Effects of Casein Hydrolysate Containing Val-Pro-Pro and Ile-Pro-Pro on Muscle Pump, Muscle Hypertrophy, and Motivation in Resistance-Trained Men: A Placebo-Controlled, Double-Blind, Parallel-Group Comparison Study

Original Research

Takuro Ohigashi [1], Koki Sato [1], Misaki Hatanaka [1], Masaaki Yasue [2], Shohei Nakashima [1], Yuri Miyamoto [3], Yumi Aoyagi [3], Shukuko Ebihara [4], Toshiharu Namba [5] and Motoyuki Tagashira [1]

[1] *Technology Research & Development Department I, Research and Development Headquarters, Asahi Group Foods, LTD, Ibaraki, Japan*
[2] *Food Ingredient Business Headquarters, Asahi Group Foods, LTD., Tokyo, Japan*
[3] *Production Development Department II, Research and Development Headquarters, Asahi Group Foods, LTD., Tokyo, Japan*
[4] *Chiyoda Paramedical Care Clinic, Tokyo, Japan*
[5] *CPCC Inc., Tokyo, Japan*

Open Access

Published: January 7, 2026

Journal of Exercise and Nutrition: *2026, Volume 9 (Issue 1): 2*

ISSN: 2640-2572

Abstract

Introduction: The purpose was to investigate the effects of lactotripeptides (LTP) immediately after training.

Methods: This randomized, placebo-controlled, double-blind, parallel-group comparison study included males who undertook leg strength training every 2 weeks for ≥3 months. Thirty-six participants received placebo, low-dose (LD) (Val-Pro-Pro 0.7 mg/Ile-Pro-Pro 1.0 mg) or high-dose (HD) (Val-Pro-Pro 1.4 mg/Ile-Pro-Pro 2.0 mg) lactotripeptides daily for 4 weeks. Muscle pump, muscle hypertrophy, fatigue, and training motivation were evaluated.

Results: In the HD group, thigh circumference before exercise, lean body mass versus baseline and thigh circumference after exercise versus placebo significantly increased (p=0.002, 0.031, 0.032). In the LD group, subjective questionnaire scores related to muscle pump versus placebo significantly improved (p=0.042). Thigh circumference changes, before and after exercise, and subjective questionnaire scores, regardless of dosage, significantly correlated (p=0.026). Individuals with flow-mediated dilation (FMD) <7% showed a trend toward increased FMD in the HD group (p=0.081). Significant positive correlation occurred between FMD changes and thigh circumference, before and after exercise (p=0.021). In the HD group, fatigue scores after exercise and motivation for training scores the morning after exercise versus placebo significantly improved (p=0.020, 0.043).

Conclusions: LTP intake may be beneficial for muscle pump after training and muscle hypertrophy, reduce training-induced fatigue, and enhance strength training motivation.

Key Words: fatigue; lactotripeptide; strength training

Corresponding author: takuro.ohigashi@asahi-gf.co.jp

Introduction

Muscle pump refers to the temporary swelling of muscles during resistance training. This occurs due to an increase in blood flow to the muscle through the arteries, aimed at supplying the necessary nutrients. As a result, plasma leaks out from the capillaries and, due to muscle contraction, metabolic byproducts such as lactic acid and inorganic phosphate accumulate in the muscle. The increase in osmotic pressure within the muscle cells draws more plasma into these cells, causing the muscle to temporarily expand.[1] This phenomenon is thought to induce metabolic stress on the muscles, potentially stimulating hypertrophic signaling pathways.[2–4] For bodybuilders, muscle pump is not merely a physical expansion of muscles but also a physically demanding and pleasurable self-discipline that provides a sense of satisfaction.[5,6] Concentric exercises are generally reported to be more effective than eccentric exercises for achieving muscle pump.[7]

Recently, pre-workout supplements containing ingredients that enhance nitric oxide (NO) production and increase blood flow have become popular among resistance-trained individuals. These supplements are consumed prior to an acute training bout to improve focus, motivation, performance, and muscle pump. While ingredients such as citrulline and arginine enhance NO production, there are few examples of these ingredients significantly improving muscle pump during strength training.[8–12]

The term lactotripeptides (LTP) refers to two types of tripeptides [Val-Pro-Pro (VPP) and Ile-Pro-Pro (IPP)] discovered in fermented milk using Lactobacillus helveticus, known for their angiotensin-converting enzyme (ACE) inhibitory activity. VPP is derived from β-casein in milk, while IPP is derived from both β-casein and k-casein in milk by enzymes originating from Lactobacillus helveticus.[13] It has been reported that LTP promote NO production through endothelial nitric oxide synthase (eNOS) activation and exert vasodilatory effects in humans.[14–16] Additionally, LTP have been shown to inhibit vascular contraction through ACE inhibition, with antihypertensive effects confirmed in clinical trials.[17,18] Improvements in endothelial function from LTP ingestion, via enhanced flow-mediated dilation (FMD) and pulse wave velocity, have also been observed in clinical studies.[19,20]

Therefore, LTP are expected to promote and maintain vasodilation through dual mechanisms of NO production enhancement and ACE inhibition, leading to a more efficient increase in blood flow. Although there are no studies that have directly evaluated muscle pump, clinical trials have revealed arterial vasodilation one day after training with several instances of LTP intake over 2 days,[21] suggesting a direct effect on enhancing muscle pump. The effect of LTP on muscle pump has not been directly assessed. Moreover, no study conducted thus far has rigorously examined whether long-term, continuous intake of LTP, in combination with sustained resistance training, induces changes in muscle mass. The primary objective of this exploratory study was to investigate whether LTP intake improves muscle pump after ergometer training, a concentric exercise effective for muscle pump, in individuals with a history of strength training. In addition, the study aimed to examine whether long-term, continuous intake of LTP, when combined with sustained resistance training, induces measurable changes in muscle size.

Methods

Participants

The study included men aged 20–49 years who had been performing lower body strength training (e.g., leg extensions, leg curls, dumbbell squats, deadlifts, bodyweight squats) aimed at muscle hypertrophy at least once every 2 weeks for a minimum of 3 months. Participants were excluded if they consumed supplements that affect blood flow, recently started taking supplements with health claims to improve exercise performance, were heavy alcohol drinkers (defined as consuming more than 60 g of alcohol per day), had irregular lifestyles (such as night shift workers or those with rotating shifts), or had history of severe medical diseases/conditions (including serious heart, liver, kidney, or gastrointestinal diseases)/allergies to medications and foods.

Study Design

This was a randomized, placebo-controlled, double-blind, parallel-group comparison trial. The 36 participants were randomly assigned to three groups based on allocation factors such as exercise capacity (anaerobic power test using an ergometer), changes in thigh circumference before and after exercise, and age. Participants consumed three tablets of the investigational product daily for 4 weeks. Compliance with test food intake was confirmed through the diary records of participants and the remaining number of test food packets collected after the trial. Participants maintained their usual lifestyle, recording medication intake, exercise habits, and types of exercise in their diaries. Furthermore, participants were instructed not to alter their usual dietary intake before and during the intervention period. To ensure adherence, they were required to record their daily eating habits in a dietary log, which confirmed that no changes

occurred throughout the study. They visited the clinic thrice (i.e., for a pre-test prior to the intervention, on the first day of test food intake, and after 4 weeks) for medical interviews, physical examinations, blood tests, and exercise tests (Figure 1).

