

근감소증에 대한 더덕열수추출물의 유효성과 안전성

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Efficacy and Safety of *Codonopsis lanceolata* Water Extract for Sarcopenia: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial

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This work was supported by MILAE Bioresources Co., Ltd. (Seoul, Republic of Korea). This funding source did not have any role in the design of this study nor would it have any role in the implementation, analysis, data interpretation, or decision to submit the results.

RECEIVED March 12, 2026

REVISED April 5, 2026

ACCEPTED April 8, 2026

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목적 근감소증 성인을 대상으로 더덕열수추출물이 근육량, 근력 및 신체 기능 개선에 미치는 효과와 안전성을 위약(placebo)과 비교하여 입증하고자 하였다.

방법 무작위 배정, 이중 눈가림, 대조식품 비교 인체적용시험으로 총 104명의 연구대상자가 포함되었다. 대상자들은 두 군으로 무작위 배정되어 12주간 시험 제품을 섭취하였고, 유효성 및 안전성 평가가 함께 수행되었다. 1차 평가 변수로 short physical performance battery (SPPB) 점수를 측정하였으며, 2차 평가 변수로 악력, 골격근량, 체지방량, SPPB 점수, tumor necrosis factor- α , interleukin-6, insulin-like growth factor-1, 이상 반응, 임상검사 결과 및 활력 징후를 측정하였다.

결과 SPPB 점수는 각 군 내에서 유의하게 향상되었으나, 군 간 비교에서는 유의한 차이가 없었다. 악력은 각 군 내에서는 향상되었으나, 대조군에서 실험군에 비해 유의하게 증가하였다($p<0.05$). 오른쪽 다리 근육량은 실험군에서 위약군보다 유의하게 높았다($p<0.05$). 더덕열수추출물과 관련된 약물 이상 반응 또는 중대한 이상 반응은 관찰되지 않았다.

결론 본 연구는 근감소증 성인을 대상으로 한 더덕열수추출물의 첫 임상시험이다. 12주 중재 후 신체기능과 근력에서는 군 간 유의한 차이가 없었고, 근력은 오히려 대조군에서 더 증가하였다. 한편, 오른쪽 다리 근육량만 실험군에서 유의하게 증가했으나, 전반적인 임상적 의의는 제한적이다. 향후 대상자 선정 기준, 투여 용량 및 치료 기간을 조정한 추가 연구가 필요하다. (J Korean Med Rehabil 2026;36(2):23-35)

Key words *Codonopsis lanceolata*, Sarcopenia, Randomized controlled trial

Introduction>>>>

The definition of sarcopenia has evolved. Initially, it referred to age-related muscle loss¹⁾. However, the concept has expanded to include declines in muscle mass, muscle strength, and physical performance²⁾. The European Working Group on Sarcopenia in Older People (EWGSOP) defines sarcopenia based on three criteria: low muscle strength, reduced muscle quantity and quality, and impaired physical performance³⁾. The Asian Working Group for Sarcopenia (AWGS) provides a similar definition, but acknowledges that measurement cut-off values may differ between Asian and Caucasian populations⁴⁾.

The principal mechanisms contributing to sarcopenia include neuromuscular junction dysfunction, impaired capillary blood flow, a decline in muscle satellite cells, infiltration of inflammatory cells, increased muscle protein degradation due to oxidative stress, and mitochondrial dysfunction, which may result in metabolic abnormalities, such as insulin resistance⁵⁾. Additionally, factors such as physical inactivity, malnutrition, smoking, inadequate or excessive sleep, and diabetes may increase the risk of sarcopenia⁶⁾.

Sarcopenia is estimated to affect 10~16% of the global older population⁵⁾, with prevalence rates ranging from 8% to 36% in individuals under 60 years of age and 10~27% in those over 60 years of age⁷⁾. As the number of sarcopenia patients continues to rise, the World Health Organization (WHO) officially recognized sarcopenia as a disease in 2016, assigning it the International Classification of Diseases code M62.84⁸⁾. Sarcopenia is a major contributor to physical frailty, functional impairment in the elderly, and reduced quality of life⁹⁾. Moreover, it increases mortality rates and risk of falls^{10,11)}. Patients with sarcopenia are 5.7 times more likely to incur higher hospital costs¹²⁾, with hospitalization expenses increasing by approximately 50%¹³⁾. In light of these concerns, addressing the treatment and prevention of sarcopenia has become increasingly crucial.

