EFFICACY OF CONSECUTIVE INGESTION OF TAHEEBO TEA FOR IMMUNOLOGICAL VIGOR

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Abstract

Background: Taheebo, the purple inner bark of *Tabebuia avellanedae* which is found in tropical rain forests, has being drunk as tea for the health. It seemed to have some effects for immunological functions. Thus, the present study examined the efficacy of Taheebo tea on human body.

Methods: A 12-week, double-blind, randomized, placebo-controlled study was conducted.

The criteria of subjects is SEIV (subjective examination) ≥ 90, and $18 <$ SIV (combination of the quantification of T cells, naive T cells, $CD8^+CD28^+$ T cells, B cells, and NK cells, the CD4/CD8 T cell ratio, and the naive/memory T cell ratio). By this criteria, relatively low in their immunological vigor can be selected. 34 subjects were randomized. The SIV score was measured as primary outcomes. The other outcomes were SEIV and antioxidant test.

Results: 24 subjects were in efficacy analysis. In SIV the significant difference was not found in the intergroup comparison of 24 subjects, but was observed in the intergroup comparison of the SIV ≥ 16.

Moreover, the degrees of improvement in the relieving fatigue-related QOL in the Taheebo group were significantly higher than the placebo group.

Conclusion: There results suggest that decrease of immunological vigor was suppressed by the ingestion of Taheebo tea in the group with a relatively low initial degree of immunological vigor.

Key words: Taheebo, immunological vigor, fatigue relief

INTRODUCTION

Tabebuia avellanedae Lorentz ex Griseb is a Bignoniaceae tree found in tropical rain forests in the South America Brazil's Amazon basin. Taheebo, the purple inner bark of *Tabebuia avellanedae*, has being drunk as tea for a recovery from illness and for the maintenance of health for more than 1,500 years. In the current studies, various animal models were used to demonstrate analgesic and anti-inflammatory effects,[1)2)] antidepressant-like action,[3)] and anti-obesity effect[4)] of Taheebo. Although it seemed some of these effects are related to immune system functions, Taheebo effects on those functions have not been studied.

In the present study, we targeted to reveal that Taheebo can improve immune system functions in a wide range of human subjects whose immune functions are poorer than expected.

Kaminogawa et al, have concluded that the improvement of immune function by food ingredients can be evaluated by measuring the general biomarker for innate immunity (natural killer cells and phagocytic cells such as neutrophils and macrophages) and adaptive immunity (immune cells such as T cells, B cells, and antigen presenting cells).[5)]

To measure the comprehensive immunological strength, the scoring of immunological vigor (SIV) was developed, which combines the quantification of T cells, naive T cells, $CD8^+CD28^+$ T cells, B cells, and NK cells, the CD4/CD8 T cell ratio, and the naive/memory T cell ratio.[6)7)]

In the study, a placebo-controlled double-blind trial was conducted to investigate the efficacy of Taheebo on the human immunological status by measuring the SIV, antioxidant test and subjective symptom parameters.

Materials and Methods

Subjects: This study received the approval of the Institutional Review Board of LLP Pharmaceutical Law Wisdoms (Tokyo) in accordance with the ethical standards established in the Helsinki declaration, and informed consent was obtained from all subjects. All of the business side was entrusted to JACTA (Japan Clinical Trial Association).

Candidate subjects were male and female volunteers aged 30 to 59 years, who were recruited by advertisement. They were selected according to the following criteria:

1. Healthy Japanese men and women aged 30 to 59 years with daily tiredness and fatigue;

2. With a relatively low Self-examination of immunological vigor (SEIV),[8)] 90 and over.

Table 1 Components and nutritional constituents of the test samples

Taheebo		Placebo	
Tabebuia avellanedae	100%	Calcium powder	100%

nutritional constituents / 100 g

	Taheebo	Placebo
energy	358 kcal	20 kcal
water	4.1 g	1.0 g
protein	2.9 g	0.6 g
fat	2.0 g	0.3 g
ash	8.8 g	94.5 g
carbo	82.2 g	3.6 g
Na	0.0032 g	1.32 g
Cal	3.29 g	36.9 g
K	0.188 g	0.059 g
Mag	0.0535 g	0.0843 g
Cu	0.28 mg	0.02 mg
Zn	0.77 mg	0.12 mg

The exclusion criteria is as follows:

1. With a relatively high SIV, 18 and over;
2. Previously suffered malignant tumors, heart failure, or cardiac infarction;
3. 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;
4. Taking medicines, including herbal medicines;
5. With pollen allergy;
6. Pregnant, nursing, or were likely to become pregnant during the trial;
7. Judged to be unsuitable to participate in the test by the doctor responsible for the present study.

