fortune Journals

Research Article

JOURNAL OF ORTHOPAEDICS AND SPORTS MEDICINE

ISSN: 2688-5115

Effects of a Dietary Supplement Containing Collagen - L-Arginine - Hyaluronic Acid on General Health in Elderly Patients with Musculoskeletal Complaints

Réka Fritz[1*], Pál Bóday[2], Annamária Maszlag[3], Lívia Mayer[3], and Péter Fritz[4]

Abstract

We investigated the efficacy of a liquid dietary supplement (DS) containing collagen, L-arginine, hyaluronic acid and vitamin C in elderly patients with musculoskeletal complaints. The two-month study 26 people were involved who were randomly divided into two groups (control and experimental group). At the beginning and end of the study, somatometric examinations, body composition examinations, joint function tests and laboratory tests were carried out. All subjects consumed 25 ml of DS per day and members of the experimental group also took part in physiotherapy 3 times a week. Blood lipid levels changed in parallel with the intake of DS: LDL level and the LDL/HDL ratio decreased significantly in both groups. There was a significant improvement in 3 points of the body composition test in both groups. The functional tests of the knee and hip joints showed significant improvements in the experimental group, while in the control group the DS can also bring about significant improvements in the range of motion of the joints in the passive state. The DS proves to be an excellent support for people who lead an active lifestyle. It shows clear benefits in promoting joint functionality, maintaining healthy blood lipid levels and improving body composition. It is worth noting that the effectiveness of DS also applies to people with a more sedentary lifestyle.

Keywords: Body composition; Laboratory results; Collagen and hyaluron acid oral supplementation; Articular movement improvement; C vitamin; L-arginin; Sport nutrition

Introduction

The world is undergoing a massive ageing process. According to the UN Population Profile, the number of people over 60 in high-income countries is expected to reach 366 million by 2030. Most of us can expect to live many years longer than our parents' and grandparents' generations. This increase in life expectancy is a huge achievement due to improvements in public health and healthcare [1]. Research focused on health promotion and prevention has led to a large number of studies aimed at maintaining health at an optimal level in the long term. The development of nutritional supplements to improve age-related deficits is a focus of this field of research.

For example, the efficiency of our body to produce collagen from dietary proteins decreases with age [2]. Adequate intake of vitamin C-rich foods is also essential for collagen synthesis; this vitamin helps to bind collagen-forming amino acids [3]. It is worth noting that studies indicate that vitamin C intake should be increased with age [4].

Affiliation:

[1]Doctoral School of Clinical Medicine University of Szeged, Szeged, Hungary

[2]Pál Bóday Hungarian Central Statistical Office Multi-domain Statistics Department, Budapest, Hungary

[3]Central – Eastern- European Recreational Association,6724 Szeged, Csaba street 48, Csongrád-Csanád County, Hungary

[4]Károli Gáspár University of the Reformed Church in Hungary, Faculty of Humanities and Social Sciences, Budapest, Hungary

***Corresponding Author:**

Réka Fritz, Doctoral School of Clinical Medicine University of Szeged, Szeged, Hungary.

Citation: Réka Fritz, Pál Bóday, Annamária Maszlag, Lívia Mayer, and Péter Fritz. Effects of a Dietary Supplement Containing Collagen - L-Arginine - Hyaluronic Acid on General Health in Elderly Patients with Musculoskeletal Complaints. Journal of Orthopedics and Sports Medicine. 6 (2024): 48-61.

Received: March 07, 2024
Accepted: March 15, 2024
Published: March 22, 2024

Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

Collagen plays a structural role in the human body and contributes to the mechanical, shaping and organisational properties of our tissues [5]. Collagen is a major component of connective tissue, including tendons, ligaments, skin and muscles [6]. Collagen is good for the skin, eyes, hair, nails, gums, ligaments, muscles, cartilage, joints, digestion and heart health [3,7,8].

For the development of food supplements, collagen can be extracted from pork, beef, chicken and various seafood. There is little information on the efficacy of collagen supplements. Studies generally use pre-digested (hydrolyzed) collagens that contain peptides rather than whole proteins [9,10]. Studies on the efficacy of collagen supplements for age-related body changes have shown benefits for the whole body:

- **The skin:** The skin undergoes structural changes with age. There is a deterioration in neurosensory perception, permeability and the ability to recover from injuries. Age-related changes in the composition of the skin's amino acids reduce the skin's natural ability to retain water. The amount of hyaluronic acid produced by fibroblasts decreases and collagen synthesis slows down [11].
- **Muscle mass:** The intake of collagen peptides has been found to increase lean body mass and muscle fibre diameter [7]. Research has shown that collagen supplementation promotes the synthesis of muscle proteins such as creatine and stimulates muscle growth after exercise [10].
- **Bone and joint function:** Supplementation with collagen peptides is also useful in relieving the symptoms of osteoarthritis. There is a marked improvement in pain, stiffness and physical function [12-15].
- Cardiovascular health: Oral intake of collagen has been shown to have a positive effect on blood lipids. When taken regularly, the LDL/HDL ratio is reduced [16], high blood pressure is lowered [17] and arterial stiffness is reduced [18].
- **Gastrointestinal diseases:** The glycine content of collagen reduces the risk of gastric ulcers [13]. Collagen synthesis is important for the process of repair and healing of the intestinal wall [14]. A link between inflammatory bowel disease and reduced serum collagen levels has been demonstrated [15].

Collagen supplements are increasingly in demand due to the desire to stay youthful, as they have been shown to have positive effects on many body systems [19]. The market for hydrolyzed collagen is expected to be the fastest growing, supported by its increasing use in the healthcare sector [20].

Study Aim

This study investigated the overall health effects of a dietary supplement in elderly patients with musculoskeletal complaints. The uniqueness of the dietary supplement used in this study is that while its main ingredient is hydrolyzed collagen - the current market importance and health effects of which we wrote in detail in the introduction, it also contains L-arginine and hyaluronic acid and vitamin C.

The composition of DS is specially created with the aim of strengthening each other's effects and helping absorption. The individual mechanisms of action and physiological role of these ingredients are well understood but have not yet been uniformly tested in a dietary supplement with this combination of ingredients or in the dosage administered in this study.

The impact of the dietary supplement on the reduction musculoskeletal complaints was investigated. In addition, the influence of intense exercise on the efficacy of the supplement was assessed. Laboratory tests were employed to assess any adverse effects, such as the impact of the dietary supplements on the liver and kidney.

Materials and Methods

Study design

The study was conducted at the Faculty of Health Sciences of the University of Miskolc during a 60-day study period. We formulated the following selection criteria: Elderly people (male and female) aged 60 years and older were included in the study, leading an active life, with musculoskeletal complaints (medically certified permanent or recurrent degenerative musculoskeletal complaints affecting at least two body parts or joints). We define exclusion criteria as persons who are prevented from physical activity for cardiovascular reasons.

Randomized controlled trial is employed as study design. Participants in the study were recruited on the basis of a public call for applications and were selected on a first-come, first-served basis if they met the selection criteria. Once the selection criteria were met, the final study population was formed and then randomly divided into two groups (study and control). Finally, we enrolled 30 patients: 15 in the study group and 15 in the control group. The final number of patients was 13-13, with 2-2 patients dropping out during the 60-day study period. The influence of cofounding factors: age, sex and weight is minimal as there are no significant differences between the mean of these variable in the two groups.