The treatment approaches for sarcopenia can be broadly categorized into non-pharmacological and pharmacological strategies. Nonpharmacological treatments include resistance exercise and adequate nutritional intake of proteins, vitamin D, and antioxidants. Pharmacological interventions include treatment with growth hormones, anabolic agents, androgenic steroids, myostatin inhibitors, and β -receptor blockers^{14,15)}. However, to date, no Food and Drug Administration-approved treatments or drugs specifically for sarcopenia have been developed.

Codonopsis lanceolata is a medicinal plant native to East Asia, including Korea and China¹⁶⁾, and has been extensively studied for its pharmacological properties. In vitro experiments have demonstrated its protective effects on vascular smooth muscle cells and endothelial cells¹⁷⁾, while animal studies have shown its ability to alleviate hypertension¹⁸⁾, restore smooth muscle vasorelaxation¹⁹⁾, enhance hepatic insulin sensitivity²⁰⁾, improve age-related macular degeneration²¹⁾, and reduce allergic lung inflammation²²⁾. Its safety profile has also been evaluated through oral toxicity studies²³⁾.

More preclinical research has highlighted the potential of *C. lanceolata* water extract in regulating lipid metabolism and ameliorating metabolic disorders such as obesity and hyperlipidemia^{24,25)}. Furthermore, it has demonstrated promising effects in preventing skeletal muscle atrophy and sarcopenic obesity^{26,27)}. Although one clinical study has examined its use in prehypertensive adults²⁸⁾, to the best of our knowledge, no clinical trials have directly evaluated the efficacy of *C. lanceolata* water extract in the context of sarcopenia.

In this study, we aimed to evaluate the efficacy and safety of *C. lanceolata* water extract in improving muscle mass, muscle strength, and physical performance compared with a placebo in adults with sarcopenia through a large-scale randomized clinical trial.

Materials and Methods>>>>

The study protocol has been described in detail in a previous publication²⁹⁾.

1. Research design

This randomized, double-blind, parallel-group, placebo-controlled superiority trial was conducted in accordance with the Standard Protocol Items: Recommendations for Interventional Trials 2013 statement.

Participants were recruited through in-hospital posters, external posters, and bus advertisements at the Kyung Hee University Korean Medicine Hospital at Gangdong, Seoul, South Korea. The investigator provided a detailed explanation of the trial purpose and procedures, and written informed consent was obtained from each participant. Participants were assigned screening numbers in the order in which consent was obtained and underwent screening assessments within 14 days of the baseline visit. Those who met all inclusion and exclusion criteria were randomly assigned in a 1:1 ratio to either the intervention or control group at the baseline visit. Participants consumed the assigned investigational product (IP) for 12 weeks. Follow-up visits were conducted at weeks 6 and 12 after the baseline visit, during which efficacy and safety outcomes were assessed. The first participant was screened on September 29, 2021, and the last participant completed the trial on April 27, 2023.

2. Ethics

This study was approved by the Institutional Review Board (IRB) of Kyung Hee University Korean Medicine Hospital at Gangdong on July 15, 2021 (IRB No. MLB_DDE_H01, ver. 01). The study was registered on the Clinical Research Information Service website on December 3, 2021 (registration No. PRE20211203-003).

3. Participants

1) Inclusion criteria

- (1) Participants aged 50~84 years.
- (2) Participants with muscle strength reduction, as measured using a dynamometer:
Aged 50~64: men <30 kg, women <20 kg
Aged 65~84: men <26 kg, women <18 kg
- (3) Participants who voluntarily agree to participate in the study and provide written informed consent.

2) Exclusion criteria

- (1) Participants with severe musculoskeletal abnormalities or injuries of the lower limbs (e.g., those with spinal stenosis requiring surgery and significant walking limitations).
- (2) Participants with untreated kidney disease or a serum creatinine level >2.0 mg/dL.
- (3) Participants with untreated liver disease or aspartate aminotransferase or alanine aminotransferase levels more than three times the normal upper limit at the trial site.
- (4) Participants with uncontrolled diabetes (HbA1c > 7.0%).
- (5) Participants with uncontrolled hypertension (blood pressure $\geq$ 160/100 mmHg, measured after 10 min of rest).
- (6) Participants with a significant psychiatric history or current psychiatric disorders (e.g., depression, schizophrenia, or epilepsy) or those currently taking psychiatric medications (except for those with intermittent use of sleep aids or those with adequately treated depression).
- (7) Participants with a history of malignant tumors within the last 5 years or those currently undergoing treatment (except for non-melanoma skin cancers).
- (8) Participants with Alzheimer's disease, vascular dementia, or Parkinson's disease who are unable to

communicate or walk (mild cases may be included at the discretion of the investigator).