The subjects were instructed as follows: to take the assigned items as indicated; to maintain their usual lifestyles and habits, avoiding too much food, drink, or alcohol; to avoid excessive exercise; to keep a daily record that included the intake of the assigned item (or not) and lifestyle factors during the test period, and to send the diary by mail to the study coordinator every 7 days; and to contact Japan Clinical Trial Association if they felt unwell.

Test foods: 'Taheebo NFD Marugoto' was prepared by TAHEEBO JAPAN CO., LTD. Calcium powder was used as the placebo. The nutritional constituents of the test samples are shown in **Table 1**.

Study design: This study was a randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy, along with the safety, of Taheebo ingestion on human immunity. The study was performed from November 2014 to February 2015. SIV, antioxidant test, SEIV, blood pressure, biochemical analysis of blood and urine was done. The analysis of the immune cells in the peripheral blood included the quantification of T cells, naive T cells, $CD8^+CD28^+$ T cells, B cells, and NK cells, the CD4/CD8 T cell ratio, and the naive/memory T cell ratio.

The comprehensive immunological status of each individual was measured with the SIV method. The score is calculated as follows. First, the numbers of T cells, $CD8^+CD28^+$ T cells, naive T cells, B cells, and NK cells, the CD4/CD8 T cell ratio, and the naive/memory T-cell ratio are each ranked on three levels: 1, needs improvement; 2, needs observation; and 3, safe. The seven scores are then summed to obtain the SIV, in a range of 7-21, which represents the vigor of the immune system from low to high.[6)7)]

Moreover, the SIV was evaluated into two groups according to the SIV level; namely, the SIV $\geq$ 16, and the SIV $\leq$ 15 group to evaluate the correlation of the efficacy with the SIV.

Antioxidant status was evaluated by the d-ROMs and BAP of the blood.

Subjective symptoms were measured by SEIV with Likert scales in the range of 1-5.

Regarding the analysis of efficacy, the criteria of exclusion is set as follows:

(i) Those who consumed less than 80% of the expected dose;
(ii) Those who did not adequately record;
(iii) Those who fell under the exclusion criteria after the enrollment;
(iv) Those who did not follow restrictions of the subject.

Statistical analysis: Data were expressed as Mean ± SD. For SIV,other immunological parameters, antioxidant and blood pressure, the changes from the baseline in the same group were assessed using paired t-test. And in the intergroup comparison, after confirmation if the changes from the baseline after the ingestion for 12 weeks were within normal distribution and equal variances, Student's t-test or Mann-Whitney U test were conducted. For SEIV, the changes from the baseline in the same group were assessed using Wilcoxon signed-rank test, and in the intergroup comparison, Mann-Whitney U test was used instead. For biochemical blood and urine analyses, the changes from the baseline in the same group were assessed using paired t-test (if $N < 10$, Wilcoxon signed-rank test was used instead), and in the intergroup comparison, the Student's t-test was conducted. For assessment of the subjects background in the intergroup comparison, Student's t-test was conducted.

The statistical analyses were performed with Statcel 3 (Yanai, 2011). $p < 0.05$ was considered significant.