All participants underwent blood tests, body composition measurements, somatometric tests, joint range of motion and endurance tests at the beginning and end of the study period and consumed 25 ml of the study supplement dissolved in 2 dl of water every morning throughout the study period.

The experimental group - in contrast to the control group - participated in three guided physiotherapy sessions per week throughout the study period.

Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

The habitual activity level of the control group did not change during the study period.

The ingredients of the dietary supplement tested in our study are (one dose: 500 mg vitamin C (625%RIV), 10 000 mg collagen, 40 mg hyaluronic acid (molecular weight Da (0.8-1.5)×10 6), 1075 mg L-arginine, 1074 mg glycine).

Socio-demographic data

The data of 13 people from the experimental and control groups (26 people in total) were analysed. There was 1 man in the test group and 2 men in the control group. The average age was 68.9 +/- 4.6 years in the study group and 69.9 +/- 4.9 years in the control group. The participants were mostly retired, with 2 people in the study group working in intellectual professions and three in the control group, also in intellectual professions.

Somatometric tests

- Height was measured with an InBody BSM 270, waist and hip circumference, thigh and upper arm circumference were measured manually with a tape measure and tabulated.
- A comprehensive anthropometric and body composition analysis was performed using the InBody 270 (InBody Co., Ltd., South Korea) according to the manufacturer's protocol. During the analysis, the following parameters were determined: weight (kg), total body water (l), body fat mass (kg), soft lean mass (kg), fat-free mass (kg), skeletal muscle mass (kg), percent body fat (%), visceral fat area (kg), body cell mass (kg), total body water (l), extracellular water (l), intracellular water (l), mineral mass (kg), bone mineral content (kg), protein mass (kg), basal metabolic rate (kcal) and total fitness (InBody Score).

Passive Range of Motion (PROM)

Is a scientific measure used to assess joint movement through external manipulation of the joint without the person actively tensing their muscles. It is a valuable tool in clinical practice for the diagnosis and treatment of musculoskeletal conditions and for monitoring changes in joint mobility over time. In passive range of motion, the joint of a person being exercised is completely relaxed while the external force moves the body part, e.g. a leg or arm, through the available range [21].

Stamina test

- Determination of voluntary apnea time (voluntary apnea time is the ability to hold one's breath, measured in seconds)
- 3-minute step bench test: counting the steps taken in 3 minutes and recording the maximum heart rate, then recording the heart rate measured after 1, 3 and 5 minutes of rest,
- Fatigue level at the end of the test with the Modified Borg Scale. (The Modified Borg Dyspnea Scale (MBS) is a numerical scale graded from 0 to 10 to measure patient-reported dyspnea during submaximal exercise, one of the most common and widely used measures to assess disease severity in pulmonary arterial hypertension) [20].
- Garmin Vivoactive 4 activity watch: continuous monitoring of activity, heart rate and calories burned throughout the duration of physical exercise.

Laboratory results (from peripheral venous blood)

Glycaemia; liver function (GOT, GPT, GGT), kidney function (urea, creatinine, GFR), Na, K, Mg, Ca, Fe, transferrin, iron binding capacity, inflammatory parameters (red blood cell sedimentation, CRP, LDH), White Blood Cell Count, blood lipids (cholesterol, HDL, LDL, triglyceride).

Statistical analysis

The paired t-test was used to determine the differences between the body composition variables, blood lipid parameters and exercise tests measured at the beginning and end of the study within the control and study groups, and the unpaired t-test was used at the two different sampling time points between the two groups. Chi-square test is used for blod parameters, whether the results are in or out of the reference interval. For all analyses, the p-value for the two-sided significance level was set at $p < 0.05$. Statistical analyses were performed using the IBPM SPSS Statistics Version 25 software package.

The methodology of physiotherapy sessions

Weeks 1-4 (Part A): Each training session began with a warm-up exercise about 5 minutes apart. This was followed by mobilisation exercises to improve the movement of the "stem" joints and the spine in a relieved position. This was followed by elements of a standard series of exercises to correct posture, stretch and strengthen the antigravity muscles.

Weeks 5-8 (Part B): Elements: Low-intensity cardiopulmonary training, posture correction, stretching and strengthening of the antigravity muscles, including in weight-bearing positions.

From week 5, part B was introduced, and then gradually fewer and fewer exercises from part A and more and more only elements from part B were used. Each time, the exercise programme was pulse- controlled.

Results

No side effects were reported during the entire study when taking the dietary supplement. All study participants completed the protocol as prescribed.

Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

Results of the comparative analysis of laboratory results

The blood laboratory results of the experimental and control groups before and after the intervention were compared by Chi-squared test whether the results are in or out of the reference intervals.

The laboratory analysis included the results of 26 components.

It is important to note that liver function parameters (GOT, GPT, GGT) and renal function values (urea, creatinine) also remains in the refence intervals Acording to the tests, no signicicant change can be presented in the control group, while in the experimental group in case of LDL after the experiment more results were in the reference interval (5 before, 12 after out of 13, and the change is significant (p=0.000).

Comparing the mean of blod lipid results the following results can be seen.

- Total cholesterol (normal range: <5.20 mmol/l): There was a significant (p=0.018) decrease in the experimental group by -0.4 from 5.8 to 5.4 (Figure 1A);
- LDL (normal range <3 mmol/l): the mean value of both groups showed a significant decrease, with the control group decreasing by -0.7 from 4.1 to 3.3 (p=0.003) and the experimental group by -1.0 from 3.7 to 2.7 (p=0.000) (Figure 1B);
- HDL cholesterol (normal range >1,4 mmol/l): there was a significant increase (p=0.004). in the experimental group the change increased by 0.2 from 1.7 to 1.9. In the control group by 0.07 from 1.59 to 1.66, the change was not significant (p=0.121), and is negligible from a practical point of view. (Figure 1C);
- LDL/HDL ratio (a ratio of more than 2.5 is a high cardiovascular risk, while a lower value than 2.5 indicates a low cardiovascular risk): significant reduction in both groups control p=0.006, test p=0.000), but slightly greater decrease in the study group (in the control group the value increased by -0,6 from 2.8 to 2.1, while in the experimental group the ratio changed by -0.8 from 2.3 to 1.5. also there was a significant between group difference the experimental group has significantly (p=0.027) lower value than the control group after the experiment.;

Results of a comparative study of InBody results

The results of the InBody body composition analysis before and after the intervention of the experimental and control groups were compared using the t-test.

We analysed 13 different measures of body composition, 2 of which showed no significant change: ECW (extracellular water), BMC (bone mineral content). For 8 test items, the experimental group showed a significant change based on the paired t-test, while in the control group the change was not significant (Table 1).