- (9) Participants with frailty-related hip fractures.
- (10) Participants with a history of myocardial infarction, coronary artery bypass surgery, percutaneous coronary intervention (e.g., angioplasty or stent insertion), unstable angina, heart failure classified as New York Heart Association Class III or IV, severe valvular heart disease (e.g., aortic or mitral stenosis), stroke, or untreated atrial fibrillation within the last three months.
- (11) Participants with a history of drug abuse or addiction, or those who have used oral steroids or adrenocorticoids within the last 4 weeks.
- (12) Regular consumption of more than 140 g of alcohol per week (approximately 11.25 cans of beer, 2.5 bottles of wine, or 15 shots of whiskey).
- (13) Participants with known allergies to the IP.
- (14) Participants who have taken supplements related to muscle strength improvement within the last 2 weeks.
- (15) Participants who regularly participated in aerobic or resistance training exercises within the last 3 months.
- (16) Participants who have participated in similar clinical trials within the last 3 months.
- (17) Participants who the investigator deems unsuitable for participation for any other reason.

4. Randomization and blinding

At the baseline visit, blinded staff performed stratified block randomization based on sex. The participants were randomly assigned to the intervention or control group in a 1:1 ratio. Randomization was conducted using a web-based Interactive Web Response System (IWRS), with randomization codes generated using predefined seeds to ensure reproducibility. The participants were assigned an IP number using the IWRS.

To maintain blinding, identical packaging, except for

individual IP numbers, was used for both the intervention and control groups, making the two products indistinguishable. Blinding was preserved for the participants, investigator, product manager, study nurses, and clinical trial monitors.

The randomization codes and IP numbers were managed by blinded staff who were not involved in the trial and had no association with the study. These codes were not revealed until after statistical analysis.

5. Intervention

Roots of *C. lanceolata* cultivated in Gangwon-do, South Korea, were sliced and dried prior to extraction. A total of 50 kg of dried *C. lanceolata* was extracted with water at a 1:10 ratio by circulation at 60 °C for 1 hour. The extract was then filtered through a 50-mesh (75 µm nominal) bag. The resulting filtrate was concentrated to 15 Brix at 55 °C. Dextrin was subsequently added at 50% based on the dry weight of the extract. The mixture was spray-dried under the following conditions: blowing temperature, 180~185 °C; exhaust air temperature, 87~92 °C; liquid temperature, 50 °C; and disk atomizer, 10,800 rpm. Approximately 12.5 kg of powdered *C. lanceolata* extract containing dextrin was obtained. The final *C. lanceolata* water extract used in this study was provided by MILAE Bioresources Co., Ltd. (Seoul, South Korea). The IP primarily consisted of *C. lanceolata* water extract, whereas the control product contained crystalline cellulose. Both products were white tablets, each containing 500 mg.

At the baseline and 6-week visits, participants were provided with IP. The participants were instructed to take two tablets once daily before breakfast with sufficient water for 12 weeks. Any remaining product was collected at the 6-week and 12-week visits, and adherence to the regimen was assessed.

6. Outcome measures

1) Primary outcome measures

The primary outcome measure was a change in the short physical performance battery (SPPB) score assessed at baseline and after 12 weeks. SPPB is commonly used to evaluate physical performance and to assess sarcopenia³⁰⁾. It consists of three tests that assess lower-extremity function: the standing balance test, gait velocity test, and repeated chair stand test. The gait speed test was performed twice, and the shorter time was recorded. Each task was scored from 0 (unable to perform) to 4 (best performance), with a total possible score of 12 points if all tasks were completed successfully.

2) Secondary outcome measures

(1) Change in grip strength

Grip strength was measured during screening, baseline, and at 6 and 12 weeks. This is one of the most widely used methods for assessing muscle strength. Although it primarily reflects upper limb strength, it is also associated with lower limb strength¹⁾.

Measurements were taken using a TKK-5401 digital grip dynamometer (Takei Scientific Instruments Co. Ltd., Tokyo, Japan), which can measure from 5.0 to 100 kg, with a precision of 0.1 kg. The dominant hand was measured first, followed by three alternating measurements of each hand. The highest value from either the right or the left hand was recorded as the final grip strength.