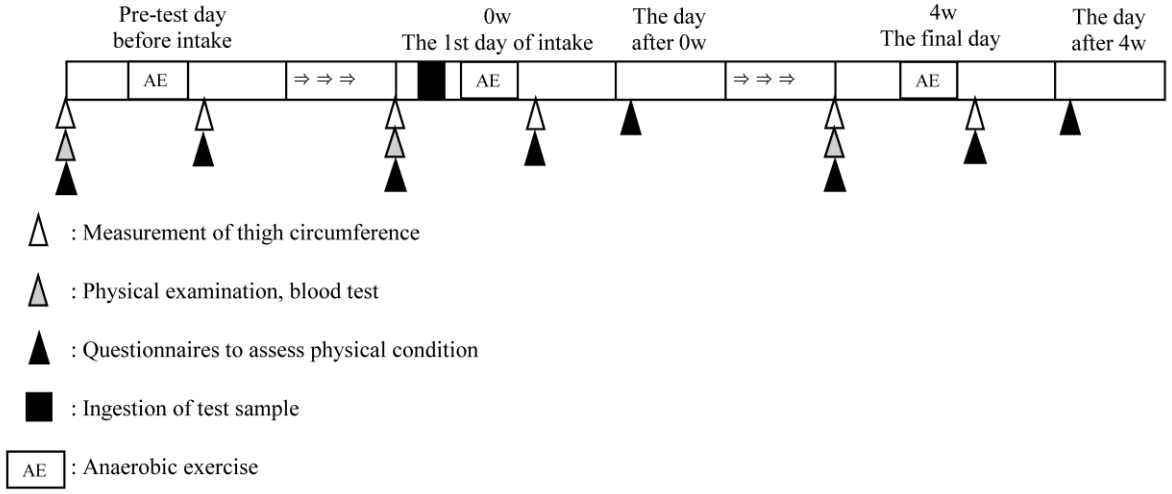


Figure 1. Schedule. 0w and 4w denote the first day and 4 weeks of test food intake, respectively.

Participants were instructed to abstain from alcohol consumption, dieting, overeating, and exercise on the day before testing. They were required to complete all food and beverage intake by 9:00 PM and to refrain from consuming anything other than water until the completion of the tests the following day. On the test day, all participants were provided with a standardized meal at the clinic at the same scheduled time. Smoking was prohibited from waking on the test day until the end of the testing session.

The trial was conducted from April 10, 2024 to May 11, 2024. The study was approved by the Ethics Committee of Chiyoda Paramedical Care Clinic on January 19, 2024. The trial adhered to the ethical principles stipulated in the Declaration of Helsinki, the "Ethical Guidelines for Medical and Health Research Involving Human Subjects" (Ministry of Education, Culture, Sports, Science and Technology; Ministry of Health, Labour and Welfare; Ministry of Economy, Trade and Industry), and the study protocol, ensuring the protection of participants' rights. The trial was pre-registered with the University Hospital Medical Information Network (UMIN) (Registration Date: February 20, 2024, UMIN Trial ID: UMIN000053655).

Supplementary Tablets (Test Samples)

To conduct an exploratory investigation, we used two dosage levels for which prior studies have demonstrated efficacy in vascular function and post-exercise fatigue.[16,20,22] The investigational product with two dosages (low-dose lactotripeptides [LD] and high-dose lactotripeptides [HD]) were manufactured as follows. Initially, casein enzymatic hydrolysate was produced according to the method described by Mizuno et al.[23] This casein enzymatic hydrolysate was subsequently mixed with excipients and lubricants, followed by tableting to obtain tablets. These tablets were further coated with a coating agent to produce tablets containing Val-Pro-Pro (VPP) and Ile-Pro-Pro (IPP) (referred to as LD and HD). The difference in VPP and IPP dosages in the test foods (LD and HD) was adjusted by varying the amount of casein hydrolysate. Placebo tablets (referred to as placebo) were manufactured by replacing the casein enzymatic hydrolysate with casein sodium. The compositions of the test foods and placebo are shown in Table 1.

Analysis by liquid chromatography-tandem mass spectrometry revealed that the three test tablets (722.4±15 mg) contained 0.7 mg VPP and 1.0 mg IPP in the LD group, and 1.4 mg VPP and 2.0 mg IPP in the HD group, whereas the placebo contained none. Nutritional analysis showed no differences in energy or sodium content among the test foods. To conduct a double-blind study, the manufactured active and placebo tablets were indistinguishable in terms of appearance, taste, and smell. Adherence was monitored by tablet count (i.e., number of tablets dispensed and returned) and the participants' daily records. Participants were instructed to consume the test foods daily, preferably prior to exercise. If pre-exercise intake was not feasible, they were permitted to consume it at any convenient time during the day. At week 0, the test food was administered before exercise upon arrival at the facility.

Table 1. Composition of test and placebo tablets used in the study by daily dose (three tablets).

Component	Unit	Placebo group	LD group	HD group
Energy	(kcal)	2.8	2.7	2.8
Protein	(g)	0.4	0.4	0.3
Val-Pro-Pro	(mg)	0	0.7	1.4
Ile-Pro-Pro	(mg)	0	1.0	2.0
Fat	(g)	<0.1	<0.1	<0.1
Carbohydrate	(g)	0.3	0.3	0.3
Sodium	(mg)	4.6	4.9	5.2
Ash	(g)	<0.1	<0.1	<0.1

HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Exercise Procedure

Measurements of thigh circumference, subjective questionnaires, and other assessments were conducted during the preliminary examination, on the first day of investigational product intake (0w), and after 4 weeks (4w).

To evaluate exercise performance (including explosive power, strength, and endurance), an anaerobic power test was conducted using a cycle ergometer (POWER MAX V3 Pro, Konami Sports Co., Ltd., Tokyo, Japan). The test involved three sets of pedaling a weighted pedal with maximum effort for 10 s, with a 120-s rest between sets. The weight load on the pedal for the first set was automatically adjusted based on the participants' sex and body weight. For the second and third sets, the weight load was automatically adjusted according to the pedal cadence (rpm) of the previous set. The load was set so that the peak of the power curve (force × velocity) occurred between the load of the first set and the third set. Additionally, the load increased progressively from the first to the third set, ensuring that the pedal cadence decreased accordingly when participants exerted maximum effort. The weight load for each set ranged from 0.1 (kp) to 12 (kp) and was set in increments of 0.1 (kp). The top of the peak of the power curve, calculated from the results of weight load and pedal cadence for three sets, was defined as "anaerobic power." Notably, the exercise protocol used in this study offers an advantage for evaluating concentric lower-limb contractions, as it allows the load to be appropriately adjusted according to individual exercise capacity to ensure maximal effort across all participants. Furthermore, previous comparisons between leg press and cycle ergometer exercises have reported that no significant differences in objective indicators of post-exercise muscle pump or muscle response.[24]

Measurements of Thigh Circumference

The method and timing of thigh circumference measurements were based on previous reports.[25,26] Measurements were taken at the midpoint of the femur (from the greater trochanter to the femoral condyle) using a tape measure. Measurements were performed immediately before and after the exercise load (within 1 minute after the anaerobic power test). Each measurement was conducted twice or thrice, and the arithmetic mean of the two measurements with a difference <0.3 cm was adopted as the thigh circumference measurement.

Questionnaires to Assess Physical Condition

To subjectively evaluate the physical condition of the participants, a five-point Likert scale was used to assess muscle pump, fatigue, and motivation for training. The scale options were: 1: Feel very strongly, 2: Feel moderately, 3: Feel the same as before, 4: Feel less than before, 5: Feel nothing at all. The muscle pump effect was evaluated immediately after the exercise load, while fatigue and motivation for training were assessed before the exercise load, immediately after the exercise load, and upon waking the next day.

FMD

FMD was measured using the UNEX EF18VG (UNEX Corporation, Aichi, Japan). A cuff was placed on the arm of the participant for occlusion, and ultrasound gel was applied to the ultrasound probe, which was subsequently placed on the arm to obtain ultrasound images. The probe was moved in parallel until the short-axis image of the blood vessel appeared on the display, at which point the probe was fixed. The center of the blood vessel's short-axis image on the screen was tapped to adjust the position of the vessel, and the baseline measurement was initiated. Next, the occlusion button on the screen was tapped to initiate a 5-min occlusion, followed by a 2-min post-release measurement.