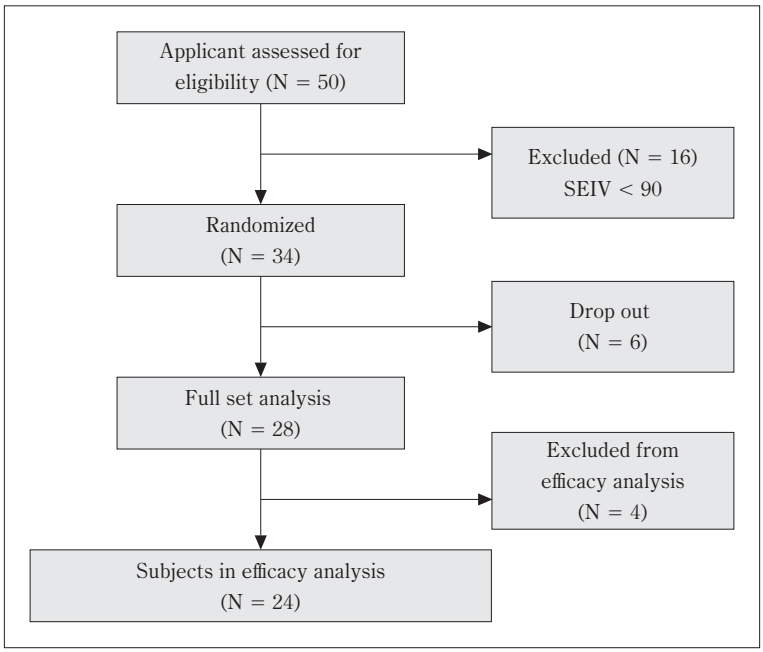

Fig. 1

Table 2　Characteristics of the subjects

	Unit	Taheebo	Placebo
Subjects (male : female)	—	11 (1 : 10)	13 (4 : 9)
Age (Mean ± SD)	y	46.2 ± 7.4	45.3 ± 6.1

RESULTS

Of 50 applicants for this study, 16 were excluded for various reasons. Overall, 34 applicants were randomly assigned to the interventions, and 6 dropped out of this study mainly due to personal reasons. Consequently, 28 subjects, of whom 13 received Taheebo and 15 received the placebo, completed the trial. Out of 28 subjects, 4 revealed to fall under the exclusion criteria for evaluation of efficacy as described in "study design". Thus, data obtained with 24 subjects were used for the analysis of efficacy (**Fig. 1**). There were no significant differences in the mean age between the groups (**Table 2**).

The results of the statistical analysis of the SIV, and other immunological parameters are shown in **Table 3**.

The SIV change in the SIV ≥ 16 group was found significantly after the ingestion of Taheebo for 12 weeks compared with that of the placebo group ($p = 0.03$) (**Table 4**).

There could not be found the change in the antioxidant status (Data not shown).

In the analysis of SEIV, a number of significant differences were observed between both groups, in the relieving fatigue QOL (Feeling of fatigue is removed by resting on weekends; $p = 0.024$, Going to bed before 12 pm; $p = 0.025$, Rarely catch a cold; $p = 0.032$, Try to take the stairs; $p = 0.018$, Never mined standing in the train; $p = 0.049$, Have hobby, not related with your job; $p = 0.016$) (**Table 5**).

For blood pressure, the SBP in Taheebo group was significantly lower versus placebo group, at 12 weeks. The DBP in Taheebo group was significantly lower versus placebo group, at 12 weeks (**Table 6**).

No severe changes were detected on the biochemical analysis of the blood.

In the urine analysis, no severe changes attributable to Taheebo ingestion were detected. No adverse effects attributable to Taheebo ingestion were observed.

DISCUSSION

The immune system functions can be ascribed to two different systems, humoral immunity and cellular immunity. Cellular immunity, T-cell-mediated, is involved in transplantation immunology and tumor immunology rather than just the removal of virus-infected cells.

On the other hand, anti-inflammatory effects of the extract from Taheebo[9)10)] have been reported, and are actually used in clinical practice.[11)] In particular, there is a report saying that beta-Lpachone from Taheebo may be effective in the treatment autoimmune encephalomyelitis modulating T-cell phenotype.[12)]

