

Effects of Foods Containing Collagen Peptides on Knee Joint Pain and Mobility: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study

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Abstract

Background: Joint function is essential for the smooth performance of daily activities. Maintenance of knee joint function and reduction in pain and other symptoms contribute to maintaining and improving quality of life (QOL). Collagen peptides have been shown to alleviate joint pain and discomfort. Therefore, we investigated the effects of foods containing collagen peptides on knee joint function in healthy adult men and women. **Methods:** Two randomized, double-blind, placebo-controlled, parallel-group studies (Trial 1 and Trial 2) were conducted. Both studies evaluated the effects of foods containing collagen peptides on knee joint function. Forty-six participants were selected for each study and randomly assigned to one of two groups: the active food group and the placebo food group. The participants consumed either the active food (containing 2.0 g/day of collagen peptides) or the placebo food for 12 weeks. Trial 1 evaluated the Japanese Orthopaedic Association (JOA) score. Trial 2 evaluated the Japanese Knee Osteoarthritis Measure (JKOM) and visual analog scale (VAS) scores. **Results:** The active food group showed significant improvements in JOA (total, I, and II scores) (Trial 1), JKOM (total, II, III, and IV scores), and VAS scores (Trial 2) compared with the placebo food group ($p < 0.05$). No adverse events attributable to the study food were observed during the study period. **Conclusions:** Our findings indicate that foods containing collagen peptides can improve mobility and relieve knee joint pain in both adult men and women.

Keywords

Collagen Peptide, Knee, Joint

1. Introduction

Joints are organs that are significantly involved in the movement of vertebrates and are composed of articular cartilage, which includes a cartilage matrix containing collagen and proteoglycans, as well as chondrocytes. They connect bones and provide mobility and stability at these junctions [1]. With aging and other factors, the homeostasis of articular cartilage is disrupted, leading to an increase in proteolytic enzymes and inflammatory cytokines in the cartilage matrix, as well as apoptosis of chondrocytes, resulting in the gradual progression of cartilage degeneration. Consequently, symptoms such as joint pain and limitations in range of motion occur [2]. Joint function is essential for the smooth performance of daily activities. According to the 2022 National Health and Nutrition Survey conducted by the Ministry of Health, Labour and Welfare of Japan, “pain in the joints of the limbs” was reported as one of the top five symptoms in both men and women [3]. Additionally, knee pain has been reported to affect quality of life (QOL) [4]. Regarding the knee specifically, a cohort study conducted in Japan [5] reported that the prevalence of knee osteoarthritis increases with age, indicating that maintaining knee joint health and reducing pain are important for maintaining and improving QOL and promoting health.

Collagen peptides are food materials derived primarily from collagen obtained from pigs, fish, and cattle and are hydrolyzed into peptides with lower molecular weights. They have been reported to reduce inflammatory cytokine levels in human trials [6]. Hydroxyproline (Hyp) is a characteristic amino acid of collagen peptides. When humans ingest collagen peptides, the blood concentrations of peptides containing Hyp, such as prolyl-hydroxyproline (Pro-Hyp), increase [7]. Furthermore, it has been reported that Pro-Hyp regulates the expression of genes involved in chondrocyte differentiation and promotes the synthesis of cartilage matrix components, such as glycosaminoglycans, in chondrocytes [8]. These findings suggest that collagen peptides containing Hyp as the main constituent amino acid may improve knee pain and mobility through their anti-inflammatory effects and the maintenance of articular cartilage homeostasis. In fact, continuous intake of foods containing collagen peptides has been reported to improve knee joint pain and mobility in patients with knee osteoarthritis [9] [10]. Furthermore, continuous intake of foods containing collagen peptides has been reported to improve knee joint pain and mobility in healthy adults who experience joint pain or discomfort [6] [11] [12].