Blood and Urine Tests

Blood tests were performed to measure the following parameters: total protein, albumin, total bilirubin, alkaline phosphatase/International Federation of Clinical Chemistry and Laboratory Medicine, lactate dehydrogenase/International Federation of Clinical Chemistry and Laboratory Medicine, aspartate aminotransferase, alanine aminotransferase, gamma glutamyltransferase, creatine kinase, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, urea nitrogen, creatinine, uric acid, sodium, potassium, chlorine, calcium, dehydroepiandrosterone sulfate, glucose, white blood cells, red blood cells, hemoglobin, hematocrit, and platelets. Urine tests were performed to measure the following parameters: protein, glucose, urobilinogen, bilirubin, and occult blood.

Body Measurements

Height was measured during the preliminary examination. Weight, body mass index (BMI), and body fat percentage were measured using the InBody570 (InBody Japan Inc., Tokyo, Japan) during the preliminary examination, on the first day of test food intake (0w), and after 4 weeks (4w). Lean body mass was calculated based on total body fat percentage and body weight.

Physiological Tests

The blood pressure (systolic and diastolic) and pulse rate were measured using the TM-2656 (A&D Company, Limited, Tokyo, Japan).

Statistical Analysis

The measured values were expressed as the mean ± standard error. Inter-group comparisons between the placebo group and each test food group, using the actual values and changes from 0w to 4w (Δ0–4w), were evaluated by Dunnett's test. Temporal comparisons between 0w and 4w using actual values were evaluated by the paired *t*-test. Inter-group comparisons of questionnaire responses between the placebo group and each test food group were evaluated by Steel's test. Temporal comparisons of questionnaire responses between 0w and 4w were evaluated by the Wilcoxon signed-rank test. Correlations between various parameters, including actual values and changes from 0w to 4w (Δ0–4w), were evaluated using Pearson's product-moment correlation coefficient. Correlations involving questionnaire responses and changes were evaluated using Spearman's rank correlation coefficient. Statistical analysis software used in this study included Microsoft Excel (Microsoft Corporation, Redmond, WA, USA), IBM SPSS Statistics (IBM Japan, Ltd., Tokyo, Japan), and Excel Statistics (Social Survey Research Information Co., Ltd., Tokyo, Japan). $P < 0.05$ was considered statistically significant.

Results

Subjects

A flow chart of participant selection is shown in Figure 2. Preliminary examinations were conducted on 111 individuals. Subjects provided informed consent to participate in the study. Of the 96 individuals who completed the preliminary examinations, those who met the inclusion criteria, did not meet the exclusion criteria, and showed no clinical abnormalities were considered eligible for the study. From these candidates, individuals with an FMD ≥10.0, a thigh circumference change of ±1.0 cm or more compared to the overall average before and after exercise using PowerMax V3 Pro, or who selected the highest rating ("1: Feel very strongly") on a five-point questionnaire immediately after exercise were excluded. Regarding changes in thigh circumference, the present study involved a limited sample size. To minimize measurement variability, participants whose changes in thigh circumference deviated substantially from the mean were excluded. Likewise, for FMD, in order to reduce variability and to accurately assess the effect of LTP—which is known to exert its benefits through improvement of vascular endothelial function—participants with excessively high baseline FMD values were excluded. Among the remaining candidates, those with relatively high exercise frequency, not taking functional supplements contributing to muscle mass increase, and not experiencing health issues after exercise that would hinder immediate thigh circumference measurement were prioritized, resulting in the selection of 36 participants.

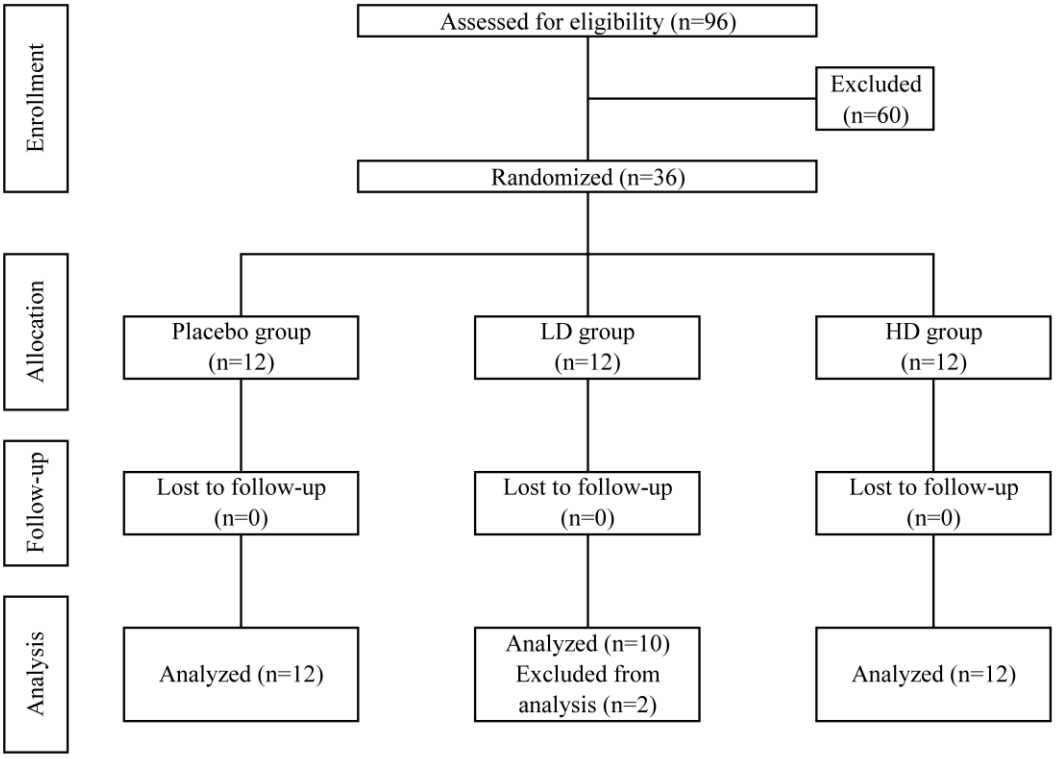


Figure 2. Flow chart of this study. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Of the 36 participants who entered the study, two were excluded (one for taking medication that reduces blood flow during the study period and one for not performing the exercise load with full effort after 4 weeks of test food intake), leaving 34 participants for analysis (Table 2).

Table 2. Participant characteristics before the ingestion of test and placebo tablets.

Characteristic	Unit	Placebo group	LD group	HD group
Number of participants	n	12	10	12
Age	years	35 ± 3.1	35 ± 2.6	35.6 ± 2.9
Height	cm	170.7 ± 1.7	172.1 ± 1.8	173.4 ± 1.2
Weight	kg	67.2 ± 2	69.6 ± 1.7	65.2 ± 2.8
Body mass index	kg/m²	23.1 ± 0.6	23.5 ± 0.6	21.6 ± 0.8
Body fat	%	18.6 ± 1.2	22.1 ± 1.7	17.9 ± 1.4
Systolic blood pressure	mmHg	114.2 ± 2.3	113.7 ± 4.2	118.8 ± 3.1
Diastolic blood pressure	mmHg	70.0 ± 2.3	72.8 ± 3	73.2 ± 2.5
Pulse rate	bpm	70.6 ± 2.4	77.5 ± 3.3	65.7 ± 3.6
FMD	%	4.7 ± 0.6	5.3 ± 0.5	6.1 ± 0.6
Anaerobic power	W/kg	9.5 ± 0.4	9.3 ± 0.4	9.5 ± 0.5
Difference in thigh circumference pre- and post-exercise	cm	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.1

Values are presented as the mean ± standard error, unless otherwise indicated. FMD, flow-mediated dilation; HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Training type and frequency, as well as adherence to the test food intake, were confirmed through lifestyle diaries. During the 4-week study period, participants performed leg training aimed at muscle hypertrophy at least once every 2 weeks. There were no statistical differences in training frequency of whole-body resistance training between the study groups (placebo group: 3.1 ± 0.4, LD group: 2.4±0.4, HD group: 2.6±0.4 sessions/week) and frequency of leg resistance training between the study groups (placebo group: 2.3±0.4, LD group: 1.7±0.3, HD group: 2.5±0.4 sessions/week). The mean adherence rate was 100% in all groups, and there was no significant difference in the ingestion rate between the groups.

