example, the items such as #4, 5, 8, 9, 16, 18, 20 and 21, which are about "want to be helpful to people and society" or "without any fatigue". POMS measures six mood swings of "Tension or Anxiety", "Depression of Dejection", "Anger or Hostility", "Vigor or Activity", "Fatigue or Inertia", and "Confusion or Bewilderment"[11]. Among them, Vigor is especially defined as a physiological and psychological energy, and it is said it is able to be examined in this psychological test. In addition, Fatigue is defined as a period of extreme tiredness which can be caused by emotional strain, physical exertion, boredom, or a general lack of rest and/or sleep, and it can be accurately evaluated in this test. Therefore, it should be considered appropriate to evaluate the subjective symptoms of bodily vigor or alleviation of temporal feeling of fatigue by using SEIV, since it not only resembles to POMS but also enables to measure bodily vigor from a standpoint of immunology. SEIV is usually used for a self-assessment of autoimmunization[12]. The function of autoimmunization declines due to various stresses. While the external stimulation can be accepted in human body as long as the amount of the stimulation is within an acceptable level. Once it exceeds the acceptability limit it disturbs the homeostasis of the internal environment of a human. This disturbance creates the stresses, and they activate the immune system, accelerate the secretion of substances such as adrenalin or glucocorticoid, and decrease an immune reaction by inhibiting the function of lymphocytes[13].

There are different types of fatigue such as physical fatigue, mental fatigue or brain fatigue. It is believed that they are caused by the active oxygen generated from a variety of stress such as mental stress derived from human relationship, body stress due to hard labor, physical stress like ultraviolet, chemical stress from chemical substances, and/or biological stress caused by viruses or bacteria[14)15)]. These stresses stimulate the secretion of the stress hormone such as adrenalin or glucocorticoid. Glucocorticoid tries to cope with the stresses by the increase in glucose metabolism or the exhibition of an anti-inflammatory effect[16)17)], whereas adrenalin tries by working on the sympathetic nervous tone[18]. Also, the super secretion of other hormones or substances occurs, and it results in the reduction in activity of the immune system such as T-cells, B-cells, NK-cells, lymphocyte cells or cytokine, the deterioration of cellular function, the increase in oxygen consumption, the decline in brain function due to inhibition of secretion of neurotransmitter serotonin, or the abnormity of incretion or metabolism[15)19)-22)]. The process described so far is regarded as the mechanism of fatigue. The fact that the scores of SEIV (as a self-assessment of autoimmunization) are high can be explained that the body increased the level of bodily vigor, since the alleviation of temporal fatigue indicates the condition of the vigor. Taheebo (the test product) contains plenty of polyphenols of Phenylethanoid Glycosides which contains hydroxyl group or methoxy group[8]. Phenylethanoid Glycosides has a very strong antioxidant activity, and possesses properties such as immunomodulatory effects[23)], neuroprotective property, anti-inflammatory and/or anticancer effect[24)]. Since the test product contains the powder of Taheebo bark and the extract directly from the bark, it is highly possible that it contained plentiful Taheebo polyphenols centering on acteoside. As described above, the main cause of fatigue or loss of bodily vigor is the active oxygen derived from stresses, and the Taheebo polyphenols (such as acteoside) contributes to removing or detoxifying it[25)26)].

It is considered that the results such as "Wake up energetically without fatigue from the previous night." (#4) and "Feeling of fatigue is reduced resting on weekends." (#5), which showed a significant difference, were produced thanks to the mechanism described above. Also, the moods such as "Enjoyment of meal" (#1), or "Indifference to standing in the train" (#17) may represent the expression of bodily vigor as a result of an anti-oxidative effect of Taheebo polyphenol. In addition, as for the items such as "Less frequency of stiff shoulder and lower back pain" (#8) and "Less symptoms of stomatitis (#11)" , it is speculated that the cells have inflammation due to the active oxygen. Since it is

reported that the Tabeebo polyphenol has an anti-inflammatory effect[4] as it downregulates the production of various chemical mediators of inflammation, the oral administration of Taheebo polyphenol performed the anti-inflammatory effect. "Catching a cold" (#9) is considered to be produced as the immune system was not inhibited and worked normally. Moreover, it is considered that the test data of "Want to be helpful to people and society" (#21) was yielded as a result of the ingestion of the test product which had improved the vigor of body, made the test subject more active and eventually contributed to the improvement of QOL among them.

