Research Article Open Access

Effects of consuming S-allyl-L-cysteine enriched garlic extract on sleep quality in Japanese adults: A randomized, double-blind, placebo-controlled, parallel-group comparative study

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Submission Date: October 31st, 2024, **Acceptance Date:** January 16th, 2025, **Publication Date:** January 24th, 2025

Please cite this article as: Hideshima W., Suzuki N., Takara T., Maru I. Effects of consuming S-allyl-L-cysteine enriched garlic extract on sleep quality in Japanese adults: A randomized, double-blind, placebo-controlled, parallel-group comparative study. *Functional Foods in Health and Disease* 2025; 15(1): 108-128. DOI: https://doi.org/10.31989/ffhd.v15i1.1493

ABSTRACT

Introduction: Sleep promotes well-being, which includes physical and mental health, but many people suffer from sleep deprivation. One of the functional components of garlic, S-allyl-L-cysteine (SAC), can reportedly improve mental fatigue and is expected to regulate the autonomic nervous system and improve sleep quality. This study investigated the effects of SAC-enriched garlic extract intake on sleep quality in healthy Japanese adults.

Methods: This was a single center, stratified (male and female with balanced randomization [1:1]), double-blind, placebo-controlled, parallel-group study conducted from September 12, 2023, to February 25, 2024. Participants consumed either the SAC-enriched garlic extract tablet (2 mg/day as SAC) or placebo (22 participants per group) for 12 weeks. The assessment items included the Oguri-Shirakawa-Azumi sleep inventory middle-aged version (OSA-MA), the Japanese version of the Pittsburgh Sleep Quality Index (PSQI-J), and St. Mary's Hospital sleep questionnaire (SMH). The primary outcome was the initiation and maintenance of sleep as measured by the OSA-MA after the 12-week intervention.

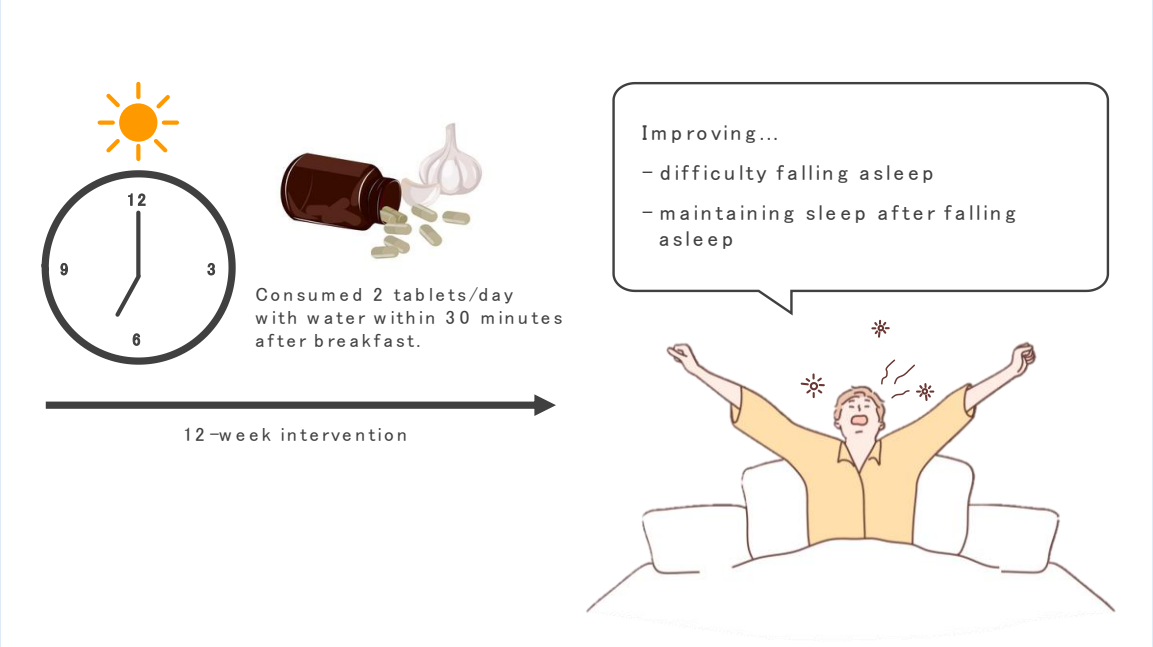
Results: The final analysis included 19 and 22 participants in the SAC and Placebo groups, respectively. An additional subgroup analysis explored the effect of SAC intake on sleep quality, with 14 and 19 participants in the SAC and Placebo

groups, respectively. After the 12-week intervention, the overall analysis showed no significant differences between groups for the primary outcome. In the subgroup analysis, however, the “Initiation and maintenance of sleep” and “Sleepiness on rising” scores in the OSA-MA significantly increased in the SAC group versus placebo. Both the overall and subgroup analyses revealed a decreased total score, subjective sleep quality (C1), and sleep latency (C2) of PSQI-J in the SAC group versus placebo. Regarding the question “How much difficulty did you have in falling asleep last night?” in the SMH, more participants in the SAC group reported “none or very little” in the overall analysis, while all participants reported “none or very little” in the subgroup analysis after the intervention.

Conclusions: SAC-enriched garlic extract relieves difficulties associated with initiating and maintaining sleep.

Keywords: garlic, S-Allyl-L-Cysteine, sleep quality, falling asleep, sleep maintenance

Trial registration number: UMIN000052187



INTRODUCTION

Garlic (*Allium sativum*) is a perennial herb of the genus *Allium*. The scales of garlic have a strong aroma and are consumed worldwide for their long-established tonic and stamina-promoting properties. Garlic releases compounds known as phytoncides that exert antistress and immune-boosting effects [1]. Sulfur-containing compounds in garlic such as S-allyl-L-cysteine (SAC), S-1-propenyl-L-cysteine (S1PC), alline, allicin, and ajoene are functionally important ingredients. Among these, SAC is the most studied, with known cardioprotective, neuroprotective, hepatoprotective, antidiabetic, antilipidemic, antihypertensive, anticancer, nephroprotective, and antidepressant activities [2]. In a recent clinical trial, we have clarified the mental fatigue-reducing effects of SAC, suggesting that it regulates the balance of the autonomic nervous system [3]. Taking this step further, we implemented this study because regulating the autonomic nervous system is also expected to improve sleep quality.

The combined impact of sleep deprivation, fragmentation, and disturbances has been linked to numerous negative health outcomes, such as a higher likelihood of developing chronic illnesses and an increased risk of mortality [4]. Adequate sleep is crucial for promoting overall well-being, both physically and mentally. The World Health Organization considers sleep a key factor in brain health [5], and the American Heart Association includes sufficient sleep duration as one of Life's Essential Eight for maintaining optimal cardiovascular health [6]. Additionally, the American Academy of Sleep Medicine and Sleep Research Society advise that adults aim for a minimum of 7 hours of sleep each night. A study of sleep duration based on sleep sensor device data [7] described that at least half of the surveyed population slept at least 7 hours, whereas approximately 15%–30% slept less than 7 hours. Meanwhile, a survey conducted by the Organization for Economic Cooperation and Development (OECD) among 33 countries in 2021 showed that Japanese people sleep for 7 hours 22 minutes on average, which is more than 1 hour less than the overall average of 8 hours 28 minutes [8]. These studies suggest the prevalence of sleep deprivation in Japan, with approximately 25% of adults being sleep-deprived. According to a study reported in 2017 [9], the annual economic loss due to sleep deprivation is estimated to be $680 billion. Thus, to maintain good health and minimize the effect on the economy, eliminating sleep deprivation is a pressing issue worldwide.