Anaerobic Power

The results of anaerobic power per body weight obtained from the anaerobic power test using the POWER MAX V3 Pro are shown in Table 3. There were no statistically significant changes over time from 0w to 4w or between the groups.

Table 3. Anaerobic power.

	Group	0w	4w	Δ0–4w
Anaerobic power (W/kg)	Placebo (n=12)	9.4 ± 0.4	9.7 ± 0.4[#]	0.3 ± 0.1
	LD (n=10)	9.5 ± 0.4	9.5 ± 0.3	0.0 ± 0.1
	HD (n=12)	9.6 ± 0.5	9.8 ± 0.5	0.2 ± 0.1

Values are presented as the mean ± standard error. [#] A trend towards significance compared to 0w ($p < 0.1$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Thigh Circumference

The results of thigh circumference measurements taken before and after training using the POWER MAX V3 Pro, as well as the changes in thigh circumference before and after exercise, are shown in Table 4.

Table 4. Thigh circumference.

	Group	0w	4w	Δ0–4w
Pre-exercise thigh circumference (cm)	Placebo (n=12)	53.0 ± 1.2	53.4 ± 1.2	0.3 ± 0.3
	LD (n=10)	54.4 ± 0.9	54.7 ± 1.0	0.3 ± 0.4
	HD (n=12)	51.1 ± 1.2	52.3 ± 1.2[##]	1.1 ± 0.3
Immediately post-exercise thigh circumference (cm)	Placebo (n=12)	54.0 ± 1.2[††]	54.1 ± 1.1[††]	0.1 ± 0.3
	LD (n=10)	55.1 ± 0.9[††]	55.6 ± 0.9[††]	0.5 ± 0.3
	HD (n=12)	52.0 ± 1.2[††]	53.1 ± 1.3[††,##]	1.1 ± 0.2**
Difference in thigh circumference pre- and post-exercise (cm)	Placebo (n=12)	1.0 ± 0.1	0.8 ± 0.1	-0.2 ± 0.2
	LD (n=10)	0.8 ± 0.1	0.9 ± 0.2	0.1 ± 0.2
	HD (n=12)	0.9 ± 0.2	0.9 ± 0.1	0.0 ± 0.2

Values are presented as the mean ± standard error. [##] Significant difference compared to 0w ($p < 0.05$). [††] Significant difference compared to pre-exercise ($p < 0.05$). ** Significant difference compared to the placebo group ($p < 0.05$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

At 0w, there were no statistically significant differences observed between the groups. In the HD group, thigh circumference before exercise significantly increased at 4w compared to 0w (p=0.002), whereas there were no changes observed in the placebo group. Additionally, the change in thigh circumference immediately after exercise (Δ0–4w) significantly increased in the HD group compared to the placebo group (p=0.032) (Figure 3).

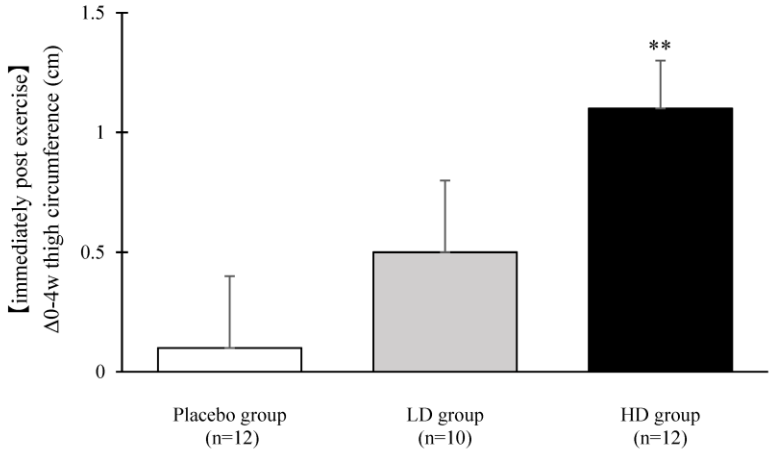


Figure 3. Comparison of mean thigh circumference immediately after exercise from 0w to 4w. ** Significant difference compared to the placebo group ($p < 0.05$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Compared to pre-exercise measurements, thigh circumference post exercise significantly increased at both 0w and 4w across all groups, indicating that the exercise using the POWER MAX V3 Pro effectively induced muscle pump (Table 4). However, there were no significant differences observed between the groups in the changes in thigh circumference before and after exercise, or in those from 0w to 4w.

Subjective Evaluation of Muscle Pump Effect Immediately After Exercise
The results of the average scores from the five-point Likert scale are shown in Table 5.

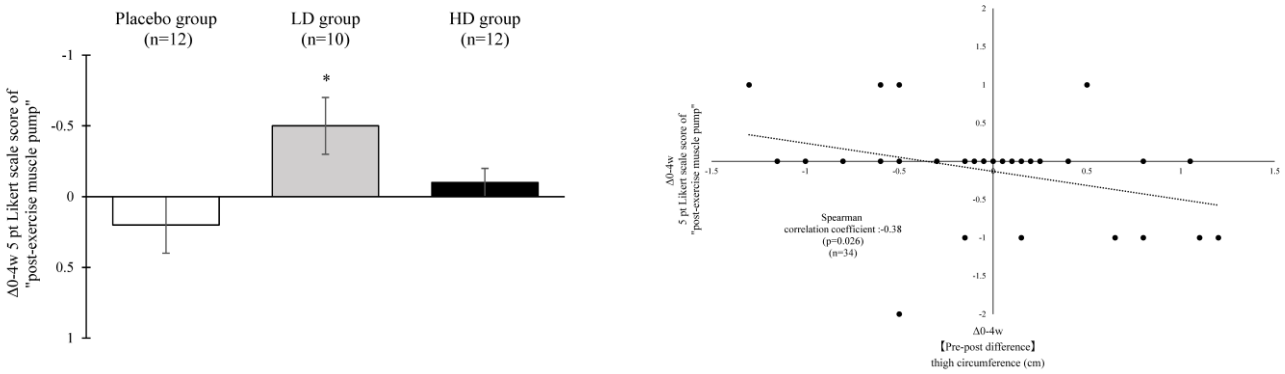
Table 5. Five-point Likert scale "post-exercise muscle pump".

	Group	0w			4w			Δ0–4w		
Post-exercise muscle pump	Placebo (n=12)	2.4	±	0.1	2.6	±	0.2	0.2	±	0.2
	LD (n=10)	2.4	±	0.3	1.9	±	0.2**,#	−0.5	±	0.2*
	HD (n=12)	2.2	±	0.2	2.1	±	0.2	−0.1	±	0.1

Values are presented as the mean ± standard error. # A trend towards significance compared to 0w ($p < 0.1$). * A trend towards significance compared to the placebo group ($p < 0.1$). ** Significant difference compared to the placebo group ($p < 0.05$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

In the LD group, the score for the muscle pump effect after training significantly improved after 4 weeks compared to the placebo group (p=0.042). There was also a trend towards the change in the difference scores of LD group before and after exercise from 0w to 4w compared to the score of the placebo group (p=0.053) (Figure 4a). Although there were no significant differences between groups in the objective measure of thigh circumference change before and after exercise, a significant negative correlation was found between the change in thigh circumference before and after exercise (Δ0–4w) and the change in the five-point Likert scale scores (Δ0–4w) (p=0.026) (Figure 4b). This indicates that participants who showed improved muscle pump effects in the subjective five-point questionnaire also showed

improvements in the objective measure of thigh circumference change before and after exercise (lower scores on the five-point questionnaire indicate greater effect).



(**a**) (**b**)

Figure 4. (a) Changes in the difference in muscle pump scores of five-point Likert scale before and after exercise from 0w to 4w. Lower scores indicate a greater effect. * A trend toward significance compared to the placebo group ($p < 0.1$). **(b)** Correlation between changes in thigh circumference before and after exercise (Δ0–4w) and changes in five-point Likert scale scores (Δ0–4w). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Body Composition

The results for body weight, BMI, body fat mass, and lean body mass are shown in Table 6.