In this study, we developed a new powdered food containing collagen peptides as the primary ingredient. Therefore, the purpose of this study was to evaluate the effects of consuming this food once daily for 12 weeks on knee joint function in healthy adult men and women. Both objective evaluations by physicians and subjective evaluations by participants are important for evaluating knee status. However, setting both as primary evaluation items in a single trial raises concerns regarding statistical multiplicity. To avoid this concern, we separated the evaluation purposes and conducted two independent, randomized, placebo-controlled, dou-

ble-blind, parallel-group trials with predefined primary evaluation items. In Trial 1, the primary evaluation item was the physician assessment, whereas in Trial 2, the primary evaluation item was the participants' subjective assessment. This study jointly presents and comprehensively evaluates the results of both trials.

2. Subjects and Methods

2.1. Study Subjects and Setting

The target sample size for Trials 1 and 2 was calculated based on reports of the effects of collagen peptides on knee joint improvement [11], with an effect size of 0.95, a significance level of 0.05 and a power of 0.80, resulting in a sample size of 19 per group. Therefore, considering dropouts and discontinuations, the sample size was set at 23 participants per group (46 in total) for each trial.

Trials 1 and 2 enrolled healthy adults who met the inclusion criteria and did not meet the exclusion criteria. The study participants were given a thorough explanation of the study procedures before the start of the study and provided written informed consent.

The inclusion criteria were as follows: 1) Males and females aged 40 to 74 years old with discomfort in the knee joints. 2) Subjects whose knee joints are judged to be not diseased by the investigator according to the Kellgren-Lawrence grade (KL grade) in X-ray at screening tests. 3) Subjects whose BMIs are less than 30. 4) Subjects who are judged not to be suffering from a disease by the investigator. 5) Subjects who can make self-judgment and are voluntarily giving written informed consent.

The exclusion criteria were as follows: 1) Have a history of and/or contract rheumatoid arthritis, or are suspected to have rheumatoid arthritis by screening tests. 2) Underwent surgery for chronic pain in joints, ligament injury or meniscus injury. 3) With knee artificial joints, etc. 4) Take joint related medicines (such as poultices, liniments, and/or analgesics, etc.) three or more times a week. 5) Have a history of and/or contract serious diseases (eg, liver disease, kidney disease, digestive disease, heart disease, respiratory disease, endocrine disease, metabolic disease and/or joint disease). 6) Can't stop using drugs and/or supplements affecting joints during the study period. 7) Have an allergy to the ingredients of active foods. 8) Are under treatment for or have a history of drug addiction and/or alcoholism. 9) Have excessive alcohol intake more than approximately 20 g/day of pure alcohol equivalent or a habit of drinking not less than 5 days a week. 10) Can't stop drinking from 2 days before the screening measurement and each measurement. 11) Are shift worker or mid-night worker. 12) With extremely irregular dietary habit. 13) Plan to travel abroad, including overseas trip, during test periods. 14) Are pregnant or planning to become pregnant or breastfeed during the study period. 15) Have donated over 200 mL of blood and/or blood components within the last one month or over 400 mL of blood and/or blood components within the last three months prior to screening tests. 16) Had participated in other clinical studies (measurement) within the last one month prior to the current study and/or are planning to participate in other clinical studies (measurement) during

the current study. 17) Are judged as unsuitable for the current study by the investigator for other reasons.

Both Trials 1 and 2 were conducted with the deliberation and approval (approval date: November 28, 2024) of the Ethics Committee of Kobuna Orthopedics Clinic (Chairman: Toshio Kawada), in accordance with the “Declaration of Helsinki, October 2013, WMA Fortaleza General Assembly (Brazil) Amendment” and the “Ethical Guidelines for Life Sciences and Medical Research Involving Human Subjects” (March 23, 2021, partially revised on March 27, 2023). Both studies were conducted under the supervision of a physician at Kobuna Orthopedics Clinic. The study plan was registered in the Clinical Trial Registration System operated by the University Hospital Medical Information Network Research Center, with registration IDs: Trial 1: UMIN000056381 (A Study on the Effect of Test Food on Knee Joint Function—A Randomized, Double-blind, Placebo-controlled, Parallel-group Study-) and Trial 2: UMIN000056382 (A Study on the Effect of Test Food on Subjective Knee Joint Symptoms—A Randomized, Double-blind, Placebo-controlled, Parallel-group Study-).