Table 3 All subject

Item	Unit	Group	Baseline	Post-intervention	Between-group difference (p-value)
SIV	—	Taheebo Placebo	15.6 ± 1.4 15.2 ± 1.0	15.0 ± 2.3 14.2 ± 1.0	0.548
T cell	/μl	Taheebo Placebo	1305.6 ± 429.0 1243.2 ± 289.9	1104.4 ± 398.0 1094.5 ± 310.0	0.140
$CD8^+CD28^+$ T cell	/μl	Taheebo Placebo	182.0 ± 70.5 203.8 ± 60.5	159.9 ± 84.8 174.2 ± 58.2	0.715
CD4/CD8 T cell ratio	ratio	Taheebo Placebo	3.5 ± 2.3 2.7 ± 1.0	3.5 ± 2.2 2.7 ± 1.1	0.777
Naive T cell	/μl	Taheebo Placebo	396.0 ± 275.1 244.5 ± 96.4	319.8 ± 258.9 181.4 ± 81.8	0.434
Naive/memory T cell ratio	ratio	Taheebo Placebo	0.8 ± 0.5 0.5 ± 0.2	0.7 ± 0.5 0.4 ± 0.2	0.907
NK cell	/μl	Taheebo Placebo	177.3 ± 65.3 269.3 ± 157.7	159.5 ± 68.3 234.1 ± 127.3	0.654
B cell	/μl	Taheebo Placebo	270.5 ± 171.0 211.2 ± 118.3	218.5 ± 131.8 165.2 ± 72.8	0.861

Taheebo N = 11, Placebo N = 13, Mean ± SD

against baseline by paired t-test

between-group differences from baseline by Student's t-test or Mann-Whitney U test

Table 4 SIV ≥ 16

Item	Unit	Group	Baseline	Post-intervention	Between-group difference (p-value)
SIV	—	Taheebo Placebo	16.7 ± 0.5 16.5 ± 0.6	16.7 ± 1.4 14.3 ± 1.0	$0.029^{\#}$
T cell	/μl	Taheebo Placebo	1526.0 ± 293.8 1482.5 ± 239.3	1327.2 ± 289.6 1186.5 ± 423.1	0.670
$CD8^+CD28^+$ T cell	/μl	Taheebo Placebo	179.8 ± 47.1 211.0 ± 89.6	172.2 ± 77.1 151.3 ± 69.5	0.242
CD4/CD8 T cell ratio	ratio	Taheebo Placebo	4.4 ± 2.7 2.7 ± 1.5	4.0 ± 2.8 2.9 ± 1.6	0.136
Naive T cell	/μl	Taheebo Placebo	561.5 ± 260.9 287.0 ± 78.2	478.5 ± 253.6 209.5 ± 44.5	0.522
Naive/memory T cell ratio	ratio	Taheebo Placebo	1.1 ± 0.5 0.4 ± 0.1	1.0 ± 0.5 0.4 ± 0.1	0.670
NK cell	/μl	Taheebo Placebo	166.3 ± 63.6 203.5 ± 85.4	173.3 ± 80.9 185.0 ± 95.3	$0.088^{\ddagger}$
B cell	/μl	Taheebo Placebo	321.5 ± 187.0 262.0 ± 172.0	273.0 ± 147.7 155.5 ± 61.4	0.832

Taheebo N = 6, Placebo N = 4, Mean ± SD

against baseline by paired t-test

$^{\ddagger}p < 0.1$, $^{\#}p < 0.05$ between-group differences from baseline by Student's t-test or Mann-Whitney U test