Table 6. Body composition parameters.

Parameter	Group	0w			4w			Δ0–4w		
Body weight (kg)	Placebo (n=12)	67.4	±	2.1	67.0	±	2.1	−0.3	±	0.3
	LD (n=10)	69.9	±	1.9	69.7	±	1.9	−0.2	±	0.4
	HD (n=12)	65.3	±	2.8	66.0	±	2.9##	0.7	±	0.2**
BMI (kg/m²)	Placebo (n=12)	23.1	±	0.6	23.0	±	0.6	−0.1	±	0.1
	LD (n=10)	23.6	±	0.7	23.6	±	0.7	0.0	±	0.1
	HD (n=12)	21.7	±	0.8	21.9	±	0.8##	0.3	±	0.1**
Body fat (kg)	Placebo (n=12)	12.8	±	1.2	12.4	±	1.2#	−0.4	±	0.2
	LD (n=10)	15.4	±	1.5	14.9	±	1.4	−0.5	±	0.3
	HD (n=12)	11.8	±	1.2	11.7	±	1.3	−0.1	±	0.3
Lean body mass (kg)	Placebo (n=12)	54.6	±	1.3	54.6	±	1.4	0.0	±	0.2
	LD (n=10)	54.5	±	1.9	54.8	±	1.9	0.3	±	0.5
	HD (n=12)	53.5	±	2.3	54.3	±	2.3##	0.9	±	0.4

Values are presented as the mean ± standard error. #A trend towards significance compared to 0w ($p < 0.1$). ## Significant difference compared to 0w ($p < 0.05$). ** Significant difference compared to the placebo group ($p<0.05$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. BMI, body mass index; HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

In the HD group, body weight (p=0.035), BMI (p=0.031), and lean body mass (p=0.031) significantly increased after 4 weeks compared to 0w, whereas there were no changes observed in the placebo group. Additionally, the changes in body weight (p=0.015) and BMI (p=0.009) (Δ0–4w) significantly improved in the HD group compared to the placebo group.

Vascular Function

There were no significant differences observed in FMD, blood pressure, or pulse rate among the participants in this study (Table 7).

Table 7. Vascular function parameters.

Parameter	Group	0w			4w			Δ0–4w		
FMD (%)	Placebo (n=12)	5.0	±	0.5	5.9	±	0.7#	1.0	±	0.5
	LD (n=10)	6.0	±	0.8	6.8	±	0.7	0.8	±	0.8
	HD (n=12)	5.3	±	0.6	6.0	±	0.7	0.7	±	0.7
Systolic blood pressure (mmHg)	Placebo (n=12)	112.5	±	2.4	113.3	±	2.5	0.8	±	2.8
	LD (n=10)	119.8	±	4.5	118.9	±	5.0	−0.9	±	3.3
	HD (n=12)	116.8	±	2.6	112.4	±	3.5	−4.3	±	3.0
Diastolic blood pressure (mmHg)	Placebo (n=12)	70.8	±	2	71.1	±	2.2	0.3	±	1.8
	LD (n=10)	75.3	±	3.6	71.2	±	2.8	−4.1	±	2.3
	HD (n=12)	70.4	±	2.1	68.7	±	3.6	−1.8	±	1.8
Pulse rate (bpm)	Placebo (n=12)	68.3	±	2.1	67.7	±	2.8	−0.6	±	2.6
	LD (n=10)	72.9	±	3.4	73.9	±	3.5	1.0	±	2.0
	HD (n=12)	64.9	±	3.6	68.3	±	3.8	3.3	±	3.0

Values are presented as the mean ± standard error. # Trend towards significance compared to 0w ($p < 0.1$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. FMD, flow-mediated dilation; HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Additionally, at 0w, there were participants with FMD <7% (i.e., borderline or endothelial dysfunction) in the placebo group (n=10), LD group (n=6), and HD group (n=10). Subgroup analysis of these participants (Table 8) showed a trend towards increased FMD in the HD group after 4 weeks compared to 0w (p=0.081), whereas there were no changes observed in the placebo group.

Table 8. FMD (subgroup analysis).

	Group	0w			4w			Δ0–4w		
FMD (%)	Placebo (n=10)	4.4	±	0.4	5.3	±	0.6	0.9	±	0.6
Participants with	LD (n=6)	4.3	±	0.6	5.4	±	0.7	1.1	±	1.2
FMD <7% at 0w	HD (n=10)	4.7	±	0.5	6.0	±	0.8#	1.3	±	0.6

Values are presented as the mean ± standard error. # Trend towards significance compared to 0w ($p < 0.1$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. FMD, flow-mediated dilation; HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Furthermore, we evaluated the relationship between FMD, an indicator of a vasodilatory effect due to the enhancement of NO production by LTP, and muscle pump. In individuals with FMD <7%, a significant positive correlation was found between the change in FMD over 4 weeks (Δ0–4w) and the change in thigh circumference before and after exercise load (Δ0–4w), which is an objective indicator of muscle pump (p=0.021) (Figure 5).

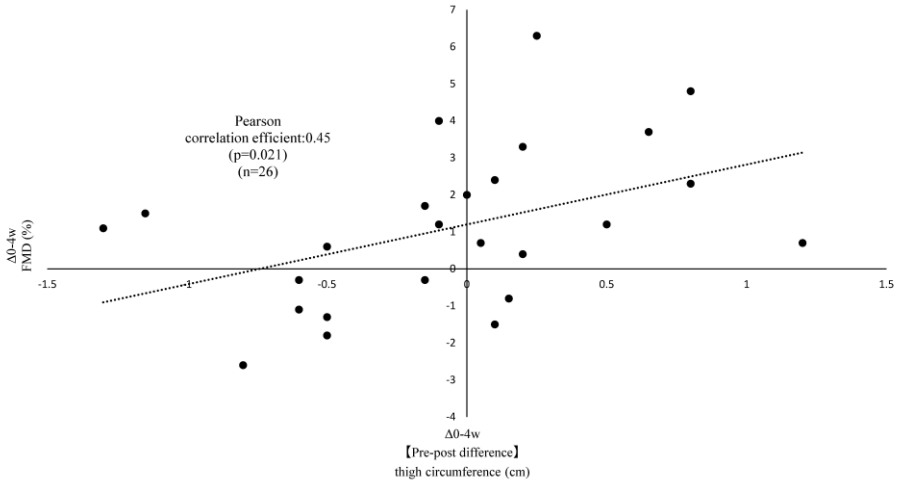


Figure 5. Correlation between changes in FMD in participants with FMD <7% (at 0w) from 0w to 4w, and changes in thigh circumference before and after exercise from 0w to 4w. 0w and 4w denote the first day and 4 weeks of test food intake, respectively. FMD, flow-mediated dilation; HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Fatigue

The change in the pre-post difference in fatigue scores of the five-point Likert scale before and after exercise from 0w to 4w ([score after exercise at 4w − score before exercise at 4w] – [score after exercise at 0w − score before exercise at 0w]) significantly improved in the HD group compared to the placebo group (Figure 6).

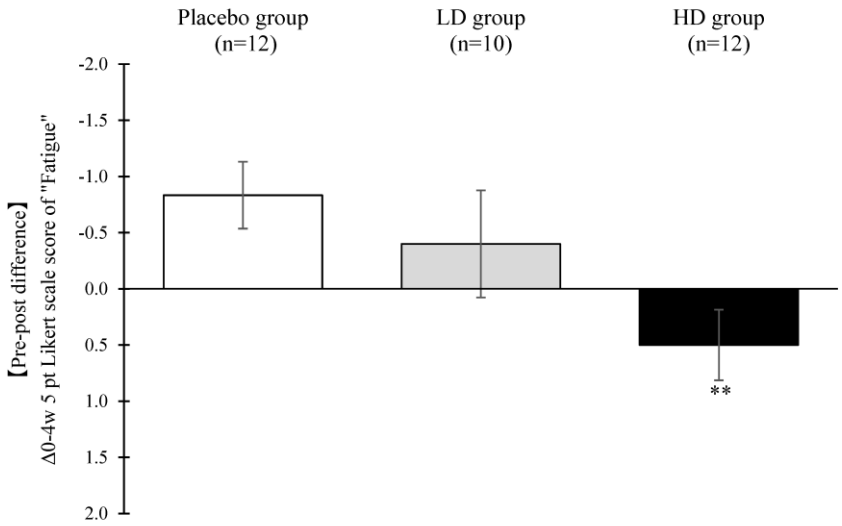


Figure 6. Changes in the pre-post difference in fatigue scores of the five-point Likert scale before and after exercise from 0w to 4w. ** Significant difference compared to the placebo group ($p < 0.05$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Motivation for Training

The results of the average scores from the five-point Likert scale at the three time points are shown in Table 9.