One way to reduce sleep deprivation is to consume dietary supplements. Amino acids, vitamin D, or melatonin are considered functional components that improve sleep quality; their sleep cycle regulation and antioxidant effects contribute to improved sleep quality [10]. SAC is also expected to improve sleep quality; it has antioxidant effects [2] and promotes the expression of clock genes that control circadian rhythms (i.e., the internal body clock) [11]. Therefore, dietary supplements containing SAC may be considered as functional foods [12,13]. They can enhance the quality of human sleep; however, there is a scarcity of knowledge on this topic. This study investigated the effects of continuous intake of SAC- enriched garlic extract on the sleep quality of healthy Japanese adults.

METHODS

Study design and ethical statement: This was a single center, stratified (male and female with balanced randomization [1:1]), double-blind, placebo-controlled, parallel-group study in Japan. The study protocol was approved by the ethics committee of the Takara Clinic, Medical Corporation Seishinkai on August 23, 2023. Afterwards, the protocol was registered at the University Hospital Medical Information Network Clinical Trials Registry (UMIN000052187). This study was conducted under the latest the guidelines stipulated in the latest Declaration of Helsinki and Ethical Guidelines for Medical and Biological Research Involving Human Subjects in Japan.

Recruit participants and eligibility criteria: Study participants were recruited online (https://www.go106.jp/), as facilitated by ORTHOMEDICO Inc. (Tokyo, Japan). Potential participants received complete information about the study via the network, and their consent was gathered electronically. Individuals affiliated with the study's sponsor and funding companies were excluded. Recruitment took place from September 6–17, 2023 and the study period was from September 12, 2023, to February 25, 2024.

This study included healthy Japanese adults aged ≥ 18 years who were judged eligible to participate in the study by the study's principal physician according to the results of the Beck depression inventory (second edition) [14,15] at screening. The exclusion criteria were as follows: (1) undergoing medical treatment or with a medical history of malignant tumor, heart failure, or myocardial infarction; (2) with a pacemaker or an implantable cardioverter defibrillator; (3) undergoing treatment for cardiac arrhythmia, liver disorder, kidney disorder, cerebrovascular disorder, rheumatism, diabetes mellitus, dyslipidemia, hypertension, any other

chronic diseases, insomnia or sleep disorder; (4) daily use/intake of medications (including herbal medicines) and dietary supplements; (5) allergies to medicines and/or food; (6) the presence of external factors that may disturb sleep; (7) having an irregular dinner time; (8) pregnant, lactating, or planning to become pregnant during this trial; and (9) enrolled in other clinical trials within the last 28 days before the agreement to participate in this trial or plan to participate another trial during this trial. The details of the eligibility criteria are registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN000052187).

The sample size was initially planned for 40 participants to maximize the budget allocation. However, to account for possible dropouts and non-compliance, the final number of participants was increased to 44, with 22 in each group.

Selection, randomization, and blinding: Among 71 participants who provided informed consent, 44 were deemed eligible by the physician. Bizen Chemical Co., Ltd. (Okayama, Japan), the sponsor and funder of this study, provided the intervention foods (test foods and placebo foods) to the contract research organization (CRO). The intervention food dispatcher of the CRO confirmed that the test and placebo foods were indistinguishable. The screening data was entered and verified by the intervention food dispatcher, who then provided the allocation controller—who was not directly involved in the study—with the identification number. Stratified block randomization was employed, considering sex as a factor (male and female). Using a computer-generated randomization list, the allocation controller randomly assigned 22 participants to each group, either the test food (SAC group) or the placebo (Placebo group). The list containing the coded test foods was made available only to the intervention food dispatcher of the CRO, who then sent the corresponding foods to participants according to the list. The allocation list was locked by the allocation controller until the scheduled key-opening day. The study team, including the sponsors, funders, principal investigator, all CRO staff (such as trial directors, trial conduct managers, monitoring personnel, statistical analysis team, and shipping staff), as well as medical institution staff, institutional review board members, contract laboratories, and any other personnel associated with the study, were all blinded to the group assignments and did not participate in the allocation process.

Intervention: Participants took 2 tablets daily within 30 minutes after breakfast with water for 12 weeks. The SAC-enriched garlic powder used in this clinical study was "SAC Garlic™ (SAC 10 mg/g powder)" manufactured by Bizen Chemical Co., Ltd. Using the powder, tablets of test and placebo foods were formulated with food additives (Table 1). The test food contained 1 mg of SAC per tablet, and thus the SAC group consumed a total of 2 mg of SAC daily. The ethics committee confirmed that the 2 types of tablets were indistinguishable.

Table 1. Composition of test foods in each tablet

Ingredient	Test food (mg)	Placebo (mg)
SAC-containing garlic powder	100.1	0
(SAC content)	(1.0)	(0)
Maltitol	78	178.1
Starch	39	39
Crystalline cellulose	35.1	35.1
Silicon dioxide	3.9	3.9
Calcium sterate	3.9	3.9

Outcomes: The medical institution conducting the study was the Medical Corporation Seishinkai, Takara Clinic, which acquired the data together with the Nerima Medical Association, Minami-machi Clinic (Tokyo, Japan), a cooperating medical institution. The Medical Corporation Seishinkai, Takara Clinic also evaluated the acquired data and managed the health of the study participants. Table 2 shows the study schedule. Previous studies [3,11] have confirmed improvements in sleep quality and fatigue at 4 weeks after the start of the test food intake. However, the Consumer Affairs Agency of Japan recommends 12 weeks or longer intervention in efficacy evaluation studies of functional foods to confirm whether the effects diminish over time [16]. Therefore, since the validity of the effect SAC intake on sleep quality was confirmed up to 4 weeks, efficacy and safety outcomes were assessed only at screening and 12 weeks after the start of the test food intake (12w).

Table 2. Study schedule

		Briefing session	Screening	Enrollment	Allocation	Examination	
						0w	12w
Registration	Eligibility screening	●		●			
	Informed consent	●					
	Other procedures	●					
	Allocation				●		
Intervention	SAC					◆	◆
	Placebo					◆	◆
Assessment	OSA-MA*		●				●
	PSQI-J		●				●
	SMH		●				●
	BDI-II		●				
	Physical measurements		●				●
	Medical questionnaire		●				●
	Daily record					◆	◆

"●" indicates the item of implementation, "◆" shows consecutive daily measurements or intake.

*OSA-MA was assessed immediately upon waking for 3 days (2 and 1 days before each examination and the day of each examination).

0w, before consumption; 12w, 12 weeks after consumption; OSA-MA, OSA sleep inventory MA version; PSQI-J, Pittsburgh Sleep Quality Index (Japanese version); SMH, St. Mary's Hospital sleep questionnaire; BDI-II, Beck depression inventory (second edition)

The Primary Outcome: The primary outcome was the measured value of the factor "Initiation and maintenance of sleep" in the Oguri-Shirakawa-Azumi sleep inventory middle-aged version (OSA-MA) at 12 weeks based on findings from a previous study [11] that suggested that improvements in sleep quality with SAC intake are attributable to enhanced sleep maintenance. The OSA-MA was administered immediately upon waking up at 3 time periods (2 days before 12w, 1 day before 12w, and the day of 12w) to investigate the state of sleep upon waking. The mean value was calculated from the Zc scores for the 3 days, with higher Zc scores indicative of better sleep.

SECONDARY OUTCOMES

OSA-MA [17]: The OSA-MA was used to investigate the state of sleep upon waking up at screening and at 12w. The measured values of "Sleepiness on rising," "Frequent dreaming," "Refreshing," "Sleep length," and each question on the OSA-MA at 12w were evaluated. The OSA-MA was administered immediately upon waking up at 3 time periods (2 days before 12w, 1 day before 12w,

and the day of 12w). The mean value was calculated from the Zc scores for the 3 days, with higher Zc scores indicative of better sleep.

The Japanese version of the Pittsburgh Sleep Quality Index (PSQI-J) [18,19]: The PSQI-J was used to examine daytime sleep conditions at screening and 12w. The measured values of the global PSQI score, subjective sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (C4), sleep disturbances (C5), use of sleep medication (C6), daytime dysfunction (C7), and each question on the PSQI-J at 12w were evaluated. Scores for C1–C7 were calculated according to the scoring method, with lower scores indicative of better sleep status.