Table 5　SEIV

Item	Group	Baseline	Post-intervention
Meal is enjoyable	Taheebo	1.6 ± 0.7	1.0 ± 0.0*
	Placebo	1.8 ± 0.7	1.4 ± 0.5 †
Meal is mostly 3 times per day	Taheebo	2.2 ± 1.5	1.7 ± 1.2
	Placebo	2.0 ± 1.1	1.5 ± 1.0*
Nutritional balance of the meal is a consideration point	Taheebo	2.3 ± 0.9	2.0 ± 1.0
	Placebo	2.5 ± 1.0	2.2 ± 0.7
Eat more meat than fish.	Taheebo	2.9 ± 1.1	2.9 ± 1.1
	Placebo	3.6 ± 0.8	3.8 ± 0.6
Meal is low in salt	Taheebo	2.3 ± 1.0	2.2 ± 0.9
	Placebo	2.6 ± 1.2	2.9 ± 0.9
Eat moderately	Taheebo	2.9 ± 1.1	2.5 ± 1.0
	Placebo	2.6 ± 1.0	2.6 ± 1.0
Eat more vegetables.	Taheebo	1.9 ± 0.9	1.7 ± 0.8
	Placebo	1.9 ± 0.9	1.8 ± 0.8
Limit intake of animal fat.	Taheebo	2.8 ± 1.1	2.4 ± 0.7
	Placebo	2.8 ± 0.9	2.6 ± 1.0
No food before bedtime.	Taheebo	2.7 ± 1.0	2.4 ± 1.1
	Placebo	3.0 ± 1.2	2.7 ± 1.5
No alcohol drinking.	Taheebo	2.7 ± 1.3	2.6 ± 1.7
	Placebo	2.7 ± 1.5	2.9 ± 1.6
Amount of drinking comparable to the standard quantity beer < 500 ml, or wine < 180 ml, or sake < 180 ml, or whiskey < 50 ml	Taheebo	1.7 ± 0.5	1.6 ± 1.2
	Placebo	2.2 ± 1.3	2.3 ± 1.8
Wake up easily in the morning	Taheebo	3.9 ± 0.8	2.7 ± 0.8*
	Placebo	4.2 ± 1.1	3.8 ± 1.1
Feeling of fatigue is removed by resting on weekends.	Taheebo	3.8 ± 1.2	2.2 ± 0.8* ┐#
	Placebo	3.8 ± 0.9	3.5 ± 1.0 ┘
Going to bed before 12 pm.	Taheebo	3.7 ± 1.3	2.9 ± 1.3 † ┐#
	Placebo	2.9 ± 1.5	3.4 ± 1.4 ┘
Get sufficient hours of sleep.	Taheebo	3.3 ± 1.3	2.5 ± 0.7
	Placebo	3.5 ± 1.1	3.1 ± 1.1
No smoking	Taheebo	1.0 ± 0.0	1.0 ± 0.0
	Placebo	1.5 ± 1.2	1.7 ± 1.4
Neither shoulder stiffness nor back problem	Taheebo	4.0 ± 1.0	3.0 ± 1.2*
	Placebo	4.0 ± 1.2	3.7 ± 1.0
Rarely catch a cold	Taheebo	3.2 ± 1.0	1.8 ± 0.9* ┐#
	Placebo	2.8 ± 1.2	2.6 ± 1.0 ┘
Rarely suffer from gastro-intestinal problem.	Taheebo	2.7 ± 1.2	1.6 ± 1.0*
	Placebo	3.0 ± 1.0	2.6 ± 1.0*
Rarely suffer from stomatitis	Taheebo	2.7 ± 1.4	1.6 ± 0.8* ┐‡
	Placebo	2.7 ± 1.2	1.2 ± 0.8 ┘
No record of the following diseases. Diabetes mellitus, Liver disease, Kidney disease, Hypertension, Hyperlipidemia, Cancer, Heart disease, Autoimmune disease, Depression	Taheebo	1.2 ± 0.4	1.0 ± 0.0
	Placebo	1.2 ± 0.8	1.2 ± 0.8
BMI < 25　BMI = BW{Kg}/(BL{m}x BL{m})	Taheebo	1.5 ± 1.2	1.1 ± 0.3
	Placebo	1.3 ± 0.9	1.2 ± 0.6
Have normal bowel movement	Taheebo	2.5 ± 1.0	2.6 ± 1.3
	Placebo	2.4 ± 1.1	2.0 ± 1.0
Try to take the stairs	Taheebo	3.3 ± 1.2	2.5 ± 1.0* ┐#
	Placebo	2.5 ± 1.3	2.7 ± 1.1 ┘
Walk up the escalator	Taheebo	2.4 ± 1.1	2.0 ± 0.9
	Placebo	2.1 ± 1.1	2.2 ± 1.1
Walk fast	Taheebo	2.5 ± 1.1	2.1 ± 1.1*
	Placebo	2.6 ± 1.0	2.2 ± 0.7 †
Never mind walking	Taheebo	2.6 ± 1.1	1.6 ± 0.7*
	Placebo	2.7 ± 1.0	2.2 ± 0.8*
Never mind standing in the train	Taheebo	3.4 ± 1.0	2.3 ± 1.3* ┐#
	Placebo	3.2 ± 0.8	3.0 ± 0.9 ┘
Use pedometer	Taheebo	3.4 ± 1.9	1.5 ± 1.3*
	Placebo	2.8 ± 1.7	2.2 ± 1.7
Never mind running when needed	Taheebo	2.9 ± 1.0	2.2 ± 1.2 †
	Placebo	3.1 ± 1.2	2.8 ± 1.2
Have a hobby of physical exercise.	Taheebo	3.3 ± 1.6	3.0 ± 1.5
	Placebo	2.8 ± 1.5	2.9 ± 1.5
Less distress/worry than usual	Taheebo	3.9 ± 0.9	3.1 ± 0.5 †
	Placebo	4.0 ± 0.8	4.0 ± 0.8
Rarely sticking to something and feeling nervous	Taheebo	3.6 ± 0.8	2.8 ± 0.8*
	Placebo	3.4 ± 1.0	3.2 ± 0.8
Enjoy talking with families and friends	Taheebo	2.3 ± 0.8	1.8 ± 0.8 †
	Placebo	2.1 ± 0.8	1.8 ± 0.7 †
Have a friend(s) listening to your complaints	Taheebo	2.4 ± 0.8	2.0 ± 0.9
	Placebo	2.5 ± 1.1	1.9 ± 1.0*
Satisfied with your daily job.	Taheebo	3.2 ± 0.8	2.5 ± 1.2*
	Placebo	3.2 ± 1.0	2.8 ± 0.9
Have a hope in the future.	Taheebo	2.7 ± 0.9	2.5 ± 1.1
	Placebo	3.2 ± 1.0	2.9 ± 0.8
Your job is beneficial for others and society.	Taheebo	2.9 ± 0.7	2.5 ± 0.7*
	Placebo	3.0 ± 0.7	2.8 ± 0.7
Have hobby, not related with your job.	Taheebo	2.5 ± 1.2	1.8 ± 1.0* ┐#
	Placebo	2.2 ± 1.2	2.3 ± 1.2 ┘
Most of daily actions, beside job, are decided by yourself.	Taheebo	3.2 ± 1.2	2.6 ± 1.2
	Placebo	3.0 ± 1.4	2.9 ± 1.3