Table 9. Five-point Likert scale "motivation for training".

Motivation for training	Group	0w	4w	Δ0–4w
Pre-exercise	Placebo (n=12)	2.6 ± 0.1	2.5 ± 0.2	−0.1 ± 0.2
	LD (n=10)	2.6 ± 0.2	2.7 ± 0.3	0.1 ± 0.3
	HD (n=12)	2.8 ± 0.2	2.4 ± 0.2##	−0.4 ± 0.1
Post exercise	Placebo (n=12)	2.6 ± 0.1	2.3 ± 0.1	−0.3 ± 0.2
	LD (n=10)	2.2 ± 0.2	2.1 ± 0.2	−0.1 ± 0.2
	HD (n=12)	2.5 ± 0.2	2.3 ± 0.2#	−0.3 ± 0.1
Post-exercise morning	Placebo (n=12)	2.4 ± 0.1	2.7 ± 0.1	0.3 ± 0.2
	LD (n=10)	2.4 ± 0.2	2.3 ± 0.2	−0.1 ± 0.1
	HD (n=12)	2.7 ± 0.2	2.3 ± 0.2##	−0.3 ± 0.1**

Values are presented as the mean ± standard error. # Trend towards significance compared to 0w ($p < 0.1$). ## Significant difference compared to 0w ($p < 0.05$). ** Significant difference compared to the placebo group ($p < 0.05$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

In the HD group, scores significantly improved after 4 weeks compared to 0w before exercise (p=0.025) and upon waking the day after exercise (p=0.046), whereas there were no improvements observed in the placebo group. Additionally, in the HD group, there was a trend towards improvement immediately after exercise at 4w compared to 0w (p=0.083), whereas there were no improvements observed in the placebo group. Furthermore, the change in scores

from 0w to 4w (Δ0–4w) upon waking the day after exercise significantly improved in the HD group compared to the placebo group (p=0.043) (Figure 7).

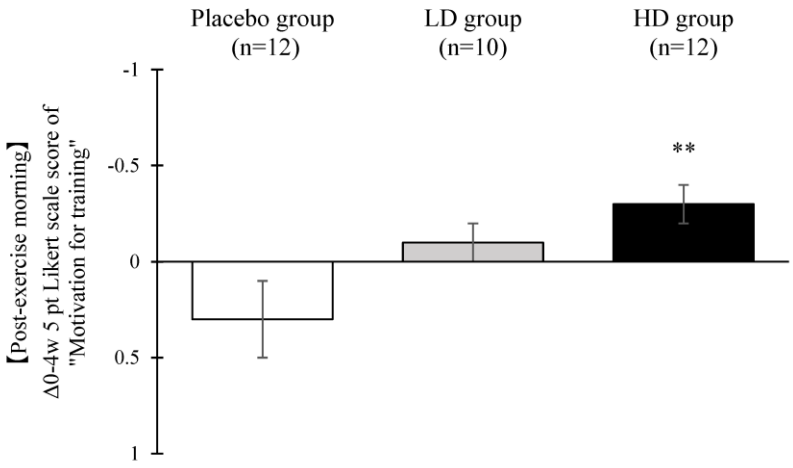


Figure 7. Changes in motivation scores of the five-point Likert scale for training upon waking the day after exercise from 0w to 4w. ** Significant difference compared to the placebo group ($p < 0.05$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

Blood and Urine Tests

The results for the mean low-density lipoprotein (LDL) cholesterol levels are shown in Table 10.

Table 10. Low-density lipoprotein cholesterol.

	Group	0w	4w	Δ0–4w
Low-density lipoprotein cholesterol (mg/dL)	Placebo (n=12)	111.9 ± 7.9	113.6 ± 9.1	1.7 ± 3.3
	LD (n=10)	125.9 ± 8.1	122.0 ± 8.2	−3.9 ± 3.6
	HD (n=12)	104.8 ± 6.3	98.3 ± 6.5##	−6.4 ± 2.4

Values are presented as the mean ± standard error. ## Significant difference compared to 0w ($p < 0.05$). 0w and 4w denote the first day and 4 weeks of test food intake, respectively. HD, high-dose lactotripeptides; LD, low-dose lactotripeptides.

In the HD group, LDL cholesterol levels significantly decreased at 4w compared to 0w (p=0.021), whereas there was no decrease observed in the placebo group. Additionally, several other parameters showed significant differences between the test food groups and significant temporal changes; nonetheless, these observations were not deemed adverse events by the principal investigator (data not shown).

Discussion

A placebo-controlled, double-blind, parallel-group comparison study was conducted to evaluate the effects of 4 weeks of continuous intake of tablets containing VPP and IPP on muscle pump, muscle hypertrophy, fatigue, and motivation in individuals with a history of lower body strength training aimed at muscle hypertrophy at least once every 2 weeks. The results showed that the intake of test food containing VPP 0.7 mg and IPP 1.0 mg per day (LD) significantly improved the subjective evaluation of muscle pump compared to placebo. VPP 1.4 mg and IPP 2.0 mg per day (HD) did not show significant differences in subjective evaluation. As explained below, HD demonstrated positive results in the objective evaluation. Although there were no significant differences between groups in the objective measure of changes in thigh circumference before and after exercise, a significant correlation was found between the subjective evaluation results and the changes in thigh circumference over 4 weeks. Therefore, participants who felt a stronger muscle pump subjectively also showed greater changes in thigh circumference. These findings may suggest that LTP intake has a beneficial effect on muscle pump immediately after exercise.

LTP has been reported to promote NO production through eNOS activation and ACE inhibitory activity, and previous studies have suggested improvements in blood flow and endothelial function.[15,16] In this study, a positive correlation

was observed between changes in FMD and objective muscle pump indicators in participants with low baseline FMD, indicating that enhanced blood flow may be associated with muscle pump. This finding aligns with existing reports on NO-promoting ingredients such as arginine and citrulline.[11] However, given that this was a short-term, small-sample exploratory study, further research is required to confirm causality. Although citrulline and arginine are widely used as NO-promoting ingredients, previous clinical trials have rarely demonstrated objective improvements in muscle pump.[9,10,27] In contrast, this study showed improvements in both subjective ratings and objective measures such as thigh circumference in the LTP group. These results suggest that LTP may exert efficacy through mechanisms distinct from citrulline and arginine, and that combining these ingredients could potentially produce greater synergistic effects. However, as this was an exploratory study with a small sample size, particularly the observed increase in FMD in the HD group should be interpreted cautiously. Because this was a subgroup analysis, it is possible that the study lacked sufficient power to detect the moderate effect ($d = 0.6$). Given the limited nature of this investigation, future studies with larger sample sizes are required to confirm these findings.