2.2. Study Methods

Both Trials 1 and 2 were randomized, placebo-controlled, double-blind, parallel-group comparison trials (allocation ratio: 1:1) consisting of a pre-observation period (1 week) and an intake period (12 weeks), totaling 13 weeks, with no methodological changes after the start of the study.

Trials 1 and 2 recruited paid volunteers, and the principal investigator enrolled the study subjects according to the inclusion and exclusion criteria. The person responsible for the statistical analysis used computer-generated random numbers to allocate subjects using a stratified block randomization method (block size 4), adjusting for sex, age, the JOA total score, and KL classification at the time of screening in Trial 1, as well as for sex, age, the JKOM total score, and KL classification in Trial 2. In both studies, the two allocated groups were assigned to the active food group and the placebo food group by the allocation manager, who was not directly involved in the study. Furthermore, the allocation manager prepared and sealed a table with the allocation results (key code) and kept it in a sealed container until the key code was disclosed after the analysis subjects were determined, thereby ensuring the blinding of persons other than the study allocation manager. Additionally, in both studies, the study food was distributed to the study participants in plain aluminum packs, with one pack containing the daily intake amount (2.6 g), ensuring blinding of both the study participants and the personnel implementing the intervention. During the study period, both Trials 1 and 2 instructed the participants not to use or consume supplements or health foods other than the study food, to maintain the same lifestyle as before the study, to avoid excessive alcohol consumption, and not to participate in other trials. Furthermore, on the test days, participants were instructed not to consume alcohol for two days before the test, not to engage in excessive exercise that would prevent conversation during exercise until the end

of the test, to finish meals by 9 p.m. the day before the test, not to eat or drink until the end of the test on the test day, and to refrain from smoking until the end of the test. The use of medications required permission from the principal investigator or subinvestigator, except during emergencies.

2.3. Intervention

During the intake period, the intervention involved the consumption of the study food. The active food used was a powdered food prepared by mixing collagen peptides with polydextrose and silicon dioxide and granulating the mixture. In the placebo food, the collagen peptides in the active food were replaced with polydextrose to make the placebo food indistinguishable from the active food. Both the active and placebo foods were designed with a daily intake amount of 2.6 g. During the intake period, the participants were instructed to dissolve one pack of the study food (active food for the active food group and placebo food for the placebo food group) in water or lukewarm water and consume it once a day. The caloric and nutritional contents per daily intake of the study foods are shown in **Table 1**. The amount of collagen peptides in the active food was 2.0 g per daily intake. The amount of collagen peptides in the active food was calculated by multiplying the amount of Hyp by a conversion factor of 8, according to the AOAC method (AOAC 990.26-1993).

Table 1. Analysis of nutrient composition values of study foods.

	Placebo food (1 pack)	Active food (1 pack)
Energy (kcal) ^a	10	10
Protein (g) ^b	0	2.3
Fat (g)	0	0
Ash (g)	2.5	0.2
Sodium (g)	0	0.007

^a. Calorie conversion factors: protein, 4; fat, 9; carbohydrates, 4; ^b. Nitrogen protein conversion factor: 6.25.

2.4. Test Items

The tests were conducted three times: before intake, at 6 weeks after intake, and at 12 weeks after intake. In Trial 1, the evaluation was conducted by physicians using the Japanese Orthopaedic Association criteria for evaluating the treatment outcomes of knee pain disorders (JOA) [13]. In Trial 2, the participants evaluated themselves using the Japanese Knee Osteoarthritis Measure (JKOM) [14] and a subjective questionnaire using the visual analog scale (VAS) method. The primary evaluation items were the knee JOA in Trial 1 and JKOM and VAS in Trial 2. There were no changes in the outcomes after the start of the study.

Knee JOA is an evaluation of the knee by a physician, assessing four items for

each knee: I “Pain on walking ability,” II “Pain on ascending or descending stairs,” III “Range of motion,” and IV “Joint effusion.” I is a 7-point evaluation with a maximum score of 30 points, II is a 6-point evaluation with a maximum score of 25 points, III is a 6-point evaluation with a maximum score of 35 points, and IV is a 3-point evaluation with a maximum score of 10 points, with higher scores indicating milder symptoms. The total score of both knees for each item and the total score of both knees for all four items were used for evaluation.