The St. Mary's Hospital sleep questionnaire (SMH) [20]: The SMH was used to examine daytime sleep conditions at screening and 12w. The measured values in the questions on the SMH (Appendix 1) at 12w were evaluated.

Statistical analysis: Two-tailed tests were used for the statistical analyses in this study with the significance level set at 5%. The software used was the Windows version of SPSS Ver. 23.0 (IBM Japan, Ltd., Tokyo, Japan). Since the analysis focused on the primary outcome, the study did not consider the multiplicity of occurrence in the secondary outcomes.

Regarding the participants' characteristics, sex was expressed as the number of males and females in the group. Other items were expressed as their mean and standard deviations (SD). The data from the OSA-MA (factor scores and each question) and PSQI-J were presented as their mean and SD. The difference between the SAC and Placebo groups (SAC group minus Placebo group; at screening: mean difference, after the intervention: estimated marginal means [EMM] difference) and 95% confidence interval (CI) were displayed. The data at screening was compared between groups using Welch's *t*-test for baseline data, whereas the post-intervention data was compared via an analysis of covariance (ANCOVA) with baseline values as covariate and group as factor. Each question of the PSQI-J and SMH was expressed as the minimum (Min), median (Med), maximum (Max), quartile range (first quartile; Q1, third quartile; Q3) and rank sum for each group, utilizing the Mann-Whitney *U* test for comparisons between groups. For the "yes/no" items of SMH, the 95% CI of the applicable percentage for each group and the difference in applicable ratio between groups (SAC group minus Placebo group) was calculated. The chi-squared test was used to compare applicability percentage between groups. The subgroup analyses in this study used the same analytical methods as for the overall analysis.

RESULTS

Participant flow and analysis set: Fig. 1 shows the follow-up flow chart for our study participants. Although all participants received the allocated intervention, 3 participants in the SAC group opted out of the examination at 12w due to personal reasons. The analysis dataset definition was based on ICH-E9 [21], and the analysis dataset for the efficacy endpoints was the full analysis set (FAS). The data set used for the safety endpoints was the safety analysis population, wherein 3 participants (3 in the SAC group) with missing post-assignment data (physical measurements, urinalysis, and peripheral blood tests) were excluded from the analysis. There were 41 participants in the FAS (Placebo group, n = 22; SAC group, n = 19). The background of the participants is shown in Table 3.

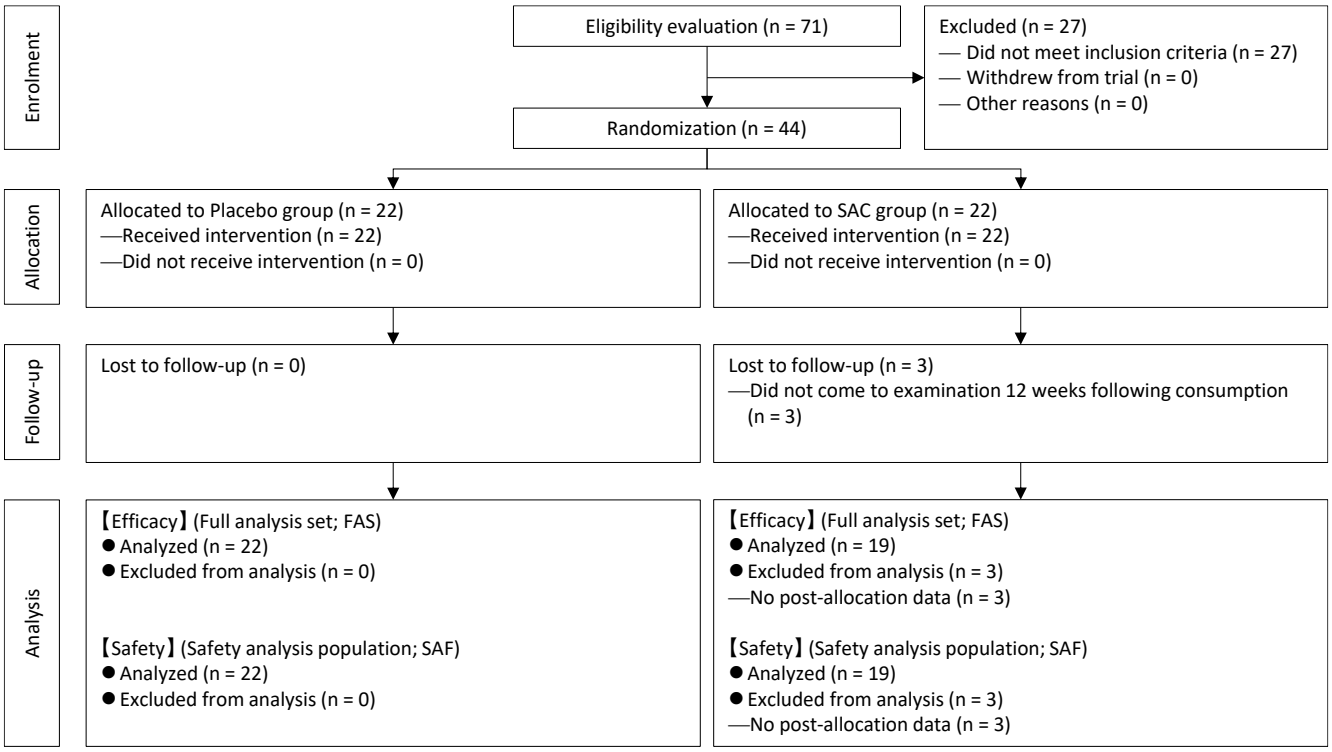


Figure 1. Participant flowchart

Table 3. Demographic data

Items	Unit	Intention to treat		Full analysis set	
		Placebo group (n = 22)	SAC group (n = 22)	Placebo group (n = 22)	SAC group (n = 19)
Sex	male/female	11/11	11/11	11/11	9/10
Age	years	45.7 (14.3)	45.8 (12.4)	45.7 (14.3)	45.3 (12.2)
Height	cm	163.9 (7.5)	165.1 (8.9)	163.9 (7.5)	164.9 (9.3)
Body weight	kg	60.5 (11.6)	62.3 (12.2)	60.5 (11.6)	62.6 (12.4)
Body mass index	kg/m^2	22.4 (3.3)	22.7 (3.3)	22.4 (3.3)	22.9 (3.4)
Systolic blood pressure	mmHg	117.4 (14.1)	115.5 (18.8)	117.4 (14.1)	111.8 (12.2)
Diastolic blood pressure	mmHg	74.0 (10.3)	72.9 (13.8)	74.0 (10.3)	70.1 (9.7)

Sex is shown by the number of participants in the group, and other items are shown by mean and standard deviation.

An additional subgroup analysis was conducted to explore the impact of the intake of SAC on sleep quality. A literature review examining the association between subjective and objective sleep-in healthy adults found that mid-awakenings were strongly associated with sleep quality and sleep efficiency, while high mid-awakenings were associated with poor sleep quality [22]. Since those with higher C5 scores in PSQI-J are deemed to have more mid-awakenings [23], we constructed a subgroup of those whose C5 scores in PSQI-J at screening were within 2SD in the FAS and examined the effect of SAC on those with a similar level of mid-awakenings (i.e., similar sleep quality). The number of participants in the subgroup analysis dataset was 33 (Placebo group, n = 19; SAC group, n = 14).

OSA-MA: For the factor scores, there were no significant differences between groups in the overall analysis (Table

4.1, Figure 2). Regarding each question, the SAC group scored significantly higher in "Question 4_I am relaxed/I am stressed" (P = 0.027) and "Question 16_My sleep was light/My sleep was deep" (P = 0.044) versus the Placebo group at 12w (Table 4.1).

In the subgroup analysis, "Sleepiness on rising" (P = 0.045) and "Initiation and maintenance of sleep" (P = 0.038) were significantly higher in the SAC group versus the Placebo group at 12w (Table 4.2, Figure 2).