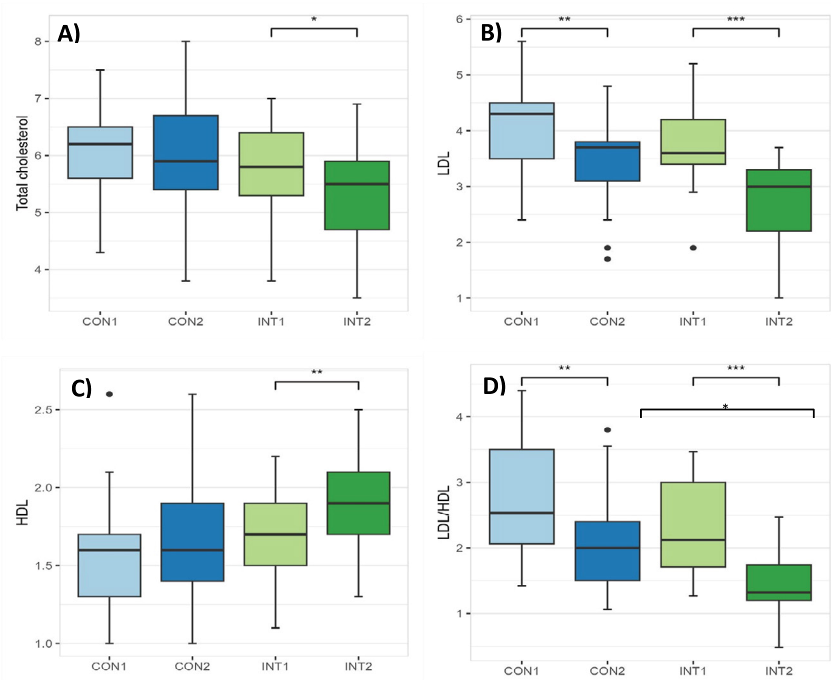


Figure 1: (A) Total cholesterol. (B) LDL. (C) HDL. (D) LDL/HDL. The names of the groups are abbreviated by: CON1: initial status of the control group, CON2: final status of the control group. INT1: initial state of the experimental group, INT2: final state of the experimental group. Significance level are indeicated by asterisk (*),***: p<0,001 , **: p<0,01 *:p<0,05.

Citation: Réka Fritz, Pál Bóday, Annamária Maszlag, Lívia Mayer, and Péter Fritz. Effects of a Dietary Supplement Containing Collagen - L-Arginine - Hyaluronic Acid on General Health in Elderly Patients with Musculoskeletal Complaints. Journal of Orthopedics and Sports Medicine. 6 (2024): 48-61.

Table 1: Comparing changes in body composition.

	Mean				SD				T-test (significance)			
									paired		independent	
	CON 1	CON 2	INT 1	INT 2	CON 1	CON 2	INT 1	INT 2	CON1-CON2	INT1-INT2	CON 1-INT1	CON 2-INT2
TBW (Total Body Water) (liter)	34.3	34.4	32.3	33	4.6	4.3	4.9	5.2	0.744	0.003	0.292	0.472
ICW (Intracellular Water) (liter)	20.9	20.9	19.8	20.7	2.7	2.6	3.0	3.5	0.809	0.013	0.359	0.813
ECW (Extracellular Water) (liter)	13.4	13.4	12.4	12.7	2.0	2.0	1.9	2.1	0.727	0.065	0.225	0.392
Protein (kg)	9.0	9.1	8.6	9.1	1.1	1.1	1.3	1.4	0.666	0.000	0.344	0.964
Minerals (kg)	3.4	3.4	3.1	3.3	0.6	0.6	0.5	0.5	0.286	0.000	0.175	0.551
BFM (Body Fat Mass) (kg)	28.5	27.7	27.7	25.6	10.1	10.0	7.7	7.3	0.002	0.000	0.83	0.543
SMM (Skeletal Muscle Mass) (kg)	25.2	25.3	23.9	24.5	3.5	3.4	3.9	4.2	0.773	0.002	0.355	0.601
BMI (Body Mass Index) (cm/m2)	28.0	27.6	28.1	27.2	4.9	4.9	4.4	4.1	0.014	0.05	0.95	0.816
PBF (Percent Body Fat) (%)	37.6	36.6	38.3	35.7	9.4	8.9	6.4	6.4	0.068	0.000	0.815	0.785
BMR (Basal Metabolic Rate) (kcal)	1378.5	1381.9	1319.1	1345.2	133.2	126.3	143.6	163.5	0.717	0.022	0.284	0.527
VFL (Visceral Fat Level)	13.5	12.8	13.4	12.0	5.3	5.4	4.2	4.2	0.013	0.000	0.968	0.687
VFA (Visceral Fat Area) (cm2)	140.9	138.2	138.1	127.8	63.8	60.7	41.2	40.6	0.353	0.000	0.897	0.611
BMC (Bone Mineral Content) (gramm)	2.8	2.9	2.6	2.6	0.5	0.5	0.4	0.4	0.302	0.160	0.165	0.174

However the between-subject (control and experimental groups) comparison did not bring significant results in the 13 different measures. The names of the groups are abbreviated in the Table: CON1: initial status of the control group, CON2: final status of the control group. INT1: initial state of the experimental group, INT2: final state of the experimental group.

- *TBW (total body water):* There was a significant (p=0.003) increase in the experimental group by 0.8 from 32.2 to 33.0. (Figure 2A);
- *ICW (intracellular water):* There was a significant (p=0.013) increase in the experimental group by 0.9, from 19.8 to 20.7. (Figure 2B);
- *Protein:* There was a significant (p=0.000) increase in the experimental group by 0.5, from 8.6 to 9.1. (Figure 2C);
- *Minerals:* There was a significant (p=0.000) increase in the experimental group by 0.2 from 3.1 to 3.3 (Figure 2D);
- *SMM (skeletal muscle mass):* There was a significant (p=0.002) increase in the experimental group by 0.6 from 23.9 to 24.5. (Figure 2E);
- *PBF (percentage body fat):* There was a significant (p=0.000) decrease in the experimental group by - 2.4 from 38.3 to 35.7. (Figure 2F);
- *BMR (basal metabolic rate):* There was a significant (p=0.022) increase in the experimental group by 26.1 from 1319.1 to 1345.2. (Figure 2G);
- *VFA (visceral fat area):* There was a significant (p=0.000) decrease in the experimental group by -10.7 from 138.1 to 127.8. (Figure 2H)