(2) Change in muscle mass and muscle index

Skeletal muscle mass (SMM) was measured at baseline and 12 weeks using dual-energy x-ray absorptiometry (DXA), which is one of the most widely used methods for assessing body composition¹⁾. The participants underwent the scan while wearing light clothing, with all metal accessories removed, and the measurements were obtained through a continuous transverse scan from the head to the toes. The skeletal muscle index (SMI) was calculated at baseline and 12 weeks using the following

formula:

$$\text{SMI} = \text{SMM (kg)} / \text{body weight (kg)} \times 100$$

Appendicular skeletal muscle mass (ASM) was measured at baseline and 12 weeks using DXA. The appendicular skeletal muscle mass index (ASMI) was calculated at baseline and at 12 weeks using the formula:

$$\text{ASMI} = \text{ASM (kg)} / \text{height}^2 \text{ (m}^2\text{)}$$

(3) Change in body fat

Body fat mass (BFM) and body fat percentage (%BF) were measured at baseline and 12 weeks using DXA. Free fat mass (FFM) was calculated at baseline and 12 weeks using the following formula:

$$\text{FFM} = \text{lean (muscle)} + \text{bone mineral content}$$

(4) Change in SPPB score

The SPPB score was assessed at baseline and after 6 weeks. The score for each SPPB item was evaluated at baseline and at 6 and 12 weeks.

(5) Change in tumor necrosis factor- α (TNF- α), interleukin (IL)-6, and insulin-like growth factor-1 (IGF-1)

TNF- α , IL-6, and IGF-1 were measured at baseline and at 12 weeks. Inflammatory markers TNF- α and IL-6 are associated with a decrease in muscle mass and strength, and may inhibit IGF-1 production and biological activity³¹⁾.

(6) Adverse events (AEs)

AEs were assessed at 6 and 12 weeks. Non-directive questioning was used to explore events with the participants at each visit. Additionally, AEs were identified through voluntary reports from participants, physical examinations, laboratory tests, or other evaluations.

(7) Laboratory tests and vital signs

Hematological tests, blood chemistry tests, and urinalysis were conducted at screening and at 12 weeks. Systolic blood pressure, diastolic blood pressure, pulse, and body temperature were measured at screening, baseline, and at 6 and 12 weeks. Blood pressure and pulse rate were measured after 10 min of rest in a seated position using the same FT-500R PLUS automatic blood pressure monitor (Jawon Medical Co. Ltd., Gyeongsan, South Korea).

7. Sample size

The change in SPPB score was used to calculate the sample size. A type I error probability (α) of 0.05 and a type II error probability (β) of 0.15 were set, yielding a statistical power ($1-\beta$) of 85%. The effect size for the difference in the SPPB score changes between the groups was assumed to be 0.6667. A meaningful change of 1.0 point in the SPPB score was estimated with a coefficient of variation of 1.5. Based on these criteria, 41 participants were included in each group. Considering a dropout rate of 20%, the final sample size was 104.

8. Statistical analysis

The primary efficacy analysis was conducted using the per protocol set (PPS), which included participants who completed the clinical trial in compliance with the study protocol. The full analysis set (FAS), based on the intention-to-treat principle and including all randomized participants, was used as a supportive analysis population. Safety analyses were performed using a safety analysis set (SAS) comprising participants with at least one safety-related data point.

Unless otherwise specified, all statistical analyses were performed with a two-sided significance level of 5%. For continuous variables, the number of participants, means, and standard deviations are reported. For categorical variables, frequencies and percentages are reported. Demographics, medication use, and medical histories were summarized using the PPS population.

In the FAS, missing data were handled using the last observation carried forward method. In the PPS and SAS populations, missing values were analyzed using the observed-case approach without imputation.

For outcome variables—including SPPB and its sub-item scores, handgrip strength, SMM, SMI, ASM, ASMI, BFM, %BF, FFM, TNF- α , IL-6, and IGF-1—changes from baseline were summarized by group using the mean,

standard deviation, median, minimum, and maximum. Least-squares means and standard errors, adjusted via a fitted general linear model (GLM), were also presented. Between-group comparisons were conducted using a GLM. If additional covariates were identified as influencing the outcome variables, they were included as independent variables. For skewed data, non-parametric methods such as the Wilcoxon rank-sum test were applied. Within-group changes were assessed using paired t-tests or Wilcoxon signed-rank tests.