This study found a potential effectiveness of training using the POWER MAX V3 Pro in some data related to muscle pump. However, the objective data on muscle pump volume between groups showed large variability, and there were no significant differences recorded compared to the placebo group. Increasing the number of participants and designing trials targeting participants more sensitive to LTP effects, considering vascular function effects, may provide clearer data on objective muscle pump volume. In the HD group (test food containing VPP 1.4 mg and IPP 2.0 mg), there were no statistically significant results obtained for subjective muscle pump evaluation. Nonetheless, both subjective and objective evaluations showed higher average scores at 0w and maintained similar scores after 4 weeks. In contrast, the placebo group showed lower scores in both subjective and objective evaluations over 4 weeks. Previous reports indicated that a single daily intake of VPP 1.4 mg and IPP 2.0 mg, the same amount as that administered to the HD group, reduced muscle soreness after training.[22] Therefore, the HD group may have shown higher scores at 0w due to the immediate effects of a single intake, and the effects may have been maintained after 4 weeks.

Interestingly, in this study, the HD group showed significant improvements in thigh circumference and lean body mass over time, and significant improvements in thigh circumference after training, including muscle pump effects, compared to the placebo group. This is the first time, to our knowledge, that such positive effects of LTP have been observed. It has been reported that muscle pump is effective for muscle hypertrophy. Hirono et al reported a significant positive correlation between muscle pump and muscle hypertrophy in participants who performed resistance training thrice per week for 6 weeks.[4] In a review, Schoenfeld and Contreras reported that muscle pump activates hypertrophic signaling pathways, such as the mechanistic target of rapamycin (mTOR) and mitogen-activated protein kinase (MAPK) pathways, by strengthening the structure against pressure exerted on the cytoskeleton and cell membrane.[1] However, lean body mass in this study was assessed using bioelectrical impedance analysis (BIA), which does not allow differentiation between fluid shifts and true muscle hypertrophy, representing a methodological limitation. Therefore, these results suggest that LTP intake may improve objective muscle pump and could be effective for muscle hypertrophy; as further verification is needed to determine whether the observed increase in lean body mass reflects true muscle hypertrophy.

Furthermore, this study suggested that daily intake of HD test food containing VPP 1.4 mg and IPP 2.0 mg for 4 weeks significantly reduced fatigue before and after training compared to placebo. Previous reports have shown effects of a single intake of LTP on muscle soreness and fatigue.[22] Hamasaki et al reported that LTP intake improved cerebral blood oxygen levels,[28] while Iwasa et al showed that LTP intake suppressed the decrease in maximal oxygen consumption and improved glucose metabolism during resistance training.[29] Therefore, LTP may enhance oxygen transport to peripheral tissues and favor glucose metabolism, suppressing anaerobic metabolism. Additionally, it was considered that the intake of LTP might have improved metabolism and reduced fatigue due to increased blood flow.

This study also suggested that daily intake of test food containing VPP 1.4 mg and IPP 2.0 mg improved motivation for training before, immediately after, and the day after training. Although the detailed mechanism underlying motivation improvement is unclear, LTP has been reported to increase cerebral blood flow velocity and improve cognitive function related to increased cerebral blood oxygen levels.[28,30] These effects of LTP on the brain may contribute to improved focus and motivation for exercise. There are few studies evaluating the relationship between muscle pump and motivation. However, the subjective feeling of improved muscle pump and effective muscle hypertrophy during the study period may have led participants to feel the effects of strength training, enhancing their motivation. Additionally, the reduction in fatigue from LTP intake may have contributed to increased motivation for exercise. Further studies are needed to elucidate the mechanisms underlying motivation improvement.

Moreover, this study suggested a significant reduction in LDL cholesterol with daily intake of test food containing VPP 1.4 mg and IPP 2.0 mg. Statin therapy in patients with hypercholesterolemia has been reported to reduce LDL cholesterol through vasodilation via NO production.[31] Therefore, it is suggested that LTP intake in this study reduced LDL cholesterol through the promotion of vasodilation.

Nevertheless, the present study had several limitations. Specifically, we were unable to rigorously monitor or control the participants' daily protein intake and exercise intensity. Training intensity and volume were not standardized across participants; therefore, if differences in training volume existed between individuals, the muscular adaptations to exercise could have varied substantially. Consequently, to enable a more definitive interpretation of changes in muscle mass, future studies should control training volume and verify outcomes under standardized conditions. Additionally, lean body mass was assessed using bioelectrical impedance analysis, which does not allow for the exclusion of fluid-related influences. These methodological constraints may have affected the accuracy of the results. In future studies, we plan to implement stricter controls regarding protein intake and physical activity levels, as well as utilize dual-energy X-ray absorptiometry for lean body mass measurement. These improvements will enable a more precise evaluation of the hypertrophic effects of LTP. Finally, since no previous studies have investigated the effects of LTP intake on muscle pump or muscle mass, it was not possible to perform a sample size calculation. Therefore, this study was positioned as an exploratory investigation with a small sample size of only 12 participants per group. Consequently, the statistical power was limited and may not have been sufficient to detect moderate effects, increasing the risk of false negatives for borderline results. Based on the findings of this study, further confirmatory trials should be conducted in the future.

No adverse events attributable to the test food were observed, including dry cough—a symptom commonly associated with ACE inhibitors. Furthermore, previous studies involving excessive intake of foods containing VPP and IPP have not reported any adverse events.[32] Based on these findings, the test food is considered to pose no safety concerns.

Conclusions

This exploratory study investigated the effects of 4 weeks of continuous intake of tablets containing VPP and IPP on muscle pump immediately after exercise in strength trained individuals. The results suggested significant increases in thigh circumference and lean body mass over 4 weeks in the HD group. Additionally, thigh circumference immediately after exercise significantly increased in the HD group compared to the placebo group over 4 weeks. Subgroup analysis of individuals with FMD <7% suggested a trend of increased FMD over 4 weeks in the HD group. A significant positive correlation was observed between the change in FMD and the change in thigh circumference before and after exercise. In the LD group, subjective questionnaire scores for muscle pump significantly improved, showing a significant difference compared to the placebo group. The HD group also showed a significant reduction in subjective fatigue scores compared to the placebo group. Furthermore, the HD group demonstrated significant improvements in motivation for training, as indicated by subjective questionnaire scores, over 4 weeks, with significant differences recorded compared to the placebo group. These results suggest that continuous intake of tablets containing VPP and IPP for 4 weeks may enhance muscle pump effects, increase muscle mass, reduce training-induced fatigue, and improve motivation for training in individuals with a habit of strength training.

Funding: This research was funded in part by Asahi Quality & Innovations, Ltd. The funder had no role in the design, collection, analysis, or interpretation of data.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Chiyoda Paramedical Care Clinic (protocol code 15000088 and date of approval: January 19, 2024).

Informed Consent Statement: Subjects provided informed consent to participate in the study.
Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors on request.

Acknowledgments: We thank Yoshiko Yasaka for technical support and the staff of CPCC Co., Ltd. for data collection. We also thank all volunteers for participating in this study.

Conflicts of Interest: The authors declare no conflicts of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

Abbreviations

The following abbreviations are used in this manuscript:

ACE	Angiotensin-converting enzyme
BMI	Body mass index
eNOS	Endothelial nitric oxide synthase
FMD	Flow-mediated dilation
HD	High-dose lactotripeptides
IPP	Ile-Pro-Pro
kp	Kilopond
LD	Low-dose lactotripeptides
LDL	Low-density lipoprotein
LTP	Lactotripeptides
MAPK	Mitogen-activated protein kinase
mTOR	Mechanistic target of rapamycin
NO	Nitric oxide
VPP	Val-Pro-Pro