Unit : Point
Taheebo N = 11,　Placebo N = 13,　Mean ± SD
† $p < 0.1$, * $p < 0.05$ against baseline by Wilcoxon signed-rank test
‡ $p < 0.1$, # $p < 0.05$ between-group differences from baseline by Mann-Whitney U test

Table 6 Blood Pressure

Item	Unit	Group	Baseline	Post-intervention	Between-group difference (p-value)
SBP	mmHg	Taheebo Placebo	122.2 ± 18.2 113.5 ± 10.5	113.5 ± 17.2* 116.5 ± 13.7	0.039#
DBP	mmHg	Taheebo Placebo	80.0 ± 11.6 70.6 ± 10.0	76.0 ± 12.7 74.0 ± 12.3	0.041#

Taheebo N = 11, Placebo N = 13, Mean ± SD

*$p < 0.05$ against baseline by paired t-test

#$p < 0.05$ between-group differences from baseline by Student's t-test or Mann-Whitney U test

This study was conducted during winter time. Due to severe circumstances, many subjects decreased their SIV.

A placebo-controlled double-blind trial revealed that the ingestion of Taheebo for 12 weeks prevented the decrease of the SIV significantly, versus the placebo group in the level of SIV 16 and 17.

To investigate the efficacy of Taheebo on health, we measured health-related QOL using a self-rating questionnaire.

The degrees of improvement in the relieving fatigue-related QOL were higher from 12 weeks in the Taheebo group than the placebo group.

Also Taheebo group was more significantly improved in blood pressure than the placebo. Meanwhile, no change was found in the antioxidant effect. That is thought to be due to mistreatment of blood after the drawing blood.

These results suggests that Taheebo can prevent the decrease of the comprehensive immunological strength and enhance fatigue relieving.

CONCLUSION

The efficacy of consecutive ingestion Taheebo tea for immunological vigor was evaluated in relatively low immunological vigor subjects. The intervention was conducted in winter.

The results suggest that the consecutive Taheebo ingestion may prevent the decrease of immunological vigor in a little bit low immunological vigor subjects and improve relieving fatigue.

In addition, no adverse events were observed, indicating that Taheebo tea is a safe and useful food.

CONFLICT OF INTEREST

The authors state no conflicts of interest.

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