The JKOM is an evaluation of the knee by the participants themselves, and JKOM I “The degree of knee pain” was evaluated using the VAS method over the past few days. In the VAS evaluation, the left end of a 100 mm line represents no pain and the right end represents the most severe pain experienced, with participants indicating their current state on the line; the length from the left end is the VAS score. Additionally, there are four items with a total of 25 questions: II “Pain and stiffness in knees” and III “Condition in daily life” for answering questions regarding the state of the knee in daily life over the past few days, IV “General activities” for answering questions about activity restrictions due to the knee over the past month, and V “Health conditions” for answering questions about health status over the past month. Each question was evaluated on a 5-point scale, with the mildest option being 0 points, the most severe option being 4 points, and the intermediate options being 1, 2, or 3 points depending on the symptoms. The VAS score for I, the subtotal scores for II, III, IV, and V, and the total score for II to V (JKOM total score) were used for evaluation.

The knee subjective questionnaire is an evaluation of the knee by the participants themselves, using the VAS method to evaluate knee pain in recent situations such as “bending and stretching the knee,” “climbing and descending stairs,” “standing up from a sitting position,” and “bending down to pick up something dropped on the floor.” In each evaluation, the left end of a 100 mm line represents no pain and the right end represents the worst imaginable pain, with participants indicating their current state on the line; the length from the left end is the VAS score used for evaluation.

Additionally, in both trials, weight (BMI) measurement, blood pressure and pulse examination, blood tests and urinalysis were conducted at before intake and 12 weeks of intake to confirm safety. Furthermore, to confirm the background of the participants, a physical examination was conducted only before intake to measure height, weight (BMI), KL classification based on radiographic findings of the knee joint, and a blood test for rheumatoid factors.

Study participants were provided with a dietary diary and a participant diary and were instructed to record the following survey items daily from one week before the start of intake to the day before the 12 weeks intake.

The survey items included (1) study food intake status, (2) the presence or absence of changes in physical condition, (3) the presence or absence of changes in living conditions, (4) the presence or absence of menstruation (women only), (5) use of medications (medications, newly designated quasi-drugs, and new-range quasi-drugs), (6) the presence or absence of exercise, and (7) dietary content.

2.5. Statistical Analysis

The analysis population was set as the Per-Protocol Set (PPS), and intergroup comparisons were made between the active and placebo food groups for each test score. The VAS score was analyzed using an independent t-test, and the other scores were analyzed using the Mann-Whitney U test, with a significance level of 5% for all tests. Statistical analyses were performed using IBM SPSS Statistics version 28. The background of the study participants was shown as mean $\pm$ standard deviation, and other data were shown as mean $\pm$ standard error. No additional analyses were conducted, and no adjustments were made for multiple testing across multiple items and time points.

3. Results

3.1. Analysis Subjects

The number of study participants enrolled in Trial 1 was 46 (17 men, 29 women), with no dropouts after randomization. The study began with 46 participants, with 23 participants allocated to each group. There were no dropouts during the study period, and 46 participants completed the study. Additionally, as no study participants met the rejection criteria after the study, including non-adherence to the protocol, 46 participants were included in the analysis. The number of study participants enrolled in Trial 2 was 46 (9 men, 37 women), with no dropouts after randomization, and the study began with 46 participants, with 23 participants allocated to each group, and no dropouts after randomization. During the study period, one male and one female in the placebo food group met the discontinuation criteria (discontinuation due to the judgment of the principal investigator for reasons unrelated to the study food) and dropped out, resulting in 44 participants completing the study. Additionally, as no study participants met the rejection criteria after the study, including non-adherence to the protocol, 44 participants (8 men and 36 women) were included in the analysis for Trial 2.

The period from recruitment of study participants to the end of follow-up was from December 2024 to May 2025 for both Trials 1 and 2, and the study was concluded when all participants completed follow-up. The background of the analysis subjects in Trials 1 and 2 is shown in **Table 2**, and a flowchart illustrating the process from enrollment to analysis is shown in **Figure 1**.