The number and percentage of participants experiencing AEs, drug-related AEs, and serious adverse events (SAEs), along with 95% two-sided confidence intervals and the total number of events were summarized by group. Between-group comparisons of incidence rates were performed using the chi-square test or Fisher's exact test.

For the laboratory test results, continuous variables were summarized using the mean and standard deviation for each group. Between-group differences were analyzed using unpaired t-tests or the Wilcoxon rank-sum test, and within-group (pre- and post-treatment) comparisons were performed using paired t-tests or the Wilcoxon signed-rank test. For categorical variables, shift tables showing frequencies and percentages were presented and within-group comparisons were performed using McNemar's test.

Vital signs were summarized as means and standard deviations by group. Between-group comparisons of changes were analyzed using unpaired t-tests or the Wilcoxon rank-sum test, and within-group comparisons using paired t-tests or the Wilcoxon signed-rank test.

9. Data management and monitoring

All data collected and utilized in the study were entered by an independent third-party researcher. To ensure participant anonymity, each participant was identified only by a unique identification number, thereby preventing identification of individual participants by third parties. The data files were password-protected, with access restricted to the designated third-party researcher.

Monitoring was conducted through regular on-site visits and telephone communications by an external monitor.

Results»»»»

1. General characteristics

In total, 113 participants were screened for eligibility. Of these, nine participants were excluded, and 104 were randomized. During the trial, three participants in the intervention group and one in the control group withdrew, resulting in 100 participants completing the study (49 in the intervention group and 51 in the control group). Subsequently, one additional participant in the control group was excluded due to a previously undetected vio-

lation of the exclusion criteria (Fig. 1).

The mean age of participants was 59.76 ± 6.56 years in the intervention group and 60.50 ± 8.03 years in the control group, with no significant difference between the groups. No significant differences were observed between

Table I. Baseline Characteristics

Characteristic	Intervention group (n=49)	Control group (n=50)	p-value*
Sex, n (%)			0.7223
Male	6 (12.24)	5 (10.00)	
Female	43 (87.76)	45 (90.00)	
Age (years)	59.76 ± 6.56	60.50 ± 8.03	0.9525
Body height (cm)	158.79 ± 7.15	158.08 ± 6.34	0.6022
Body weight (kg)	58.14 ± 8.06	57.54 ± 9.64	0.4539

Values are expressed as mean±standard deviation or n (%).

*Compared between groups.