Additionally, the SAC group also had significantly higher scores for "Question 4_I am relaxed/I am stressed" (P = 0.022), "Question 11_I feel uncomfortable/I feel comfortable" (P = 0.035), "Question 14_I can answer a survey quickly and easily right now/It's troublesome to answer" (P = 0.032), and "Question 16_My sleep was light/My sleep was deep" (P = 0.035) versus the Placebo group at 12w (Table 4.2).

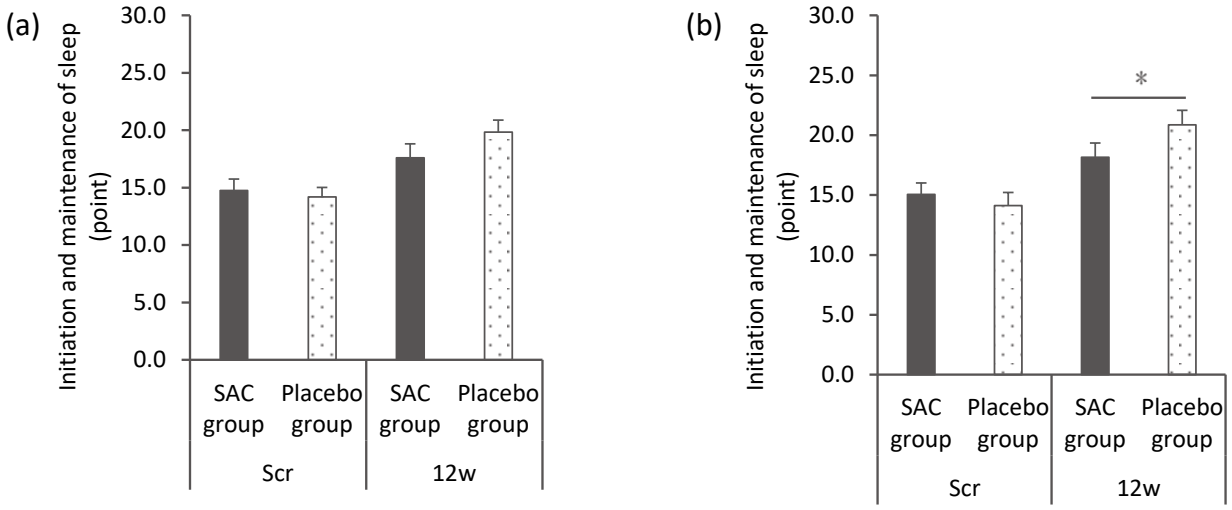


Figure 2. The changes in the primary outcome ("Initiation and maintenance of sleep" as measured by the OSA-MA)
The changes in each analysis (a, overall analysis; b, subgroup analysis) are shown as mean and standard error (SE) at Scr, and as estimated marginal mean and SE at 12w. OSA-MA, OSA sleep inventory MA version; Scr, screening (baseline); 12w, 12 weeks after consumption.

PSQI-J: For the component scores, global PSQI score (P = 0.031), subjective sleep quality (C1) (P = 0.004), and sleep latency (C2) (P = 0.032) were significantly lower in the SAC group than in the Placebo group at 12w (Table 5.1). At screening, the SAC group scored significantly higher in the question, "During the past month, how often have you had trouble sleeping because you wake up in the middle of the night or early morning?" (P = 0.023) versus the Placebo group (Appendix 2.1). At 12w, the SAC group had significantly lower scores for the questions "During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 minutes?" (P = 0.009), "During the past month, how would you rate your sleep quality overall?" (P = 0.007) versus the Placebo group (Appendix 2.1).

In the subgroup analysis, global PSQI score (P = 0.035) and subjective sleep quality (C1) (P = 0.007) were significantly lower in the SAC group than in the Placebo group at 12w (Table 5.2). At screening, the SAC group scored significantly higher for the question, "During the past month, how often have you had trouble sleeping because you wake up in the middle of the night or early morning?" (P = 0.017) versus the Placebo group (Appendix 2.2). At 12w, the SAC group scored significantly lower for the questions "During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 minutes?" (P = 0.025), "During the past month, how would you rate your sleep quality overall?" (P = 0.039), and "During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?" (P = 0.024) versus the Placebo group (Appendix 2.2).

Table 4.1. Comparison of OSA-MA factor scores among the FAS population

Items	Time point	Placebo group (n = 22)				SAC group (n = 19)				Group comparison		
		Mean	SD	EMM	95%CI	Mean	SD	EMM	95%CI	Δ	95%CI	*P*
Sleepiness on rising	Screening	15.7	4.2	-	-	17.1	4.9	-	-	1.4	(–1.5, 4.3)	0.323
	12w	18.6	5.0	19.0	(17.0, 21.0)	21.8	5.6	21.4	(19.2, 23.6)	2.4	(–0.6, 5.3)	0.117
Question 2 I am concentrated / I am not concentrated	Screening	16.7	4.8	-	-	19.1	5.7	-	-	2.3	(–1.0, 5.7)	0.171
	12w	18.5	5.5	19.1	(16.8, 21.5)	22.3	6.5	21.6	(19.1, 24.1)	2.5	(–1.0, 5.9)	0.153
Question 4 I am relaxed / I am stressed	Screening	15.0	4.9	-	-	16.1	5.1	-	-	1.0	(–2.2, 4.2)	0.522
	12w	18.6	6.4	18.9	(16.6, 21.3)	23.2	6.4	22.8	(20.3, 25.3)	3.9	(0.5, 7.3)	0.027*
Question 8 I feel clearheaded / I feel foggy headed	Screening	14.3	4.8	-	-	16.4	6.0	-	-	2.1	(–1.4, 5.6)	0.232
	12w	18.6	6.1	19.0	(16.4, 21.6)	21.1	6.3	20.7	(17.9, 23.5)	1.7	(–2.2, 5.5)	0.379
Question 14 I can answer a survey quickly and easily right now / It's troublesome to answer	Screening	16.5	5.7	-	-	16.8	4.9	-	-	0.3	(–3.1, 3.7)	0.859
	12w	18.6	5.6	18.7	(16.5, 20.9)	20.6	6.0	20.6	(18.1, 23.0)	1.8	(–1.4, 5.1)	0.263
Initiation and maintenance of sleep	Screening	14.7	4.7	-	-	14.2	3.6	-	-	–0.6	(–3.2, 2.1)	0.670
	12w	17.6	5.6	17.4	(15.5, 19.3)	19.8	4.6	20.0	(18.0, 22.1)	2.6	(–0.2, 5.4)	0.068
Question 3 I slept well / I didn't sleep well	Screening	13.7	5.1	-	-	14.1	5.9	-	-	0.4	(–3.1, 3.9)	0.832
	12w	17.1	5.6	17.2	(15.1, 19.4)	19.5	5.8	19.4	(17.1, 21.7)	2.2	(–1.0, 5.3)	0.168
Question 7 I often dozed off until I fell asleep / I was less likely to doze off until I fell asleep	Screening	15.8	7.2	-	-	16.4	7.0	-	-	0.6	(–3.9, 5.1)	0.790
	12w	17.2	7.2	17.3	(14.4, 20.2)	19.8	6.8	19.7	(16.6, 22.8)	2.5	(–1.8, 6.7)	0.247
Question 10 I fell asleep right away / I didn't sleep right away	Screening	11.5	6.4	-	-	11.8	4.5	-	-	0.3	(–3.2, 3.7)	0.863
	12w	15.8	7.4	15.8	(12.8, 18.8)	18.4	6.7	18.4	(15.1, 21.6)	2.6	(–1.8, 7.0)	0.247
Question 13 I woke up frequently during sleep / I didn't wake up during sleep	Screening	17.3	5.9	-	-	15.3	4.2	-	-	–2.0	(–5.2, 1.2)	0.212
	12w	19.6	8.4	19.1	(16.1, 22.1)	20.5	6.0	21.1	(17.9, 24.3)	2.0	(–2.4, 6.4)	0.360
Question 16 My sleep was light / My sleep was deep	Screening	15.4	5.6	-	-	13.4	6.6	-	-	–2.0	(–5.9, 1.9)	0.296
	12w	18.3	7.1	17.8	(15.2, 20.3)	20.9	6.4	21.6	(18.9, 24.3)	3.8	(0.1, 7.6)	0.044*