Therefore in this study, the test group could stop the generation of active oxygen, inhibit the decrease of immunity and recover from the disorder of the body after ingesting the test product containing plenty of Taheebo polyphenol; in other words, it can be said that it could recover bodily vigor and alleviation of temporal feeling of fatigue.

Secondary Findings

In this study we examined the safety of the test product by blood test and urine test. In the blood test, a significant difference was observed in the changes of total cholesterol, potassium, phosphorus, urea nitrogen, creatinine, and serum glucose. On the other hand, in the urine test we observed significant difference in the change of urine specific gravity. In either case, since the difference was within a range of baseline and a shade of difference, the investigator judged it as the range of physiological variation (or clinically safe).

During the study, five (5) subjects stopped the test due to personal reasons such as work or bodily discomfort, and they were not related to the adverse event caused by the test product. Therefore, based upon the medical interview, blood test and urine test, we observed no harmful influence against biochemical and/or physiological matters of the subjects. These results indicated the safety of the ingestion of the test product for the 12-weeks test period.

General information

The product used in this test is the tablet-type food which contains the extract from Taheebo tea and the ingredients from bark of Taheebo. The ingestion of this type of "simple and convenient" food can omit the process such as decocting of the bark or boiling of water; therefore it contributes to the daily habituation of ingestion. It is reported that chronic fatigue, which is triggered as a result of non-recovery from fatigue for a long time, leads to a decrease of more than 50% of daily activity[27]. In the modern "stress-sick" society of Japan, people tend to suffer from irregular life styles, and these styles accumulate their fatigue, both physically and psychologically. Therefore, if they can recover from the fatigue and strengthen their bodily vigor just by the everyday ingestion of tablet-type foods, it contributes to the increase of the volume of activity and the increase in healthy population, the improvement of QOL and the enlivenment of social life.

Limitations

In this study we used SEIV, a type of immunological indicator, for evaluating the level of bodily vigor and the alleviation of a temporal feeling of fatigue. Since the subjective impression plays an important role in the feeling of bodily vigor and alleviation of temporal feeling of fatigue, the examination of subjective symptoms is usually applied for evaluating these feelings[28)29)]. Also, POMS (Profile of Mood States) is often used as an indicator of mental fatigue since it is aimed at evaluating the effect on humans from subjective aspects such as mood or emotion[30)31)]. Now the relationship between POMS and biomarker is being researched[32)], and therefore it is highly creditworthy. SEIV, on the other hand, is a test developed by Hirokawa and colleagues for assessing the bodily vigor and alleviation of temporal feeling of fatigue from immunological index, and its question items have a high similarity to those of POMS. Therefore, it is considered as a relevant measure for evaluating a feeling of fatigue, there is no test evaluating the definite resemblance between them, though. In addition, the feeling of fatigue is often quantified by various biomarkers such as Heart Rate Variability[33)], Biogenic Amines[34)] or blood lactate level[35)]. Theoretically, SEIV used in this study is considered relevant for evaluating the alleviation of a temporal feeling of fatigue, but if we also utilize the other measures such as the quantification of fatigue level by the biomarkers explained above or the investigation of other subjective symptom at the same time and compare all the test results, it is highly possible to obtain more objective and versatile outcomes. This point is subject for further scrutiny.

5. CONCLUSION

In conclusion, we found out that the ingestion of the tablet containing Taheebo polyphenol for 12 weeks resulted in the improvement of human bodily vigor and alleviation of temporal feeling of fatigue. In addition, no safety-related matter occurred during 12-weeks test period.

CONFLICT OF INTEREST

All parts of this study were funded by TAHEEBO JAPAN CO., LTD. All authors state that the study was conducted in the absence of any other relationships that could be interpreted as a conflict of interest.

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