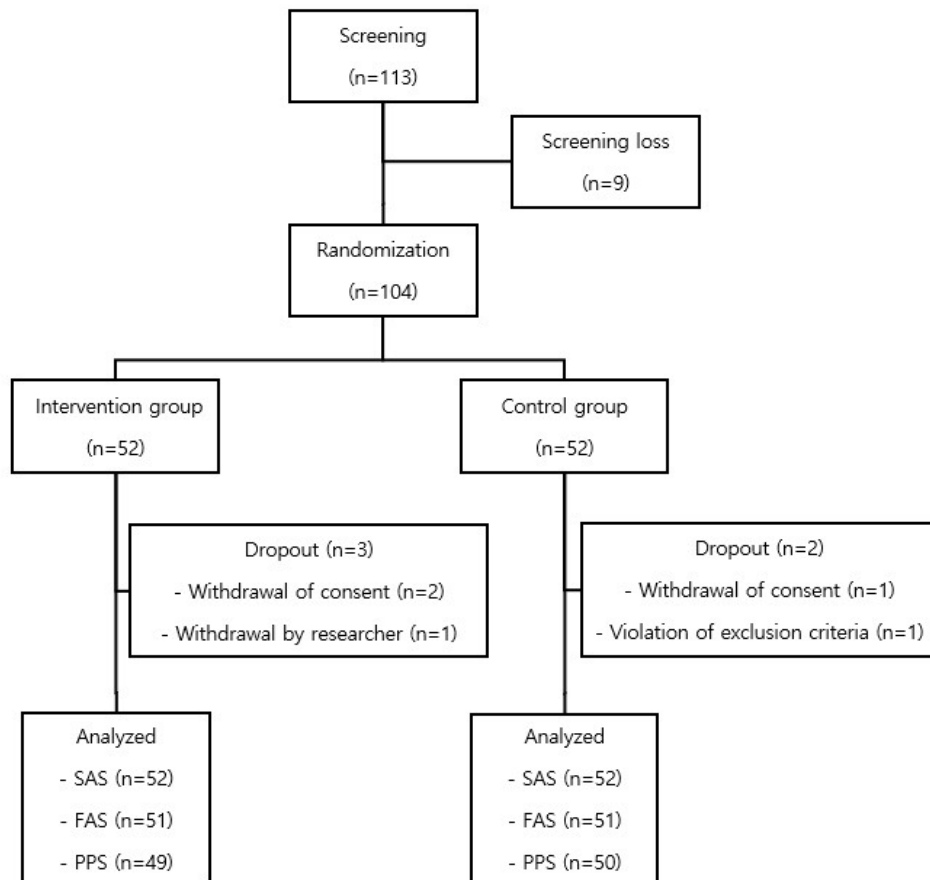


Fig. 1. Study flow chart. SAS: safety analysis set, FAS: full analysis set, PPS: per protocol set.

the groups in sex distribution, height, or weight (Table I). Medical history, prior and concomitant medication use, lifestyle factors, physical activity, and dietary intake were comparable between the groups, with no significant differences.

2. Primary outcome measure

After 12 weeks of supplementation, the mean change in the SPPB score from baseline was 0.88 ± 1.55 in the intervention group and 0.90 ± 1.13 in the control group, and both changes were significant ($p < 0.0001$ for both). However, no significant between-group difference was observed ($p = 0.6053$).

In the subgroup analysis of participants aged < 65 years, the SPPB score increased by 0.92 ± 1.36 in the intervention group and by 0.97 ± 0.93 in the control group, and both changes were significant ($p < 0.0001$). The between-group differences were not significant ($p = 0.4297$). In participants aged ≥ 65 years, the mean change was 0.75 ± 2.09 in the intervention group ($p = 0.2406$), and 0.69 ± 1.60 in the control group ($p = 0.2500$); neither change was significant. No significant differences were observed between the groups ($p = 0.7973$) (Table II).

3. Secondary outcome measures

1) Change in grip strength

At 6 weeks, handgrip strength increased by 1.89 ± 3.84 kg in the intervention group and 2.72 ± 3.06 kg in the control group; both increases were significant ($p < 0.0001$ for both). However, the between-group differences were not significant ($p = 0.0726$). At 12 weeks, handgrip strength increased by 2.73 ± 4.95 kg in the intervention group and by 4.33 ± 3.98 kg in the control group; both changes remained significant ($p < 0.0001$ for both). The increase was significantly greater in the control group than in the intervention group ($p = 0.0165$) (Fig. 2).

2) Change in muscle mass and index

No significant differences were observed between the groups in the changes from baseline to week 12 in SMM, SMI, ASM, or ASMI.

Analysis of limb muscle mass (arms and legs) showed that the right leg muscle mass significantly increased in the intervention group but decreased in the control group. The increase was significantly greater in the intervention group than in the control group ($p = 0.0111$). Changes in

Table II Change in SPPB Score from Baseline to Week 12

	Baseline (mean $\pm$ SD)	Week 12 (mean $\pm$ SD)	p-value*	p-value†
Intervention group (n=49)	10.27 $\pm$ 1.74	11.14 $\pm$ 1.34	<0.0001	0.6053
Control group (n=50)	10.20 $\pm$ 1.68	11.10 $\pm$ 1.22	<0.0001	
Intervention group (age<65, n=37)	10.54 $\pm$ 1.69	11.46 $\pm$ 0.99	<0.0001	0.4297
Control group (age<65, n=37)	10.22 $\pm$ 1.57	11.19 $\pm$ 1.13	<0.0001	
Intervention group (age $\geq$ 65, n=12)	9.42 $\pm$ 1.68	10.17 $\pm$ 1.80	0.2406	0.7973
Control group (age $\geq$ 65, n=13)	10.15 $\pm$ 2.03	10.85 $\pm$ 1.46	0.2500	

SPPB: short physical performance battery, SD: standard deviation.

*Compared within groups.

†Compared between groups.

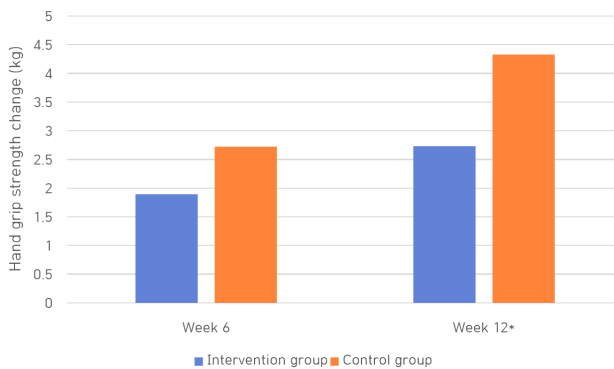


Fig. 2. Hand grip strength change after 6 and 12 weeks. * $p < 0.05$.