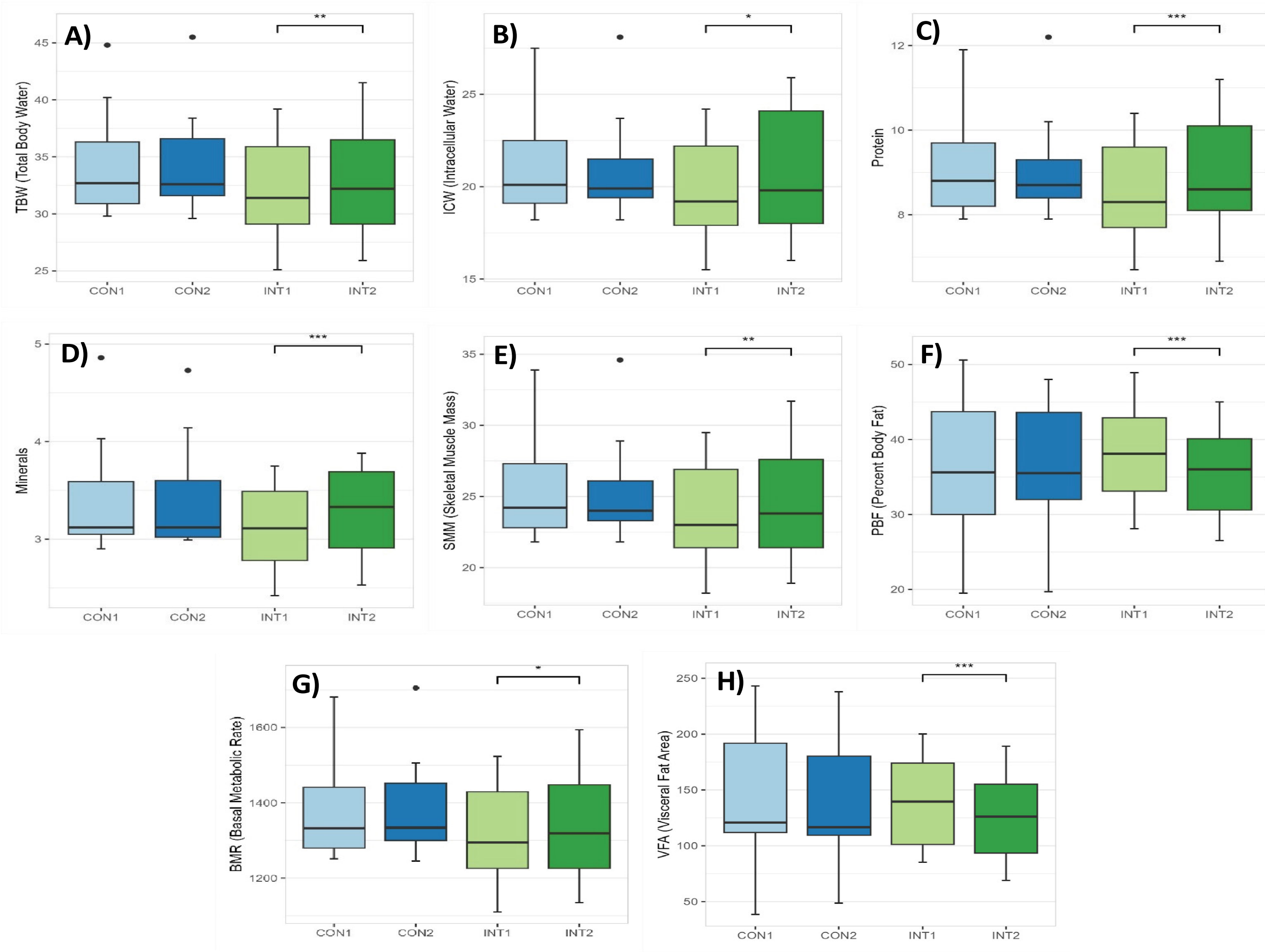


Figure 2: (A) (TBW) total body water. (B) (ICW) intracellular water. (C) Protein. (D) Minerals. (E) (SMM) skeletal muscle mass. (F) (PBF) percent body fat. (G) (BMR) basal metabolic rate. (H) (VFA) visceral fat area. The names of the groups are abbreviated by: CON1: initial status of the control group, CON2: final status of the control group. INT1: initial state of the experimental group, INT2: final state of the experimental group. Significance level are indeicated by asterisk (*),***: p<0,001, **: p<0,01 *:p<0,05.

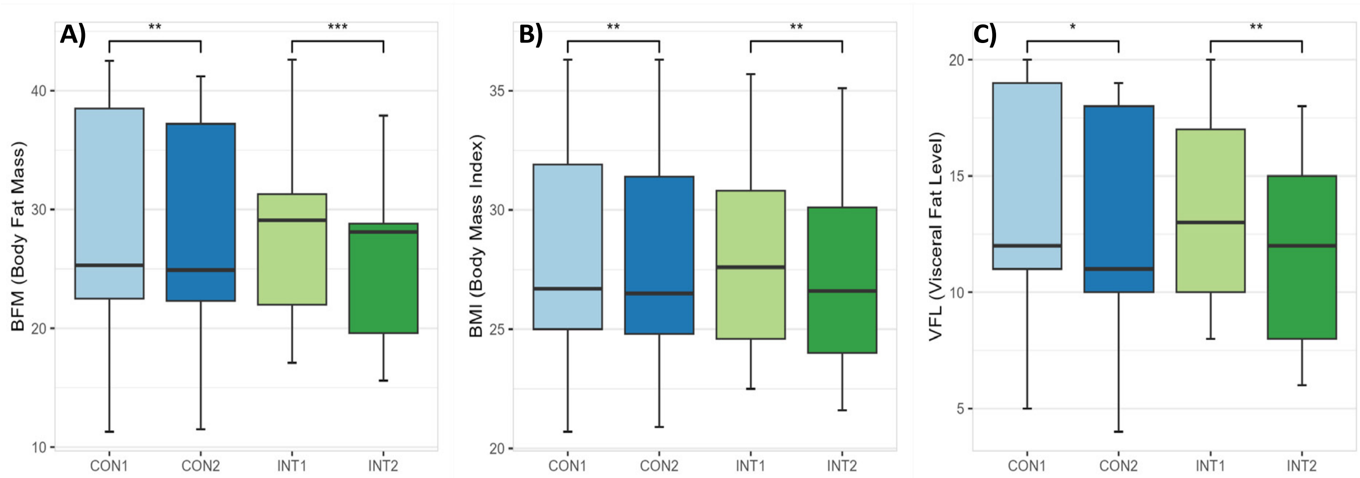


Figure 3: (A) BFM (Body Fat Mass). (B) BMI (Body Mass Index). (C) VFL (Visceral Fat Level). The names of the groups are abbreviated by: CON1: initial status of the control group, CON2: final status of the control group. INT1: initial state of the experimental group, INT2: final state of the experimental group. Significance level are indeicated by asterisk (*),***: p<0,001, **: p<0,01*:p<0,05.

Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

Range of motion testing of hip and knee joints (passive range of motion - PROM)

In 3 test items, the experimental group showed a significant change in the basis of the paired t-test, while the change was not significant in the control group, and 1 test item showed significant change in the control group while the change in the experimental group was not significant. The names of the groups are abbreviated in the Table 2: CON1: initial status of the control group, CON2: final status of the control group. INT1: initial state of the experimental group, INT2: final state of the experimental group.

- Hip ROM fl L: There was a significant (p=0.008) increase in the experimental group by 7.7 from 109.2 to 116.9 (Figure 4A);
- Knee ROM fl R: There was a significant (p=0.006) increase in the experimental group by 5.3 from 111.8 to 117.1. (Figure 3B);
- Knee ROM fl L: There was a significant (p=0.006) increase in the experimental group by 5.9, the change was significant (p=0.001) from 112.3 to 118.2 (Figure 4C);
- Knee ROM ext R: There was a significant (p=0.004) decrease in the control group by 3.3 from 5.5 to 2.8 (Figure 4D)

In 2 test items, the change was significant for both groups according to the t-test:

- Hip ROM fl R: The mean increased by 6.3 from 109.8 to 116.1 (p=0.018) in the control group and by 7.8 from 109.2 to 116.9 (p=0.000) in the experimental group (Figure 5A);
- Knee ROM ext L: The mean decreased by -4.2 from 6.2 to 2.5 in the control group (p=0.000) and by -4.5 from 6.3 to 1.8 in the experimental group (p=0.000) (Figure 5B)

Results of the parameters measured during the physiotherapy session

Among the parameters tested at the experimental group, exercise time (p=0.011), maximum heart rate (0.002) and calorie consumption during exercise (p=0.012) showed significant changes (Table 3).