Items	Time point	Placebo group (n = 22)				SAC group (n = 19)				Group comparison		
		Mean	SD	EMM	95%CI	Mean	SD	EMM	95%CI	Δ	95%CI	*P*
Frequent dreaming	Screening	22.6	7.2	-	-	20.6	6.5	-	-	–2.0	(–6.3, 2.4)	0.364
	12w	24.0	6.2	23.6	(21.3, 25.8)	22.9	5.6	23.4	(20.9, 25.8)	–0.2	(–3.6, 3.1)	0.898
Question 9 I had many nightmares / I didn't have nightmares	Screening	23.4	7.2	-	-	22.8	7.0	-	-	–0.6	(–5.1, 3.9)	0.782
	12w	25.0	6.3	24.8	(22.4, 27.3)	24.1	6.6	24.3	(21.6, 26.9)	–0.6	(–4.2, 3.0)	0.750
Question 12 I dreamed often / I didn't dream	Screening	21.8	8.3	-	-	18.5	7.1	-	-	–3.3	(–8.1, 1.5)	0.176
	12w	23.0	6.9	22.4	(19.9, 24.8)	21.7	5.8	22.4	(19.7, 25.1)	0.1	(–3.6, 3.8)	0.969
Refreshing	Screening	14.9	4.7	-	-	14.6	5.5	-	-	–0.2	(–3.5, 3.0)	0.881
	12w	18.0	5.5	17.9	(15.8, 20.0)	20.3	5.0	20.3	(18.1, 22.6)	2.4	(–0.6, 5.5)	0.118
Question 1 I'm still tired / I'm not tired	Screening	14.7	5.4	-	-	13.6	5.9	-	-	–1.1	(–4.7, 2.5)	0.543
	12w	17.8	5.3	17.6	(15.4, 19.8)	19.7	5.4	19.9	(17.5, 22.3)	2.3	(–1.0, 5.5)	0.166
Question 5 I feel sluggishness in the body / I feel nimbleness in the body	Screening	12.8	5.0	-	-	14.1	5.9	-	-	1.2	(–2.3, 4.7)	0.478
	12w	16.6	6.2	16.8	(14.4, 19.2)	18.8	5.6	18.5	(15.9, 21.1)	1.7	(–1.8, 5.2)	0.336
Question 11 I feel uncomfortable / I feel comfortable	Screening	17.0	5.7	-	-	16.2	5.8	-	-	–0.9	(–4.5, 2.7)	0.623
	12w	19.5	6.7	19.4	(16.8, 22.0)	22.4	5.8	22.6	(19.8, 25.3)	3.2	(–0.6, 7.0)	0.097
Sleep length	Screening	17.7	4.9	-	-	18.0	4.4	-	-	0.2	(–2.7, 3.2)	0.867
	12w	19.8	4.0	19.8	(17.8, 21.9)	21.8	6.0	21.8	(19.6, 24.0)	1.9	(–1.1, 4.9)	0.197
Question 6 I have an appetite / I have no appetite	Screening	16.9	7.7	-	-	19.9	7.2	-	-	3.0	(–1.7, 7.7)	0.208
	12w	20.0	5.5	20.8	(18.1, 23.4)	23.8	8.7	23.0	(20.2, 25.8)	2.2	(–1.7, 6.1)	0.259
Question 15 Sleeping time was long / Sleeping time was short	Screening	18.5	5.5	-	-	16.1	4.6	-	-	–2.5	(–5.7, 0.7)	0.123
	12w	19.5	5.7	18.8	(16.5, 21.1)	19.8	6.2	20.6	(18.1, 23.0)	1.8	(–1.6, 5.2)	0.296

OSA-MA, OSA sleep inventory MA version; SD, standard deviation; EMM, estimated marginal mean; Δ, Difference between groups (SAC group – Placebo group); 95%CI, 95% confidence interval; 12w, 12 weeks after consumption. *$P < 0.05$

Table 4.2. Comparison of OSA-MA factor scores among the FAS population with similar sleep quality

Items	Time point	Placebo group (n = 19)				SAC group (n = 14)				Group comparison		
		Mean	SD	EMM	95%CI	Mean	SD	EMM	95%CI	Δ	95%CI	*P*
Sleepiness on rising	Screening	16.0	3.5	-	-	17.3	5.6	-	-	1.3	(–2.2, 4.9)	0.445
	12w	18.7	4.4	19.0	(16.8, 21.2)	22.9	6.2	22.5	(19.9, 25.1)	3.5	(0.1, 6.9)	0.045*
Question 2 I am concentrated/ I am not concentrated	Screening	17.0	3.5	-	-	18.6	6.6	-	-	1.6	(–2.4, 5.7)	0.410
	12w	18.5	5.0	18.9	(16.4, 21.5)	22.9	7.4	22.4	(19.4, 25.4)	3.4	(–0.5, 7.4)	0.086
Question 4 I am relaxed / I am stressed	Screening	15.2	4.7	-	-	15.7	5.7	-	-	0.5	(–3.3, 4.3)	0.789
	12w	18.7	6.2	18.9	(16.4, 21.3)	23.6	6.3	23.4	(20.5, 26.2)	4.5	(0.7, 8.3)	0.022*
Question 8 I feel clearheaded / I feel foggy headed	Screening	14.4	4.8	-	-	16.9	6.6	-	-	2.5	(–1.8, 6.8)	0.241
	12w	18.7	6.1	19.1	(16.1, 22.0)	22.4	6.8	21.9	(18.5, 25.4)	2.9	(–1.7, 7.4)	0.215
Question 14 I can answer a survey quickly and easily right now / It's troublesome to answer	Screening	17.1	5.1	-	-	17.7	5.4	-	-	0.7	(–3.1, 4.5)	0.724
	12w	18.5	4.7	18.6	(16.4, 20.9)	22.6	5.6	22.4	(19.8, 25.1)	3.8	(0.3, 7.3)	0.032*
Initiation and maintenance of sleep	Screening	15.1	4.2	-	-	14.1	4.1	-	-	–0.9	(–3.9, 2.1)	0.533
	12w	18.1	5.2	17.9	(15.9, 19.9)	20.9	4.6	21.2	(18.8, 23.5)	3.3	(0.2, 6.4)	0.038*
Question 3 I slept well / I didn't sleep well	Screening	13.7	4.8	-	-	13.9	6.8	-	-	0.2	(–4.2, 4.6)	0.929
	12w	17.8	5.4	17.8	(15.5, 20.2)	20.6	6.3	20.6	(17.9, 23.3)	2.8	(–0.8, 6.3)	0.129
Question 7 I often dozed off until I fell asleep / I was less likely to doze off until I fell asleep	Screening	16.5	7.1	-	-	17.2	7.8	-	-	0.7	(–4.7, 6.1)	0.796
	12w	17.7	6.9	17.8	(14.7, 20.9)	20.1	7.1	20.0	(16.4, 23.6)	2.2	(–2.6, 7.0)	0.348
Question 10 I fell asleep right away / I didn't sleep right away	Screening	11.6	6.5	-	-	11.8	4.7	-	-	0.2	(–3.8, 4.1)	0.937
	12w	15.8	7.6	15.8	(12.4, 19.2)	19.4	6.7	19.3	(15.4, 23.3)	3.5	(–1.7, 8.7)	0.176
Question 13 I woke up frequently during sleep / I didn't wake up during sleep	Screening	17.4	5.3	-	-	14.4	3.8	-	-	–3.0	(–6.2, 0.2)	0.067
	12w	20.3	7.8	19.7	(16.6, 22.9)	21.8	5.2	22.6	(18.9, 26.3)	2.8	(–2.1, 7.8)	0.254