Table 2. Participant characteristics.

Parameter	Trial 1		Trial 2	
	Placebo food group (n = 23)	Active food group (n = 23)	Placebo food group (n = 21)	Active food group (n = 23)
Male/Female	8/15	9/14	4/17	4/19
KL grade (0/I)	11/12	11/12	10/11	10/13

Continued

Age (years old)	53.1 ± 7.9	54.5 ± 5.6	54.0 ± 7.4	53.3 ± 7.8
Height (cm)	162.7 ± 7.6	163.8 ± 7.6	158.0 ± 7.3	160.0 ± 7.8
Body weight (kg)	57.9 ± 8.4	60.4 ± 10.3	55.0 ± 9.3	58.1 ± 11.0
Body mass index (kg/m ²)	21.9 ± 2.8	22.4 ± 2.8	21.9 ± 2.8	22.6 ± 3.2
JOA total score (point)	184.1 ± 5.6	183.5 ± 4.9	—	—
JKOM total score (point)	—	—	22.9 ± 6.4	22.1 ± 10.2

Values are expressed as means ± SDs. No significant difference was observed.

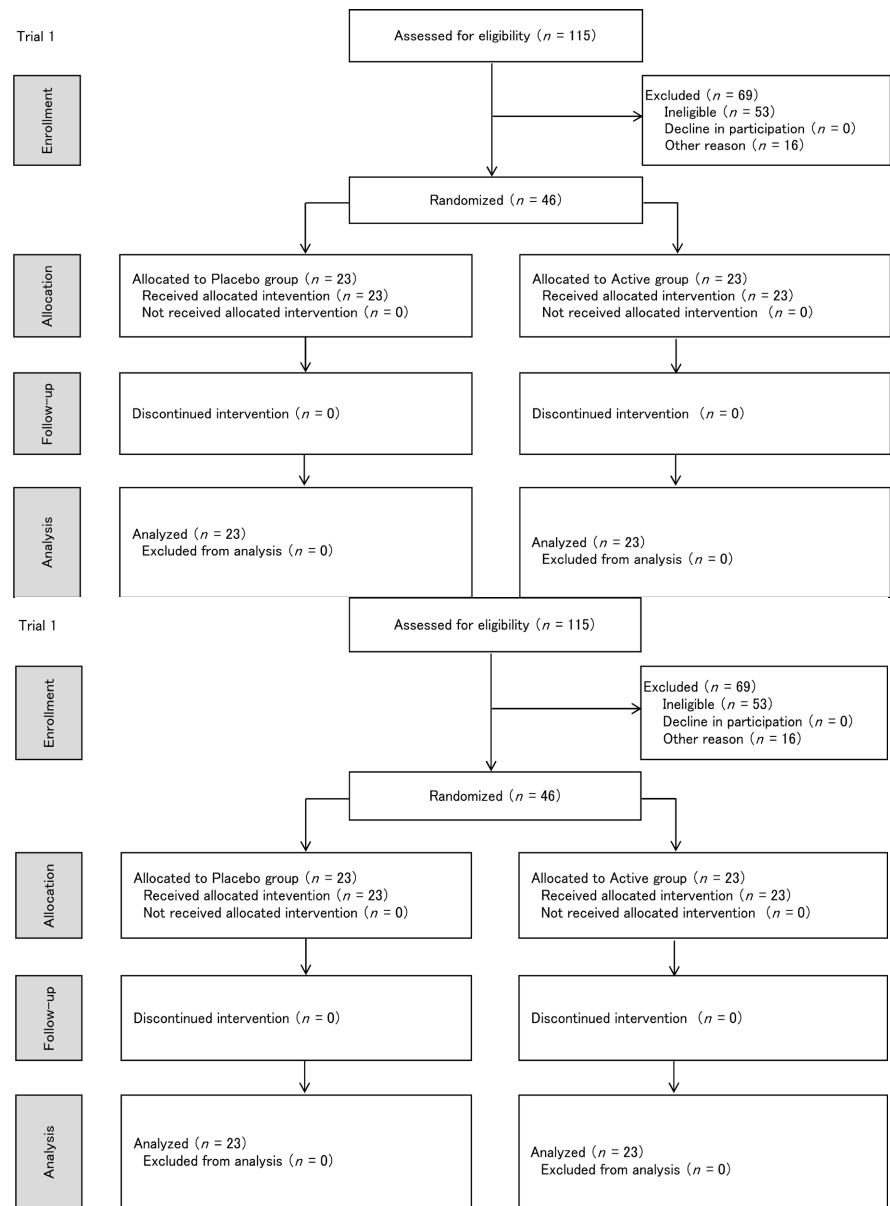


Figure 1. Flow diagram of progress through phases of randomized, double-blind, placebo-controlled, parallel-group study.

3.2. Analysis Results

The results of knee JOA in Trial 1 are shown in **Table 3**. Intergroup comparisons revealed significant differences in the JOA total score, JOA I score, and JOA II score at 12 weeks after intake ($p < 0.05$). However, no significant differences were observed between the groups in the JOA III and JOA IV scores.

The JKOM results in Trial 2 are presented in **Table 4**. Intergroup comparisons revealed significant differences in the JKOM total score, JKOM II score, JKOM III score, and JKOM IV score at 12 weeks after intake ($p < 0.05$). In contrast, no significant differences were observed between the groups in JKOM I and JKOM V scores.

The results of the VAS questionnaire on knee sensation in Trial 2 are presented in **Table 5**. Intergroup comparisons revealed significant differences in the VAS scores for pain when bending and stretching the knee, pain when climbing and descending stairs, pain when standing up from a sitting position, and pain when bending down to pick up something dropped on the floor at 12 weeks after intake ($p < 0.05$).