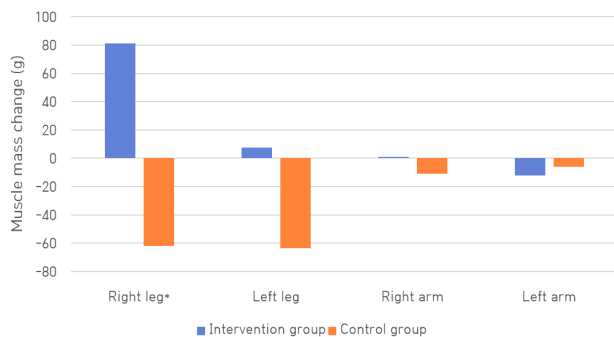


Fig. 3. Muscle mass change after 12 weeks. * $p < 0.05$.

the left leg and right arm muscle mass followed a similar pattern: an increase in the intervention group and a decrease in the control group; however, no significant between-group differences were observed. Left arm muscle mass decreased in both groups; however, the difference was not significant (Fig. 3).

3) Change in body fat content

No significant differences were observed between the groups in the changes from baseline in BFM, %BF, or FFM.

4) Change in the SPPB scores

There was no significant difference in the change in total SPPB scores between the intervention and control groups from baseline to week six. However, in the gait velocity test, the control group showed a significantly greater increase in score compared with the intervention group

($p=0.0415$), indicating a larger improvement in walking speed. No significant differences were observed between the groups in terms of changes in other SPPB subcomponent scores.

5) Change in TNF- α , IL-6, and IGF-1

There were no significant differences between the two groups in the changes from baseline in TNF- α , IL-6, and IGF-1 levels.

6) Adverse events

In the intervention group, 21 AEs, including pharyngitis and hyperlipidemia, were reported by 16 participants, whereas 23 AEs, including pharyngitis and back pain, were reported by 17 participants in the control group. No significant differences were observed between the groups. All reported AEs were mild and were deemed unrelated to the *C. lanceolata* water extract, and no SAEs were observed.

7) Laboratory tests and vital signs

No statistically or clinically significant changes were observed in laboratory test results. No significant differences in vital signs were observed between the groups.

Discussion>>>>>

We conducted a randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy and safety of *C. lanceolata* water extract for improving muscle mass, strength, and physical performance in adults with sarcopenia. In alignment with the diagnostic criteria of sarcopenia, including a decline in muscle strength, muscle quantity and quality, and physical performance, the SPPB was used to assess physical performance, a dynamometer was used to measure muscle strength, and DXA was used to quantify muscle mass. No significant differences were observed between the intervention and control groups in the primary outcome (SPPB score) or most

secondary outcomes, indicating that the intervention did not demonstrate efficacy in this trial.

Diagnostic criteria for sarcopenia have been continuously revised. The EWGSOP updated its criteria in 2010³²⁾ and 2019³⁾, while the AWGS revised its guidelines in 2014⁴⁾ and 2019³³⁾. Given that the concept of sarcopenia is relatively recent, its definition and diagnostic thresholds require further refinement. For example, EWGSOP defines low handgrip strength as <30 kg for men and <20 kg for women, whereas the AWGS sets the thresholds at 26 kg and 18 kg, respectively. Age criteria also differ; the EWGSOP focuses on individuals aged 65 years and older, whereas the International Working Group on Sarcopenia does not specify an age threshold. Furthermore, other studies have used various diagnostic criteria^{34,35)}. Inclusion criteria were based on expert consensus among Korean Medicine Rehabilitation specialists with over 10 years of clinical experience. Participants aged 50~64 years were included if handgrip strength was <30 kg for men or <20 kg for women, while those aged 65~84 years were included if handgrip strength was <26 kg for men or <18 kg for women, reflecting an age-associated decline in muscle strength.

Sarcopenia contributes to physical disability and reduced quality of life and was officially recognized as a disease by the WHO in 2016. Treatment strategies require a multifaceted approach involving both non-pharmacological (e.g., nutrition and exercise) and pharmacological (e.g., anti-inflammatory agents) interventions³⁶⁾.