Items	Time point	Placebo group (n = 19)				SAC group (n = 14)				Group comparison		
		Mean	SD	EMM	95%CI	Mean	SD	EMM	95%CI	Δ	95%CI	*P*
Question 16 My sleep was light / My sleep was deep	Screening	15.9	5.1	-	-	13.3	7.4	-	-	–2.7	(–7.4, 2.1)	0.258
	12w	19.2	6.2	18.6	(15.9, 21.3)	22.4	6.5	23.1	(20.0, 26.2)	4.5	(0.3, 8.7)	0.035*
Frequent dreaming	Screening	22.0	7.3	-	-	19.9	6.3	-	-	–2.1	(–7.0, 2.8)	0.385
	12w	23.7	6.5	23.3	(21.0, 25.6)	24.3	4.3	24.8	(22.1, 27.5)	1.5	(–2.1, 5.1)	0.403
Question 9 I had many nightmares / I didn't have nightmares	Screening	22.8	7.5	-	-	22.3	6.8	-	-	–0.5	(–5.6, 4.6)	0.842
	12w	24.6	6.7	24.5	(21.9, 27.1)	25.4	5.0	25.5	(22.5, 28.5)	1.0	(–3.0, 4.9)	0.619
Question 12 I dreamed often / I didn't dream	Screening	21.3	8.3	-	-	17.6	7.1	-	-	–3.7	(–9.2, 1.8)	0.179
	12w	22.8	7.2	22.1	(19.7, 24.6)	23.2	4.7	24.2	(21.3, 27.1)	2.1	(–1.8, 5.9)	0.282
Refreshing	Screening	14.7	4.3	-	-	15.1	6.1	-	-	0.4	(–3.6, 4.3)	0.850
	12w	18.0	5.4	18.1	(15.7, 20.4)	21.1	5.2	21.0	(18.3, 23.7)	2.9	(–0.7, 6.5)	0.107
Question 1 I'm still tired / I'm not tired	Screening	14.4	5.2	-	-	14.1	6.3	-	-	–0.3	(–4.6, 3.9)	0.867
	12w	17.9	5.3	17.9	(15.4, 20.4)	19.7	5.8	19.8	(16.9, 22.7)	1.9	(–2.0, 5.7)	0.325
Question 5 I feel sluggishness in the body / I feel nimbleness in the body	Screening	12.5	4.9	-	-	14.5	6.2	-	-	2.0	(–2.1, 6.1)	0.333
	12w	16.7	6.2	17.0	(14.3, 19.7)	19.6	5.6	19.2	(16.1, 22.4)	2.2	(–2.0, 6.4)	0.291
Question 11 I feel uncomfortable / I feel comfortable	Screening	17.2	5.2	-	-	16.6	6.6	-	-	–0.6	(–5.0, 3.8)	0.792
	12w	19.3	6.5	19.2	(16.4, 22.0)	23.8	5.9	23.9	(20.6, 27.2)	4.7	(0.3, 9.0)	0.035*
Sleep length	Screening	17.3	4.4	-	-	18.6	4.8	-	-	1.3	(–2.1, 4.6)	0.445
	12w	19.6	4.3	19.8	(17.5, 22.0)	23.2	5.7	22.9	(20.3, 25.6)	3.2	(–0.3, 6.7)	0.074
Question 6 I have an appetite / I have no appetite	Screening	16.8	7.0	-	-	21.9	7.2	-	-	5.0	(–0.1, 10.1)	0.055
	12w	20.4	5.7	21.3	(18.5, 24.2)	26.7	7.7	25.5	(22.1, 28.9)	4.1	(–0.4, 8.7)	0.075
Question 15 Sleeping time was long / Sleeping time was short	Screening	17.8	4.6	-	-	15.4	5.0	-	-	–2.5	(–6.0, 1.0)	0.155
	12w	18.8	5.6	18.2	(15.5, 20.8)	19.6	6.8	20.5	(17.4, 23.6)	2.3	(–1.8, 6.5)	0.255

OSA-MA, OSA sleep inventory MA version; SD, standard deviation; EMM, estimated marginal mean; Δ, Difference between groups (SAC group – Placebo group); 95%CI, 95% confidence interval; 12w, 12 weeks after consumption.*$P < 0.05$

Table 5.1. Comparison of PSQI-J component scores among the FAS population

Items	Time point	Placebo group (n = 22)				SAC group (n = 19)				Group comparison		
		Mean	SD	EMM	95%CI	Mean	SD	EMM	95%CI	Δ	95%CI	*P*
Global PSQI score	Screening	7.0	3.0	-	-	6.7	3.0	-	-	–0.3	(–2.2, 1.6)	0.743
	12w	5.2	3.1	5.1	(4.3, 5.9)	3.6	1.8	3.7	(2.8, 4.6)	–1.4	(–2.6, –0.1)	0.031*
subjective sleep quality (C1)	Screening	1.6	0.5	-	-	1.7	0.7	-	-	0.1	(–0.3, 0.5)	0.587
	12w	1.3	0.7	1.3	(1.1, 1.6)	0.8	0.4	0.8	(0.5, 1.0)	–0.6	(–0.9, –0.2)	0.004*
sleep latency (C2)	Screening	2.0	1.0	-	-	1.5	1.0	-	-	–0.5	(–1.1, 0.2)	0.137
	12w	1.5	1.1	1.3	(1.0, 1.6)	0.7	0.7	0.8	(0.5, 1.2)	–0.5	(–0.9, 0.0)	0.032*
sleep duration (C3)	Screening	1.1	1.0	-	-	1.2	1.0	-	-	0.1	(–0.5, 0.7)	0.826
	12w	0.8	0.9	0.8	(0.6, 1.1)	0.8	0.9	0.8	(0.5, 1.0)	–0.1	(–0.4, 0.3)	0.664
habitual sleep efficiency (C4)	Screening	0.3	0.7	-	-	0.3	0.7	-	-	0.0	(–0.5, 0.5)	0.992
	12w	0.3	0.8	0.3	(0.0, 0.5)	0.1	0.2	0.1	(–0.2, 0.3)	–0.2	(–0.6, 0.1)	0.224
sleep disturbances (C5)	Screening	1.0	0.4	-	-	1.2	0.5	-	-	0.1	(–0.2, 0.4)	0.428
	12w	0.8	0.4	0.8	(0.7, 1.0)	0.9	0.5	0.9	(0.7, 1.0)	0.0	(–0.2, 0.3)	0.842
use of sleep medication (C6)	Screening	0.1	0.5	-	-	0.0	0.0	-	-	–0.1	(–0.3, 0.1)	0.186
	12w	0.0	0.0	NA	NA	0.0	0.0	NA	NA	NA	NA	NA
daytime dysfunction (C7)	Screening	0.9	0.7	-	-	0.9	0.7	-	-	0.0	(–0.4, 0.5)	0.885
	12w	0.5	0.6	0.5	(0.3, 0.7)	0.4	0.5	0.4	(0.2, 0.6)	–0.1	(–0.4, 0.2)	0.557

PSQI-J, Pittsburgh Sleep Quality Index (Japanese version); FAS, full analysis set; SD, standard deviation; EMM, estimated marginal mean;

Δ, Difference between groups (SAC group - Placebo group); 95%CI, 95% confidence interval; 12w, 12 weeks after consumption. *$P < 0.05$; NA, Not Available

Table 5.2. Comparison of PSQI-J component scores among the FAS population with similar sleep quality