Table 3. JOA results.

Parameter	Group	Before intake	6 weeks	12 weeks	
JOA total score (points)	Placebo food (n = 23)	184.1 ± 1.2	184.3 ± 1.1	184.3 ± 1.1	
	Active food (n = 23)	183.5 ± 1.0	184.3 ± 1.2	191.3 ± 1.8	**
JOA I score (points)	Placebo food (n = 23)	52.8 ± 0.7	52.8 ± 0.7	52.8 ± 0.7	
	Active food (n = 23)	52.2 ± 0.7	52.4 ± 0.8	55.7 ± 1.0	*
JOA II score (points)	Placebo food (n = 23)	41.7 ± 0.5	42.0 ± 0.5	42.0 ± 0.5	
	Active food (n = 23)	41.3 ± 0.5	42.0 ± 0.7	45.7 ± 1.0	**
JOA III score (points)	Placebo food (n = 23)	69.6 ± 0.4	69.6 ± 0.4	69.6 ± 0.4	
	Active food (n = 23)	70.0 ± 0.0	70.0 ± 0.0	70.0 ± 0.0	
JOA IV score (points)	Placebo food (n = 23)	20.0 ± 0.0	20.0 ± 0.0	20.0 ± 0.0	
	Active food (n = 23)	20.0 ± 0.0	20.0 ± 0.0	20.0 ± 0.0	

Values are expressed as means ± SEs. Significantly different from the placebo food group (*: $P < 0.05$, **: $P < 0.01$).

Table 4. JKOM results.

Parameter	Group	Before intake	6 weeks	12 weeks	
JKOM I (mm)	Placebo food (n = 21)	44.7 ± 3.9	36.3 ± 3.8	29.5 ± 3.5	
	Active food (n = 23)	45.8 ± 4.3	32.7 ± 3.6	21.2 ± 3.6	
JKOM total score (points)	Placebo food (n = 21)	22.9 ± 1.4	18.2 ± 1.7	17.2 ± 2.0	
	Active food (n = 23)	22.1 ± 2.1	14.3 ± 1.8	9.9 ± 1.5	**
JKOM II score (points)	Placebo food (n = 21)	9.5 ± 0.5	7.5 ± 0.6	6.6 ± 0.7	
	Active food (n = 23)	9.4 ± 0.9	6.0 ± 0.7	4.1 ± 0.7	*
JKOM III score (points)	Placebo food (n = 21)	7.4 ± 0.7	5.8 ± 0.9	5.4 ± 0.9	
	Active food (n = 23)	6.7 ± 0.9	4.0 ± 0.8	2.3 ± 0.5	**
JKOM IV score (points)	Placebo food (n = 21)	3.5 ± 0.3	3.0 ± 0.3	3.3 ± 0.4	
	Active food (n = 23)	3.4 ± 0.4	2.6 ± 0.3	2.1 ± 0.3	*
JKOM V score (points)	Placebo food (n = 21)	2.5 ± 0.2	2.0 ± 0.2	1.9 ± 0.2	
	Active food (n = 23)	2.6 ± 0.2	1.7 ± 0.2	1.4 ± 0.2	