Preclinical investigations have shown that *C. lanceolata* suppresses body weight gain and fat accumulation in animal models and reduces serum triglyceride and total cholesterol levels²⁴⁾. Additionally, it promotes muscle protein synthesis by activating the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (Akt)/mammalian target of rapamycin complex 1 (mTORC1) pathway and inhibits muscle protein degradation by downregulating the expression of muscle RING finger-1 (MuRF1) and muscle atrophy F-box protein (Atrogin-1)²⁵⁾. Furthermore, it suppresses lipid accumulation in skeletal muscles by modu-

lating PI3K/Akt signaling and lipid metabolism²⁶⁾. To the best of our knowledge, this is the first clinical trial to evaluate the efficacy of aqueous *C. lanceolata* extract in adults with sarcopenia. Despite these promising preclinical findings, this clinical trial did not demonstrate improvements in clinically relevant outcomes, highlighting a discrepancy between preclinical and clinical evidence.

In this study, both groups demonstrated significant improvements in SPPB scores over 12 weeks; a subgroup analysis revealed that individuals under 65 years experienced greater improvements than those aged 65 years or older. However, no significant between-group differences were observed, suggesting that the improvements in SPPB scores were not attributable to the intervention. Similarly, the grip strength increased significantly in both groups, with a significantly greater increase in the control group after 12 weeks. Among the lean mass outcomes assessed using DXA, only right leg muscle mass showed a significantly increase in the intervention group compared to the control group.

Regarding physical performance, the maximum SPPB score was 12, and the average score after 12 weeks exceeded 11 in both groups, with marginally higher scores in the intervention group. This ceiling effect may have limited the ability to detect differences.

The greater increase in grip strength observed in the control group may be explained by several factors, including a learning effect from repeated dynamometer measurements, incidental increases in physical activity, lower baseline handgrip strength leading to regression to the mean, and potential floor effects providing additional room for improvement. The slightly faster gait velocity observed in the control group may be attributed to these same factors.

Among the body composition outcomes, only right leg muscle mass showed a significantly greater increase in the intervention group. However, this isolated finding should be interpreted with caution, as it was not accompanied by consistent improvements in overall muscle mass, strength, or physical performance.

Although this is the first study to evaluate the aqueous extract of *C. lanceolata* in the context of sarcopenia, its safety is supported by its long history of traditional use in East Asian medicine. No significant differences in adverse events or clinically meaningful changes in laboratory test results were observed between the groups. No serious adverse events occurred, and the extract appeared to be safe over a 12-week period.

This study had some limitations. First, although lifestyle factors such as smoking, diet, physical activity (assessed using the international physical activity questionnaire), and alcohol consumption were assessed pre- and post-intervention and no significant differences were found between the groups, it was not possible to completely control for these confounding variables. As exercise and diet are the core treatments for sarcopenia, stricter control of these factors is necessary in future studies.

Second, in participants under 65 years of age, a ceiling effect may have masked larger improvements compared with older individuals. Adjusting the inclusion criteria, such as by using lower baseline SPPB scores for younger participants, may yield more meaningful results. Third, the intervention duration may have been insufficient to observe meaningful clinical effects.

Overall, the findings consistently indicate a lack of efficacy of the intervention across primary and most secondary outcomes. In conclusion, *C. lanceolata* water extract did not demonstrate efficacy in improving muscle strength or physical performance in adults with sarcopenia. Although a partial increase in regional muscle mass was observed, its clinical significance remains uncertain. Future trials should focus on adults under 65 years with moderate sarcopenia, apply stricter inclusion criteria, and evaluate long-term effects across different treatment durations.

Conclusions>>>>

This randomized controlled trial evaluated the efficacy and safety of aqueous *C. lanceolata* extract in 104 adults with sarcopenia. After 12 weeks of intervention:

1. No significant differences were observed between groups in changes in SPPB scores.
2. Grip strength increased significantly more in the control group than in the intervention group.
3. Right leg lean mass measured by DXA increased significantly more in the intervention group than in the control group.
4. No significant differences in adverse events were found, and no drug-related or serious adverse events occurred.

These results suggest that although *C. lanceolata* water extract did not significantly improve physical performance or muscle strength, it may modestly increase regional muscle mass. Further clinical studies with refined inclusion criteria, optimized dosing strategies, and extended treatment durations are warranted to confirm these findings.

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