Items	Time point	Placebo group (n = 19)				SAC group (n = 14)				Group comparison		
		Mean	SD	EMM	95%CI	Mean	SD	EMM	95%CI	Δ	95%CI	*P*
Global PSQI score	Screening	6.9	2.4	-	-	6.8	3.0	-	-	–0.1	(–2.1, 1.9)	0.911
	12w	5.1	2.9	5.1	(4.1, 6.1)	3.4	1.9	3.5	(2.3, 4.6)	–1.6	(–3.1, –0.1)	0.035*
subjective sleep quality (C1)	Screening	1.6	0.5	-	-	1.9	0.5	-	-	0.2	(–0.1, 0.6)	0.227
	12w	1.2	0.6	1.2	(1.0, 1.5)	0.7	0.5	0.7	(0.4, 1.0)	–0.6	(–1.0, –0.2)	0.007*
sleep latency (C2)	Screening	2.0	0.9	-	-	1.4	1.2	-	-	–0.6	(–1.3, 0.2)	0.143
	12w	1.5	1.0	1.3	(1.0, 1.7)	0.6	0.7	0.8	(0.4, 1.2)	–0.5	(–1.0, 0.0)	0.061
sleep duration (C3)	Screening	1.1	1.0	-	-	1.4	0.9	-	-	0.3	(–0.4, 1.0)	0.369
	12w	0.8	1.0	0.9	(0.7, 1.2)	0.9	0.8	0.8	(0.5, 1.1)	–0.1	(–0.6, 0.3)	0.526
habitual sleep efficiency (C4)	Screening	0.3	0.7	-	-	0.3	0.8	-	-	0.0	(–0.5, 0.6)	0.933
	12w	0.2	0.7	0.2	(0.0, 0.5)	0.0	0.0	0.0	(–0.3, 0.3)	–0.2	(–0.6, 0.2)	0.284
sleep disturbances (C5)	Screening	1.0	0.0	-	-	1.0	0.0	-	-	NA	NA	NA
	12w	0.8	0.4	0.8	(0.7, 1.0)	0.9	0.4	0.9	(0.7, 1.1)	0.0	(–0.3, 0.3)	0.909
use of sleep medication (C6)	Screening	0.1	0.5	-	-	0.0	0.0	-	-	–0.1	(–0.3, 0.1)	0.331
	12w	0.0	0.0	NA	NA	0.0	0.0	NA	NA	NA	NA	NA
daytime dysfunction (C7)	Screening	0.8	0.7	-	-	0.9	0.7	-	-	0.0	(–0.5, 0.5)	0.950
	12w	0.5	0.6	0.5	(0.3, 0.8)	0.3	0.5	0.3	(0.0, 0.6)	–0.2	(–0.6, 0.1)	0.179

PSQI-J, Pittsburgh Sleep Quality Index (Japanese version); FAS, full analysis set; SD, standard deviation; EMM, estimated marginal mean;

Δ, Difference between groups (SAC group - Placebo group); 95%CI, 95% confidence interval; 12w, 12 weeks after consumption. *$P < 0.05$; NA, Not Available

SMH*:* There were no significant differences between groups in the overall analysis (Appendix 3.1). In the subgroup analysis at 12w, the SAC group scored significantly lower for the question "How much difficulty did you have in getting off to sleep last night?" (P = 0.004) versus the Placebo group (Appendix 3.2).

DISCUSSION: SAC has been proposed to offer potential advantages in managing chronic conditions like cardiovascular disease and diabetes due to its antioxidant and anti-inflammatory properties, and it may also play a role in treating arthritis and Alzheimer's disease [2]. In addition, consuming food with potent antioxidant and anti-inflammatory effects may improve sleep quality. Reports have confirmed that insomniacs are in a state of oxidative stress [24], with a link between sleep-related disorders and immunity [25,26]. SAC can reduce mental fatigue in humans by regulating the balance of the autonomic nervous system [3] improving sleep quality when combined with its antioxidant and anti-inflammatory effects. Because the brain produces endogenous bioactive substances with sleep-inducing properties in response to the removal of oxidative stress [27], SAC's antioxidant effects are expected to reduce oxidative stress and improve sleep quality. In addition, SAC increases the expression of *Period2* (*Per2*), a clock gene [11]. In humans, *Per2* expression follows a circadian rhythm, peaking at 8 AM and reaching its lowest levels in the afternoon [28]. However, sleep deprivation attenuates the rhythmic expression of clock genes and genes associated with metabolism and antioxidant functions [29]. SAC can cross the blood–brain barrier [30], with blood SAC concentrations peaking 30 min to 2 h after ingestion [11]. Thus, SAC ingested after breakfast may reach the brain, enhancing the amplitude of *Per2* expression and other genes, normalizing circadian clock function, and improving sleep quality. This study examined the effects of consuming garlic extract-containing SAC on sleep quality in healthy Japanese men and women. The results suggest that the consumption of garlic extract-containing SAC enhances sleep quality in healthy Japanese men and women with difficulty of sleeping; they specifically report experiencing a refreshed feeling after waking up.

The OSA-MA is a psychological scale that assesses sleep introspection upon waking, with higher values indicating better conditions [31]. Although the FAS analysis showed no significant differences between groups in the primary outcome ("Initiation and maintenance of sleep" at 12w), the score was higher in the SAC group. In the subgroup analysis of the FAS population with a similar sleep quality, significant differences between groups were found in the items "Initiation and maintenance of sleep" and "Sleepiness on rising," with the SAC group showing higher values than the Placebo group similar to that of the previous study[11].

Considering the significant differences of these results, we reviewed reports of studies aimed at developing and standardizing the OSA-MA for middle-aged and older adults (i.e., individuals living in the Kanto area in Japan, lead a normal life at home, and do not have cancer, dialysis, serious heart disease, psychiatric disorders, enlarged prostate requiring surgery, severe pain, itching, etc.). A previous report found that participants aged 26–59 years (284 participants) had mean scores of 21.3 and 17.4, respectively, for "Initiation and maintenance of sleep" and "Sleepiness on rising" [17]. Therefore, we assumed that these averages were those of the general Japanese population and considered the implications of those results in the present study.

The FAS population scored lower for the "Initiation and maintenance of sleep" than the general Japanese population. After the intervention, the 95% CI upper limit did not reach 21.3 for the Placebo group but exceeded 21.3 for the SAC group, suggesting that the identified

difference was medically relevant. Another analysis conducted among the FAS population with similar sleep quality revealed that they had lower scores than the general Japanese population for "Initiation and maintenance of sleep" and "Sleepiness on rising." After the intervention, the 95% CI upper limit for "Initiation and maintenance of sleep" exceeded 21.3 points for the SAC group only, and the mean and 95% CI range for "Sleepiness on rising" exceeded 17.4 points for the SAC group only. These significant differences confirmed in the FAS population as well as in the FAS population with similar sleep quality were considered medically meaningful differences.

Higher scores for "Initiation and maintenance of sleep" indicate that individuals fell asleep more quickly and continued to sleep steadily without awakening. Additionally, higher scores for "Sleepiness on rising" indicate low levels of sleepiness upon waking. When the individuals were sleepy on waking, other items in the same direction moved in the same direction, which is statistically guaranteed [31]. After reviewing the results of each OSA-MA question for the FAS population and the FAS population with similar sleep quality, Question 16 (a sub-item of sleep maintenance) was significantly higher in the SAC group after the intervention. On the other hand, "Sleepiness on rising" had significant differences between groups were confirmed in the FAS population with similar sleep quality. Regarding its sub-items, the SAC group also showed significantly higher scores on Questions 4 ("I am relaxed/I am stressed") and 14 ("I can answer a survey quickly and easily right now/It's troublesome to answer") as well as higher scores on Question 2 ("I am concentrated/I am not concentrated"). Our previous clinical study [3] also suggested that SAC intake helped maintain concentration and reduce fatigue accumulation, which is reflected in the results of the current study. These results suggest that SAC-enriched garlic extract enhances the sense of sound sleep in healthy Japanese men and women. Additionally, it can enhance the refreshed feeling after waking up and the ability to concentrate in a group of healthy Japanese men and women who have a similar degree of difficulty sleeping.