Table 2: Comparing changes in motion testing of hip and knee.

	Mean				SD				T-test (significance)			
									paired		independent	
	CON 1	CON 2	INT1	INT2	CON 1	CON 2	INT1	INT2	CON1- ON2	INT1- INT2	CON1- INT1	CON 2- INT2
Hip_ROM_fl_R	109.5	116.2	107.2	116.5	9.4	9.8	5.4	8.7	0.026	0	0.467	0.917
Hip_ROM_fl_L	113.7	114.3	109.2	116.9	9.8	8.9	3.6	8.8	0.721	0.008	0.137	0.458
Hip_ROM_e xt_R	3.4	3.2	3.2	4.2	2.8	1.9	2.4	1.6	0.829	0.331	0.88	0.167
Hip_ROM_e xt_L	4.9	4.6	3.8	5.6	3.9	2.1	2.1	2.1	0.786	0.051	0.389	0.229
Knee_ROM_ fl_R	118.8	117.7	111.8	117.1	8.7	12.5	13.4	12.7	0.59	0.006	0.133	0.902
Knee_ROM_ fl_L	117.5	120.1	112.3	118.2	11.9	11.9	11.7	12.6	0.125	0.006	0.277	0.692
Knee_ROM_ ext_R	5.6	2.8	5.5	3.2	2.6	2.1	3.6	2.5	0.004	0.095	0.951	0.616
Knee_ROM_ ext_L	6.6	2.5	6.3	1.8	3.2	1.7	2.8	1.5	0	0	0.798	0.335

Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

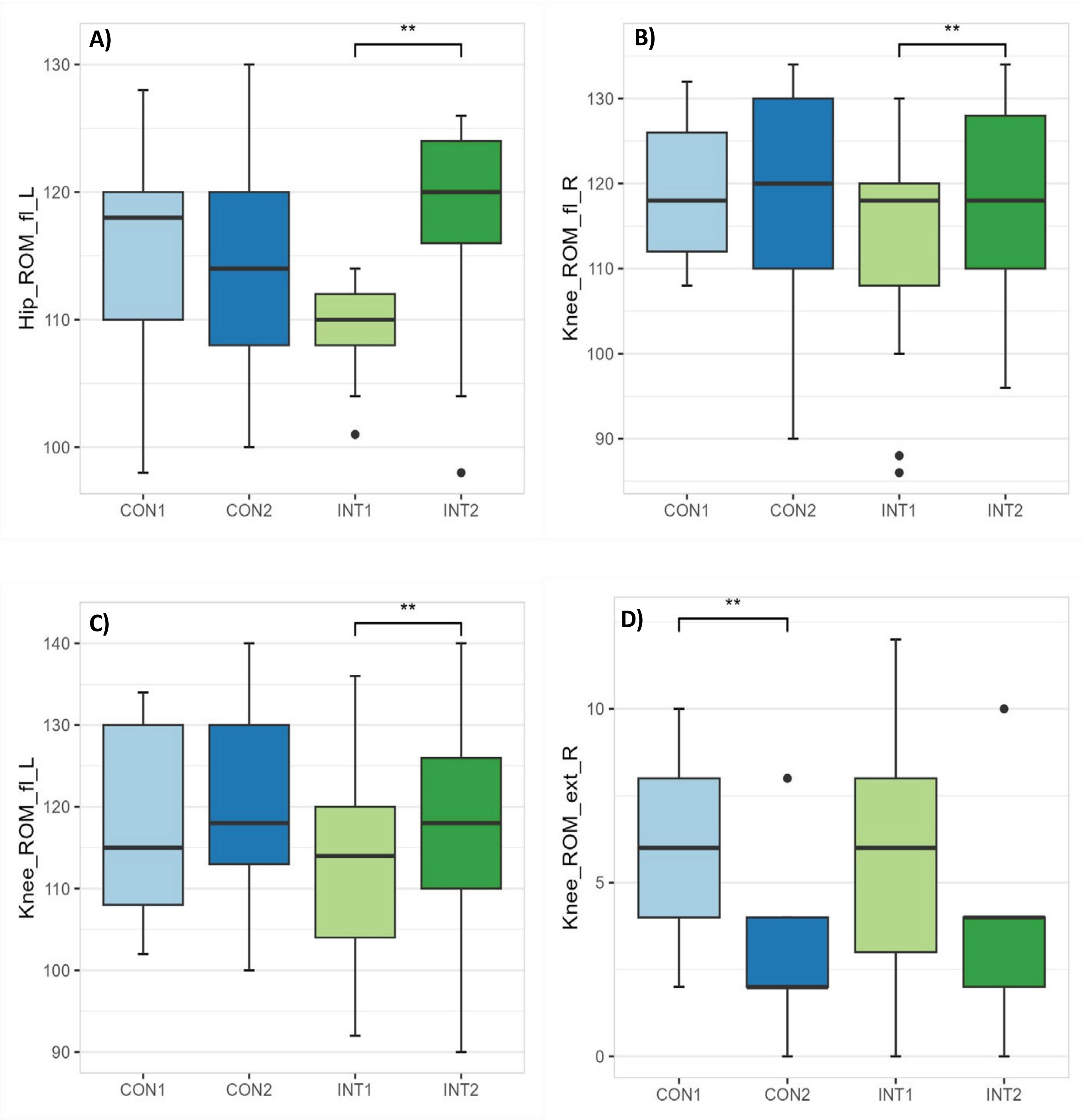


Figure 4: (A) Hip ROM fl left. (B) Knee ROM fl right. (C) Knee ROM fl left. (D) Knee ROM ext right. The names of the groups are abbreviated by: CON1: initial status of the control group, CON2: final status of the control group. INT1: initial state of the experimental group, INT2: final state of the experimental group. Significance level are indeicated by asterisk (*), ***: p<0,001 , **: p<0,01*:p<0,05.

Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

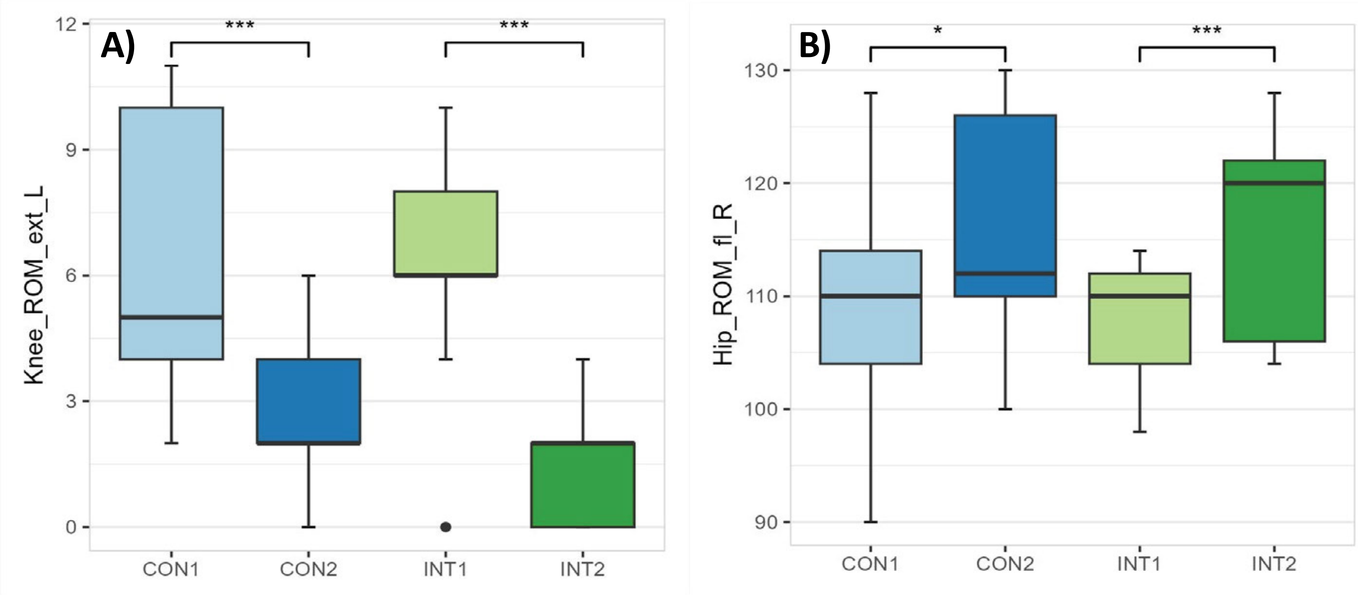


Figure 5: (A) Hip ROM fl right. (B) Knee ROM ext left. The names of the groups are abbreviated by: CON1: initial status of the control group, CON2: final status of the control group. INT1: initial state of the experimental group, INT2: final state of the experimental group. Significance level are indicated by asterisk (*), ***: p<0,001, **: p<0,01, *:p<0,05.

Table 3: Comparing changes in parameters during training.

Parameters	Initial average	SD	Final average	SD	Significance (p)
Training time (min)	42.5	1.5	45	1.1	0.011
Average heart rate (beats/min)	76.2	8.1	80.6	6	0.084
Maximum heart rate (beats/min)	97.1	8.7	114.6	8.5	0.002
Calories	134.6	46.3	169	37.7	0.012

Discussion

In this study, we investigated the health benefits of a collagen supplement in an elderly population. The special feature ofDS is that it contains L-arginine, vitamin C and hyaluronic acid in addition to the high collagen content.

The aim behind this careful formulation is to maximize the bioavailability and efficacy of the individual ingredients. By combining ingredients that work together, DS aims to achieve a more comprehensive and powerful effect on the targeted physiological processes, such as musculoskeletal health in elderly patients. While the individual mechanisms and physiological functions of these ingredients are well understood, their combined effects and optimal dosages in this particular supplement have not been widely studied.

Based on our understanding of the effects of these four key components on the human body, our findings are framed in terms of four main objectives: cardiovascular, prophylactic, nutritional and joint and musculoskeletal aspects.

Cardiovascular aspects:

In the field of biology, it is known that elevated LDL and triglyceride levels contribute to atherosclerosis and endothelial dysfunction. Various markers for early atherosclerosis have been identified, such as the ratio of LDL to HDL (LDL-C/HDL-C ratio). A ratio of more than 2.5 is considered high risk, while a lower value indicates a lower risk [22,23]. Oral intake of collagen has been shown to have positive effects on blood lipids and therefore cardiovascular health. Regular intake has been associated with a reduction in the LDL/HDL ratio [16], a reduction in high blood pressure [17] and a reduction in arterial stiffness [18].

In terms of dosage, there are notable differences in the amounts used in the various research studies. To provide a comparative perspective, we present specific examples from the literature and compare them with the results of our own research.

In a study similar to ours, in which healthy adults consumed 16 grams of collagen daily for 6 months, a reduction in the LDL/HDL cholesterol ratio and a reduction in levels of an atherosclerosis risk marker were observed [16].

Our study concurred with these findings and showed that participants who exercised regularly had a significant

Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

increase in HDL cholesterol, a decrease in total cholesterol and a decrease in average LDL cholesterol. Interestingly, the control group that did not exercise showed a non-significant decrease in total cholesterol and a non-significant increase in HDL cholesterol, both changes being so small as to be negligible from a medical point of view: However, a significant decrease in LDL cholesterol was found in the control group.

The initially high LDL/HDL ratio shows significant reduction in both groups (control p=0.006, experimental p=0.000), but slightly greater decrease in the study group (in the control group the value increased by -0,6 from 2.8 to 2.1, while in the experimental group the ratio changed by -0.8 from 2.3 to 1.5. also there was a significant between group difference the experimental group has significantly (p=0.027) lower value than the control group after the experiment.; It is noteworthy that the collagen supplement, which contains additional antiatherogenic elements such as L-arginine and vitamin C, played a decisive role in this improvement.

Based on the LDL/HDl ratio, both groups showed an improvement in atherogenic risk. The control group went from a high risk value to a low risk value, and in case of the experimental group the original low risk status decreased further.

In contrast to the mentioned aerlyer in which 16 mg of collagen was taken for 6 months (p=0.253), our study showed more significant effects with 10 grams per day, enriched with supplemental ingredients. This robust improvement in the LDL/HDL ratio, a major cardiovascular risk marker, underscores the effectiveness of supplemental collagen supplementation in achieving remarkable results in a shorter period of time.

Similar studies have been conducted in the literature. In one small study, for example, mild hypertension was reduced in 15 adult subjects by consuming 5.2 grams of collagen per day for 4 weeks [17]. Consuming 2.5 grams of collagen per day for 12 weeks reduced arterial stiffness [18]. As blood pressure and arterial stiffness were not measured in our study, a direct comparison with our results in these areas is not possible. It is important to note that the references to these studies were for illustrative purposes only and emphasized the remarkable variability in dosing rather than drawing parallels to our specific results.

Evaluation of the changes in parameters during training: The group physiotherapy sessions held three times a week under the guidance of an expert triggered adaptation processes in the participants. As a result, the maximum heart rate, the time of physical activity, i.e. the exercise time (p=0.011), increased at the end of the 60th day. The average heart rate (p=0.084) and maximum heart (p=0.002) rate also showed a significant increase, which was due to the reinforcement of the training components of the sessions.