Values are expressed as means ± SEs. Significantly different from the placebo food group (*: $P < 0.05$, **: $P < 0.01$).

Table 5. VAS results.

Parameter	Group	Before intake	6 weeks	12 weeks	
Bending and stretching the knee (mm)	Placebo food (n = 21)	46.0 ± 4.7	36.4 ± 4.0	34.4 ± 3.8	
	Active food (n = 23)	42.6 ± 4.1	28.0 ± 3.0	21.9 ± 2.9	*
Climbing and descending stairs (mm)	Placebo food (n = 21)	45.9 ± 4.7	38.0 ± 4.2	35.0 ± 4.0	
	Active food (n = 23)	42.9 ± 4.5	27.4 ± 3.3	20.5 ± 3.0	**

Continued

Standing up from a sitting position (mm)	Placebo food (n = 21)	48.9 ± 4.5	38.0 ± 4.3	34.6 ± 4.2	
	Active food (n = 23)	47.1 ± 3.6	31.9 ± 3.1	22.4 ± 3.3	*
Bending down to pick up something dropped on the floor (mm)	Placebo food (n = 21)	45.6 ± 4.3	35.3 ± 4.1	32.9 ± 4.2	
	Active food (n = 23)	44.7 ± 4.8	30.3 ± 3.7	21.1 ± 3.4	*

Values are expressed as means ± SEs. Significantly different from the placebo food group (*: $P < 0.05$, **: $P < 0.01$).

3.3. Adverse Events

During the study period, in Trial 1, mild fluctuations in blood test results were confirmed as adverse events in one case in the placebo food group and in three cases in the active food group. In Trial 2, there were three cases of mild fluctuations in blood test results and two cases of one fracture and one other unrelated event in the placebo food group. In the active food group, five cases of mild fluctuations in blood test results were confirmed. In all cases, taking into account temporal relationships and other relevant factors, the principal investigator denied any causal relationship with the study food.

4. Discussion

In this study, we investigated the effects of foods containing collagen peptides on the knees of healthy adult men and women with knee joint discomfort through a randomized, placebo-controlled, double-blind, parallel-group trial, in which participants continuously consumed foods containing collagen peptides (active food) or foods without collagen peptides (placebo food) for 12 weeks.

In Trial 1, the JOA total, JOA I, and JOA II scores at 12 weeks after the end of the intake period were significantly higher in the active food group than in the placebo food group, indicating improvement with the intake of the active food. In Trial 2, the JKOM total, JKOM II, JKOM III, and JKOM IV scores, as well as the results of the VAS questionnaire on knee sensation were significantly lower in the active food group than in the placebo food group, indicating an improvement with the intake of the active food.

Regarding the evaluation of knee pain, improvement with the intake of the active food was observed in JKOM II “Pain and stiffness in knees,” which assesses the state of the knee in daily life over the past few days, and in the subjective questionnaire on pain in specific situations such as bending and stretching the knee in daily life. However, no changes were observed in the JKOM I score, which evaluates knee pain over the past few days. The JKOM II and the subjective questionnaire on knee pain evaluate pain when performing daily activities such as bending and stretching the knee, while JKOM I is not an evaluation specifying a particular

situation; therefore, the results of JKOM I do not negate the improvement of knee pain with the intake of collagen peptides.