In other sleep assessments, after the intervention, the SAC group showed significant decreases in global PSQI score, subjective sleep quality (C1), and sleep latency (C2) compared to the Placebo group among the FAS population. Meanwhile, among the FAS population with similar sleep quality, the SAC group showed significant decreases in global PSQI score and subjective sleep quality (C1) and decreased sleep latency (C2). A study of sleep quality in 82 healthy Japanese men and women (38.8 ± 12.2 years old) showed that the global PSQI score had a mean ± SD of 3.78 ± 1.78 points [18]. The cut-off for global PSQI score is 5.5 points, with a score of ≥ 6 indicating a sleep disorder [18]. The EMM and 95% CI of the global PSQI scores for the SAC group and Placebo group, respectively, after the intervention were 3.7 (95% CI 2.8–4.6) and 5.1 (95% CI 4.3–5.9) in the FAS population, while these were 3.5 (95% CI 2.3–4.6) and 5.1 (95% CI 4.1–6.1) in the FAS population with similar sleep difficulty. In both populations, only the SAC group scored below 3.78 points in the EMM and the lower 95% CI.

Regarding specific PSQI questions, "Cannot get to sleep within 30 minutes" was significantly lower in the SAC group after the intervention for both populations. This question is scored according to the number of times the individuals had difficulty sleeping in a week. The number of individuals with difficulty of sleeping at least 3 times a week changed from 5 (22.7%) to 0 (0.0%) in the SAC group and from 10 (45.5%) to 5 (22.7%) in the Placebo group before and after the intervention in the FAS population. Meanwhile, this changed from 4 (28.6%) to 0 (0.0%) in the SAC group and from 9 (47.4%) to 4 (21.1%) in the Placebo group among the FAS population with similar sleep difficulty. The results were also similar

for “How much difficulty did you have in getting off to sleep last night?” of the SMH, which had more respondents in the SAC group reporting “none or very little” versus the placebo group in the FAS population (*P* = 0.079). On the other hand, significant differences were found in the FAS population with similar sleep quality, with all participants in the SAC group reporting “none or very little” after the intervention. In both populations, consumption of the SAC-enriched garlic extracts reduced difficulty in falling asleep, indicating that the reduced time required to fall asleep contributed to improved sleep quality. In the general Korean adult population, prolonged habitual sleep latency based on self-reporting using the PSQI has been associated with all-cause and cancer-related mortality [32]. Chronic sleep deprivation is also linked to an increased risk of chronic diseases and mortality [4]. Therefore, the current results suggest that the SAC-enriched garlic extract made it easier to fall asleep and helped maintain sleep, thereby contributing to the maintenance and promotion of good health.

One study limitation was the small sample size. In a study conducted with a small sample size that was not based on a previous study, the bias of unknown background factors may affect the results [33], despite randomization, stratification, and statistical analysis methods used to homogenize and control for background factors [34]. The results of our study, including the primary outcome, could have been affected by background factor bias due to the small number of participants. To strengthen the evidence for the effectiveness of SAC-enriched garlic extract in improving sleep quality, a validation study with a larger sample size is recommended based on the findings of this study.

According to chrononutrition, the intake of certain food components, such as carbohydrates and tryptophan, before bedtime may influence sleep [35]. However, the potential impact of these ingredients could not be assessed in this study because meal-specific diets were not included. Future studies should monitor participants’ diets using methods such as food frequency questionnaires or 24-h dietary recall, while also considering the influence of dietary habits.

In addition, this study relied on subjective sleep assessment using questionnaires. Although the OSA-MA and PSQI-J results indicated improvements in initiating and maintaining sleep, objective measures of sleep, such as sleep latency and the distribution of REM and non-REM sleep, were not obtained. Although sleep quality evaluations are subjective and based on individuals’ introspection upon waking [17], previous studies have shown that individuals with poor sleep quality tend to experience longer sleep latency, more REM or N1 non-REM sleep (shallow sleep), and less N3 non-REM sleep (deep sleep) [36]. An association between subjective sleep perception and objective sleep measures has been reported. Therefore, individuals dissatisfied with their sleep quality may exhibit sleep patterns that deviate from the ideal. Future studies should incorporate polysomnography or body movement measurements during sleep to more accurately assess the impact of SAC-enriched garlic extract on sleep quality.

Sleep quality is known to change with age, and the National Health and Nutrition Examination Survey reported that sleep duration tends to be longer in the older generation (aged ≥ 60 years) compared to those aged 40–60 years [37]. However, the physiologically necessary hours of sleep are decreased among the older generations [38], and the day-night rhythm decreases due to age-related changes in the body clock that controls the sleep-wake rhythm [39,40]. These changes induce shallower sleep and increase mid-wake and early morning awakenings even among healthy elderly people [41,42]. At screening, the study participants had age ranges of 26–71 years in the Placebo group and 27–62 years in the SAC group. Another study comparing 580 healthy adult men and women divided into age groups

(26–59 years, n = 284; and 60–75 years, n = 296) for each factor of the OSA-MA confirmed significant differences between age groups for several factors [17], suggesting that variations in the age of study participants may have affected the study results. Furthermore, there are also sex-based differences in sleep [43], which can be attributed to female hormones [43], particularly in perimenopausal women in whom insomnia occurs as a menopausal symptom [44]. Since the study population was a small group of healthy Japanese men and women with decreased sleep patterns and sound sleep, a validation study can examine the effects of the intake of garlic extract-containing SAC on sleep quality in further detail by considering age, gender, and menstrual period.

CONCLUSIONS

This study examined the effects of consuming of garlic extract-containing SAC on sleep quality in healthy Japanese men and women. The intervention led to significant modifications in various measures of sleep quality, such as "falling asleep and staying asleep" on the OSA-MA, global PSQI score, as well as sleep quality and sleep latency on the PSQI-J. These results suggest that the SAC-enriched garlic extract can help alleviate difficulties in initiating and maintaining sleep.

List of abbreviations: 12w, 12 weeks after the start of test food intake; 95%CI, 95% confidence intervals; ANCOVA, analysis of covariance; BDI-II, Beck depression inventory (second edition); BMI, body mass index; CAND, Calorie and Nutrition Diary; CRO, contract clinical trial organization; EMM, estimated marginal mean; first quartile, Ql; full analysis set, FAS; Max, maximum; Med, median; Min, minimum; ND, not detectable; OSA-MA, Oguri-Shirakawa-Azumi sleep inventory (middle-aged version); OECD, Organization for Economic Cooperation and Development; SAC, S-Allyl-L-Cysteine; SD, standard deviation; PSQI-J, Pittsburgh Sleep Quality Index (Japanese version); SMH, St. Mary's Hospital sleep questionnaire, SMH; Q3, third quartile; WHO, World Health Organization

Competing interests: The sponsor and funder of this study, Bizen Chemical Co., Ltd., entrusted ORTHOMEDICO Inc., with conducting the study. W.H. and I.M. belong to Bizen Chemical Co., Ltd., while N.S. belongs to ORTHOMEDICO Inc. The implementation of this study was a joint effort between Bizen Chemical Co., Ltd. and ORTHOMEDICO Inc. T.T. (MD), belonging to Medical Corporation Seishinkai, Takara Clinic, who served as the responsible physician for this study. The study was assigned to T.T. by ORTHOMEDICO Inc., with all associated costs covered by the company. It is important to mention that the overseeing physician has no financial interest in any companies linked to the research and has not received any fees or funding for the study.

Authors' contributions: Conceptualization, W.H. and I.M.; Data curation, N.S. and T.T.; Formal analysis, N.S.; Funding acquisition, I.M.; Investigation, N.S. and T.T.; Methodology, N.S. and T.T.; Project administration, T.T.; Resources, W.H. and I.M.; Supervision, T.T.; Visualization, N.S.; Writing—original draft preparation, W.H.; and Writing – review & editing, N.S., T.T. and I.M.

Acknowledgments and funding: The authors thank all the subjects and staff who participated in this study.

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