Prophylactic aspects:

In recent decades, numerous studies have attempted to identify substances with anti-atherogenic properties, such as vitamin C and L-arginine, and to investigate the effects of various exercise programs on blood lipid levels [23]. Regular physical activity has shown promise in lowering blood lipid levels, with both triglyceride and total cholesterol levels showing a downward trend [24]. Furthermore, a detailed breakdown of HDL and LDL cholesterol levels shows an upward trend in HDL cholesterol and a concomitant decrease in LDL cholesterol with physical activity [25]. In particular, physically active women were found to have significantly higher HDL cholesterol levels than their sedentary counterparts [26]. High-intensity exercise alone has been shown to positively alter lipoproteins in a cardiovascular manner, particularly in healthy older women [27]. Another study emphasizes the role of L-arginine in lowering blood lipids, showing that L-arginine supplementation improved lipid profiles by lowering serum concentrations of triglycerides, total cholesterol, and low-density lipoprotein cholesterol [28].

Our study is consistent with these proven associations, as patients in the study group who exercised regularly showed a notable increase in HDL cholestol, a decrease in total cholesterol and a decrease in average LDL cholesterol. Interestingly, the control group that did not exercise also showed a significant decrease in LDL cholesterol.

This suggests that while these changes are indeed significant in patients who are both physically active and taking a dietary supplement, individuals who rely solely on a dietary supplement show even more favorable results. The superiority of the results is particularly evident in the reduction of LDL cholesterol, where significant values are achieved, which in itself underlines the efficacy of the dietary supplement.

Nutritional aspects:

The administration of L-arginine has been associated with an inhibition of visceral fat accumulation [29]. Further studies have highlighted the anti-atherogenic effect of L-arginine and vitamin C [30]. L-arginine, known for its versatility, exhibits pronounced anti-ageing effects, including reduced risk of vascular and heart disease, reduced erectile dysfunction, improved immune response and inhibition of gastric acidity [31]. There is much evidence to suggest that oral administration of L-arginine within the physiological range may be beneficial to the health of both men and women by increasing the synthesis of nitric oxide (NO) and thus blood flow to tissues (e.g. skeletal muscle). NO is a vasodilator, a neurotransmitter, a regulator of nutrient metabolism and a killer of bacteria, fungi and parasites [32-39]. In addition, there is evidence that oral hyaluronic acid supplementation is effective against obesity [32].

fortune Journals
Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

In our study, a significant reduction in body fat mass, body mass index and visceral fat percentage was observed in both groups, a result that we attribute to the synergistic anti-adipogenic and metabolism- stimulating effects of the supplement's ingredients. Positive changes were observed in visceral fat area, basal metabolic rate, percentage body fat and skeletal muscle mass, which, although not significant compared to the control group, still represent a positive change in body composition. In particular, the test group that exercised regularly showed significant positive changes, which underlines the effect of physical activity. Encouragingly, the group that relied solely on the dietary supplement also showed improvements.

Looking at somatometric studies, a direct correlation between waist circumference and visceral fat is known [33]. In our study, a significant reduction in abdominal volume was observed in the study group (by 3,91 cm (p=0.010) from 96,47 cm to 92,56 cm according to t-test), which correlated with a significant reduction in visceral fat area (VFA) and visceral fat level (VFL).

Articular-, musculoskeletal aspects:

The use of collagen has shown remarkable benefits in people with chronic knee pain, manifested in a reduction in pain and an improvement in range of motion (ROM) [32]. The positive effects also extend to the relief of symptoms associated with osteoarthritis, with significant improvements in pain, stiffness and physical function [12].

In terms of orthopedic changes, taking collagen proves to be a comprehensive solution that improves bone strength, density and mass. It also contributes to improved joint stiffness, mobility and functionality and ultimately reduces pain [35]. In the field of sports nutrition, it is known that joint and ligament injuries can be reduced by appropriate macro- and micronutrient supplementation and collagen replacement [36].

Oral administration of hyaluronic acid can have a positive therapeutic effect in patients with early osteoarthritis [37].

Hyaluronic acid is naturally present in synovial fluid, where it acts as a lubricant and shock absorber. Some studies suggest that taking hyaluronic acid can improve joint mobility and relieve pain. Oral administration of hyaluronic acid leads to an improvement in osteoarthritis biomarkers, namely higher HA concentrations in the synovial fluid [38].

Arginine supplementation may therefore be beneficial by increasing nitric oxide (NO) synthesis and thus blood flow to tissues: e.g. skeletal muscle [39].

Maintaining and gradually increasing range of motion can be promoted by targeted exercises, including mobility and stretching exercises [21].

In our study, the experimental group showed significant improvements in range of motion (ROM) of the knee and hip joints, emphasizing the positive effect of collagen supplementation. Interestingly, the control group showed significant improvements in joint range of motion under passive conditions even without physiotherapy (e.g. hip ROM fl R, knee ROM ext L).

Limitations of the study:

Despite the limitation of a small sample size, which is common in this and other cited studies, it is important to note that such a sample size can provide a common baseline for comparisons. This common baseline can be seen as a strength of the research as it provides a foundation for more accurate correlations and findings. Based on these findings, future studies with larger samples can be designed to further substantiate and extend these initial conclusions.

The gender ratio is not balanced, as the selection criteria were based on the order of application and fulfilment of the selection criteria.

Conclusions

The results of our modest pilot study indicate that the use of dietary supplements can make an important contribution to the promotion and prevention of joint, cardiovascular and nutritional health.

The dietary supplement we studied, which contains collagen, hyaluronic acid, vitamin C and L-arginine, is proving to be an effective aid for people with an active lifestyle. It shows significant benefits in improving joint functionality, stabilizing blood lipid levels and reducing areas of fat and abdominal girth — a collective improvement that brings significant health benefits.

Remarkably, the effectiveness of the supplement is also present in individuals with a more sedentary lifestyle. Even when used as the sole dietary supplement, it proves beneficial by lowering the cardiovascularly relevant LDL/HDL ratio and targeting specific fat areas of the body. Although the effect is not as pronounced as in people with an active lifestyle, the supplement still shows efficacy in improving joint pain when used as part of a diet. Overall, these results underline the versatility and positive health effects of the supplement, which is suitable for both active and passive lifestyles. In the future, we plan to study its effects in other groups, such as younger patients and athletes, with a larger number of test items.

Highlights

- Collagen, hyaluronic acid, L-arginine and vitamin C have a positive effect on cholesterol levels.
- The consumption of collagen improves joint mobility.
- The consumption of collagen improves body composition.

Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

- Consuming collagen during sport significantly improves joint mobility.

Authors' contributions: PF, RF, contributed to the original idea, study design and the conception of the work. PF, LM, and AM supervised the study, performed measurements. PB performed the statistical analysis. PF, RF wrote the main manuscript text. PF, RF, PB, LM, and AM revised and edited the manuscript. All authors approved the final version of the article.

Consent for publication: Not applicable.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the the Regional/Institutional Science and Research Ethics Committee (BAZ County Central Hospital and University Teaching Hospital (BORS – 10/2022).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: All data generated and analyzed during the current study are included in this published article [and its supplementary information file]. The raw datasets are available from the corresponding author on reasonable request. (Dr. Péter Fritz; peterfritz@kre.hu)

Competing interests: The authors report there are no competing interests to declare.

Conflicts of Interest: The sponsors had no role in the design, execution, interpretation, or writing of the study.

Acknowledgments: The authors thank the Superfoods Ltd.