Regarding the evaluation of difficulty in knee movements, significant improvement with the intake of the active food was observed in JOA I “Pain on walking,” JOA II “Pain on ascending or descending stairs,” JKOM III “Condition in daily life,” which assesses the state of the knee in daily life over the past few days, and JKOM IV “General activities,” which assesses the frequency of going to events or department stores, difficulty or restrictions on usual activities due to knee pain, and the frequency of giving up going out over the past month. Although no changes were observed in JKOM V “Health conditions,” JKOM V is a question about one’s health status over the past month and the adverse effects on health due to the state of the knee and is not a direct evaluation index for knee pain or movement. Therefore, the results of JKOM V do not negate the improvement in knee pain and functional movement with the intake of collagen peptides. Additionally, JOA III “Range of motion” and JOA IV “Joint effusion” were evaluated as full marks in the collagen peptide-containing food intake group, suggesting that no abnormalities in knee bending and stretching or swelling were observed in the participants of this trial according to the examining physician’s findings.

The mechanism of improvement in knee pain and movement in daily life observed in this trial can be attributed to the maintenance of articular cartilage homeostasis and anti-inflammatory effects based on existing knowledge. When humans ingest collagen peptides, Hyp, Hyp-Gly, and Pro-Hyp-Gly are detected in the blood, with Pro-Hyp detected at particularly high concentrations [7]. It has been reported that Pro-Hyp is taken up by chondrocytes in animal experiments [15] and promotes the synthesis of glycosaminoglycans by chondrocytes in cell experiments [8]. Furthermore, it has been reported that the intake of collagen peptides improves knee joint pain and reduces inflammatory markers [6]. Therefore, the intake of collagen peptides contributes to the maintenance of articular cartilage homeostasis and anti-inflammatory effects by transporting peptides such as Pro-Hyp to joint tissues, thereby improving knee pain and movement in daily life in adult men and women.

Additionally, the safety of collagen peptides was confirmed in this trial. No adverse events attributable to the intake of collagen peptide-containing foods were observed, suggesting that there are no safety issues associated with the long-term intake of collagen peptide-containing foods.

However, this study had some limitations. This study targeted healthy adults with knee joint discomfort; therefore, the effects on individuals with diseases such as rheumatoid arthritis are unknown. Future research should be conducted with a wider range of participants to confirm the effects of collagen peptides on improvements in knee pain and movement.

5. Conclusion

Collagen peptide-containing foods have been shown to improve knee pain and

movement during daily activities in healthy adult men and women with knee joint discomfort.

Author Contributions

Conceptualization, T. Kamiya and K. Takagaki; Methodology, R. Komatsuzawa; Validation, N. Matsuoka; Formal analysis, A. Kamiya and N. Matsuoka; Investigation, A. Kamiya; Writing-Original Draft Preparation, A. Kamiya and K. Toda; Supervision, K. Takagaki and Y. Kobuna; Writing-Review & Editing, T. Morikawa and S. Takashima; Visualization, K. Toda and N. Matsuoka; Project Administration, S. Takashima and T. Kamiya. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

This study was conducted in accordance with the Declaration of Helsinki and approved by The Ethics Committee of Kobuna Orthopedics Clinic (approval date: 28 November 2024; approval number: Trial 1: MK-2411-05, Trial 2: MK-2411-06).

Informed Consent Statement

Informed consent was obtained from all participants involved in the study.

Data Availability Statement

The data used in this manuscript are not publicly available because of commercial restriction, but are available on reasonable request.

Conflicts of Interest

This study was commissioned by Toyo Shinyaku Co., Ltd. to K.S.O., Inc. The test food used in this study was provided by Toyo Shinyaku Co., Ltd. Eight of the authors (A. Kamiya, N. Matsuoka, K. Toda, R. Komatsuzawa, T. Morikawa, S. Takashima, T. Kamiya, and K. Takagaki) are employees of, and receive their salaries from, Toyo Shinyaku Co., Ltd. Y. Kobuna, a physician affiliated with Kobuna Orthopedics Clinic, conducted this study as the principal investigator under contract with K.S.O., Inc.

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