References

1. Schoenfeld BJ, Contreras B. The muscle pump: potential mechanisms and applications for enhancing hypertrophic adaptations. Strength Cond J. 2014;36:21–25. doi: 10.1097/SSC.0000000000000021
2. Takarada Y, Nakamura Y, Aruga S, Onda T, Miyazaki S, Ishii N. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J Appl Physiol. 2000;88:61–65. doi: 10.1152/jappl.2000.88.1.61
3. Wackerhage H, Schoenfeld BJ, Hamilton DL, Lehti M, Hulmi JJ. Stimuli and sensors that initiate skeletal muscle hypertrophy following resistance exercise. J Appl Physiol. (1985) 2019;126:30–43. doi: 10.1152/japplphysiol.00685.2018
4. Hirono T, Ikezoe, T, Taniguchi M, et al. Relationship between muscle swelling and hypertrophy induced by resistance training. J Strength Cond Res. 2020;36:359–364. doi: 10.1519/JSC.0000000000003478
5. Monaghan L. Looking good, feeling good: The embodied pleasures of vibrant physicality. Sociol Health Illn. 2001;23:330–356. doi: 10.1111/1467-9566.00255
6. Schwarzenegger A, Dobbins, B. The New Encyclopedia of Modern Bodybuilding. Simon and Schuster; 1998:68–69.
7. Vieira A, Blazevich A, Souza N, et al. Acute changes in muscle thickness and pennation angle in response to work-matched concentric and eccentric isokinetic exercise. Appl Physiol Nutr Metab. 2018;43:1069–1074. doi: 10.1139/apnm-2018-0055
8. Trexler ET, Keith DS, Schwartz TA, et al. Effects of citrulline malate and beetroot juice supplementation on blood flow, energy metabolism, and performance during maximum effort leg extension exercise. J Strength Cond Res. 2019;33:2321–2329. doi: 10.1519/JSC.0000000000003286
9. Gonzalez AM, Spitz RW, Ghigiarelli JJ, Sell KM, Mangine GT. Acute effect of citrulline malate supplementation on upper-body resistance exercise performance in recreationally resistance-trained men. J Strength Cond Res. 2018;32:3088–3094. doi: 10.1519/JSC.0000000000002373
10. Gonzalez AM, Yang Y, Mangine GT, Pinzone AG, Ghigiarelli JJ, Sell KM. Acute effect of L-citrulline supplementation on resistance exercise performance and muscle oxygenation in recreationally resistance trained men and women. J Funct Morphol Kinesiol. 2023;8:88. doi: 10.3390/jfmk8030088
11. Bürkle F, Doll J, Neide A, Gantz S, Tsitlakidis S, Fischer C. New perspectives for investigating muscular perfusion response after dietary supplement intake: an exploratory, randomized, double-blind, placebo-controlled crossover trial in healthy young athletes using contrast-enhanced ultrasound (CEUS). J Int Soc Sports Nutr. 2022;19:397–416. doi: 10.1080/15502783.2022.2097018
12. Gonzalez AM, Townsend JR, Pinzone AG, Hoffman JR. Supplementation with nitric oxide precursors for strength performance: a review of the current literature. Nutrients 2023;15:660. doi: 10.3390/nu15030660
13. Armin MK, Marco GV. Cardioprotective peptides from milk processing and dairy products: from bioactivity to final products including commercialization and legislation. Foods 2022;11:1270–1293. doi: 10.3390/foods11091270
14. Yamaguchi N, Kawaguchi K, Yamamoto N. Study of the mechanism of antihypertensive peptides VPP and IPP in spontaneously hypertensive rats by DNA microarray analysis. Eur J Pharmacol. 2009;620:71–77. doi: 10.1016/j.ejphar.2009.08.005

15. Hirota T, Nonaka A, Matsushita A, et al. Milk casein-derived tripeptides, VPP and IPP induced NO production in cultured endothelial cells and endothelium-dependent relaxation of isolated aortic rings. Heart Vessels 2011;26:549–556. doi: 10.1007/s00380-010-0096-y
16. Hatanaka M, Kanzato H, Nadaoka I, et al. Beneficial effect of lactotripeptide on peripheral blood flow in healthy volunteers: a randomized placebo-controlled double-blind study. Jpn Pharmacol Ther. 2021;49:73–82.
17. Nakamura Y, Yamamoto N, Sakai K, Okubo A, Yamazaki S, Takano T. Purification and characterization of angiotensin I-converting enzyme inhibitors from sour milk. J Dairy Sci. 1995;78:777–783. doi: 10.3168/jds.S0022-0302(95)76689-9
18. Sano J, Ohki K, Higuchi T, et al. Effect of casein hydrolysate, prepared with protease derived from Aspergillus oryzae, on subjects with high-normal blood pressure or mild hypertension. J Med Food 2005;8:423–430. doi: 10.1089/jmf.2005.8.423
19. Nakamura T, Mizutani J, Ohki K, et al. Casein hydrolysate containing Val-Pro-Pro and Ile-Pro-Pro improves central blood pressure and arterial stiffness in hypertensive subjects: a randomized, double-blind, placebo-controlled trial. Atherosclerosis 2011;219:298–303. doi: 10.1016/j.atherosclerosis.2011.06.007
20. Uchida N, Osawa K, Oki K, et al. Effect of tablets containing lactotripeptides (VPP, IPP) on vascular endothelial function in healthy subjects -a randomized, double-blind, placebo-controlled trial. Jpn Pharmacol Ther. 2016;44:1025–1034.
21. Tagawa K, Ra SG, Choi Y, Maeda S. Lactotripeptides supplementations alleviate the decrease in maximal isometric force following high-intensity eccentric exercise: a randomized, placebo-controlled, double-blinded clinical trial. Am J Phys Med Rehabil. 2018;97:370–374. doi: 10.1097/PHM.0000000000000867
22. Iwasa M, Aoi W, Nakayama A, et al. Milk casein hydrolysate alleviates muscle soreness and fatigue after downhill walking exercise in middle-aged to elderly men. Ann Sports Med Res. 2015;2:1045. doi: 10.47739/2379-0571/1045
23. Mizuno S, Nishimura S, Matsuura K, Gotou T, Yamamoto N. Release of short and proline-rich antihypertensive peptides from casein hydrolysate with an Aspergillus oryzae protease. J Dairy Sci. 2004;87:3183–3188. doi: 10.3168/jds.S0022-0302(04)73453-0
24. Steele J, Butler A, Comerford Z, et al. Similar acute physiological responses from effort and duration matched leg press and recumbent cycling tasks. Peer J. 2018;28;6:e4403. doi: 10.7717/peerj.4403
25. Freitas ED, Poole C, Miller RM, et al. Time course change in muscle swelling: high-intensity vs. blood flow restriction exercise. Int J Sports Med. 2017;38:1009–1016. doi: 10.1055/s-0043-118342
26. Wilson JM, Lowery RP, Joy JM, Loenneke JP, Naimo MA. Practical blood flow restriction training increases acute determinants of hypertrophy without increasing indices of muscle damage. J Strength Cond Res. 2013;27:3068–3075. doi: 10.1519/JSC.0b013e31828a1ffa
27. Greenberg D, Emerson, K, Ojalvo SP, Sylla S, Komorowski J. Inositol-stabilized arginine silicate reduces exercise induced muscle damage and increases perceived energy. J Exerc Nutr. 2023;6:5. doi: 10.53520/jen2023.103141
28. Hamasaki A, Akazawa N, Yoshikawa T, et al. Combined effects of lactotripeptide and aerobic exercise on cognitive function and cerebral oxygenation in middle-aged and older adults. Am J Clin Nutr. 2019;109:353–360. doi: 10.1093/ajcn/nqy235
29. Iwasa M, Aoi W, Mune K, et al. Fermented milk improves glucose metabolism in exercise-induced muscle damage in young healthy men. Nutr J. 2013:12:83. doi: 10.1186/1475-2891-12-83
30. Akazawa N, Hamasaki A, Tanahashi K, et al. Lactotripeptide ingestion increases cerebral blood flow velocity in middle-aged and older adults. Nutr Res. 2018;53:61–66. doi: 10.1016/j.nutres.2018.03.009
31. John S, Schlaich M, Langenfeld M, et al. Increased bioavailability of nitric oxide after lipid-lowering therapy in hypercholesterolemic patients. Circulation 1998;98:211–216. doi: 10.1161/01.cir.98.3.211
32. Ishida Y, Shibata Y, Fukuhara I, Yano Y, Takehara I, Kaneko K. Effect of an excess intake of casein hydrolysate containing Val-Pro-Pro and Ile-Pro-Pro in subjects with normal blood pressure, high-normal blood pressure, or mild hypertension. Biosci Biotechnol Biochem. 2011;75:427–433. doi: 10.1271/bbb.100560.