References

1. Dixon A. The United Nations Decade of Healthy Ageing requires concerted global action. Nature Aging 1 (2021): 2.
2. Varani J, Dame MK, Rittie L, et al. Decreased collagen production in chronologically aged skin: roles of age-dependent alteration in fibroblast function and defective mechanical stimulation. Am J Pathol 168 (2006): 1861-1868.
3. Fritz P, Mayer L, Pető A, et al. A kollagén szerepe és hatása az emberi szervezetre = The role and effect of collagen on the human body. Recreation 10 (2020): 8-11.
4. Harrison FE. A critical review of vitamin C for the prevention of age-related cognitive decline and Alzheimer's disease. J Alzheimers Dis 29 (2012): 711-726.
5. Ricard-Blum S. The collagen family. Cold Spring Harbor perspectives in biology 3 (2011)
6. Lodish H, Berk A, Matsudaira P, et al. Molecular Cell Biology, 5th ed.; W. H. Freeman, New York, USA 15 (2005).
7. Line S, Rhodes C, Yamada Y. Molecular Biology of Cartilage Matrix. In Cellular and Molecular Biology of Bone. Noda, M.; Academic press, Cambridge, Massachusetts, USA (1993): 539-555.
8. León-López A, Morales-Peñaloza A, Martínez-Juárez VM et al. Hydrolyzed Collagen-Sources and Applications. Molecules (Basel, Switzerland) 24 (2019): 4031.
9. Kirmse M, Oertzen-Hagemann V, de Marées M, et al. Prolonged Collagen Peptide Supplementation and Resistance Exercise Training Affects Body Composition in Recreationally Active Men. Nutrient 11 (2019): 1154.
10. Farage MA, Miller KW, Elsner P, et al. Characteristics of the Aging Skin. Advances in wound care 2 (2013): 5-10.
11. Zdzieblik D, Oesser S, Baumstark MW, et al. Collagen peptide supplementation in combination with resistance training improves body composition and increases muscle strength in elderly Sarcopenic men: A randomised controlled trial. The British journal of nutrition 114 (2015): 1237-1245.
12. Lugo JP, Saiyed ZM, Lane NE. Efficacy and tolerability of an undenatured type II collagen supplement in modulating knee osteoarthritis symptoms: a multicenter randomized, double-blind, placebo-controlled study. Nutritional Journal 15 (2016): 14.
13. Tariq M, Al Moutaery AR. Studies on the antisecretory, gastric anti-ulcer and cytoprotective properties of glycine. Research communications in molecular pathology and pharmacology 97 (1997): 185-198.
14. Graham MF, Drucker DE, Diegelmann RF, et al. Collagen synthesis by human intestinal smooth muscle cells in culture. Gastroenterology 92 (1987): 400-405.
15. Koutroubakis IE, Petinaki E, Dimoulios P, et al. Serum laminin and collagen IV in inflammatory bowel disease. Journal of clinical pathology 56 (2003): 817-820.
16. Tomosugi N, Yamamoto S, Takeuchi M, et al. Effect of Collagen Tripeptide on Atherosclerosis in Healthy Humans. Journal of Atherosclerosis and Thrombosis 24 (2017): 530-538.
17. Saiga-Egusa A, Iwai K, Hayakawa T, et al. Antihypertensive effects and endothelial progenitor cell activation by intake of chicken collagen hydrolysate in pre- and mild- hypertension. Bioscience Biotechnology, and Biochemistry 73 (2009): 422-424.
18. Igase M, Kohara K, Okada Y, et al. A double-blind, placebo-controlled, randomised clinical study of the

Fritz R, et al., J Ortho Sports Med 2024
DOI:10.26502/josm.511500142

effect of pork collagen peptide supplementation on atherosclerosis in healthy older individuals. Bioscience, Biotechnology, and Biochemistry 82 (2018): 893-895.

19. Choi FD, Sung CT, Juhasz M, et al. Oral Collagen Supplementation: A Systematic Review of Dermatological Applications. Journal of Drugs in Dermatology: JDD 18 (2019): 9-16.

20. Collagen Market Size, Share & Trends Analysis Report By Source (Bovine, Porcine), By Product (Gelatin), By Application (Food & Beverages, Healthcare), By Region, And Segment Forecasts 2020- 2027. Available online: https://www.grandviewresearch.com/industry-analysis/collagen-market (accessed on 24 Oct 2020).

21. Range of Motion. Available online: https://www.physio-pedia.com/Range_of_Motion (accessed on 19 May 2023).

22. Banerjee D, Kamuren J, Baird GL, et al. The Modified Borg Dyspnea Scale does not predict hospitalization in pulmonary arterial hypertension. Pulmonary circulation 7 (2017): 384-390.

23. Enomoto M, Adachi H, Hirai Y, et al. T. LDL-C/HDL-C Ratio Predicts Carotid Intima-Media Thickness Progression Better Than HDL-C or LDL-C alone. Jorunal of Lipids (2011): 549137.

24. Haskell WL. The influence of exercise on the concentrations of triglyceride and cholesterol in human plasma. Exercise and Sport Sciences Reviews 12 (1984): 205-44.

25. Halverstadt A, Phares DA, Wilund KR, et al. Endurance exercise training raises high-density lipoprotein cholesterol and lowers small low-density lipoprotein and very low-density lipoprotein independent of body fat phenotypes in older men and women. Metabolism 56 (2007): 444-50.

26. Kokkinos PF, Fernhall B. Physical activity and high density lipoprotein cholesterol levels: what is the relationship? Sports Medicine 28 (1999): 307-14.

27. Fahlman MM, Boardley D, Lambert CP, et al. Effects of endurance training and resistance training on plasma lipoprotein profiles in elderly women. The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences 57 (2002): B54-B60.

28. Hadi A, Arab A, Moradi S, et al. et al. The effect of l-arginine supplementation on lipid profile: a systematic review and meta-analysis of randomised controlled trials. The British Journal of Nutrition 122 (2019): 1021-1032.

29. Kujawska-Łuczak M, Suliburska J, Markuszewski L, et al. The effect of L-arginine and ascorbic acid on the visceral fat and the concentrations of metalloproteinases 2 and 9 in high-fat-diet rats. Endokrynologia Polska 66 (2015): 526-532.

30. Bogdańsk P, Suliburska J, Szulińska M, et al. L-Arginine and vitamin C attenuate pro-atherogenic effects of high-fat diet on biomarkers of endothelial dysfunction in rats. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 76 (2015): 100-106.

31. Gad MZ. Anti-aging effects of l-arginine. Journal of Advanced Research 1 (2010): 169-177.

32. Park BG, Park YS, Park JW, et al. Anti-obesity potential of enzymatic fragments of hyaluronan on high-fat diet-induced obesity in C57BL/6 mice. Biochemical and Biophysical Research Communications 473 (2016): 290-295.

33. Ross R, Neeland IJ, Yamashita S, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. Nature reviews. Endocrinology 16 (2020): 177-189.

34. Zdzieblik D, Oesser S, Gollhofer A, et al. Corrigendum: Improvement of activity-related knee joint discomfort following supplementation of specific collagen peptides. Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme 42 (2017): 1237.

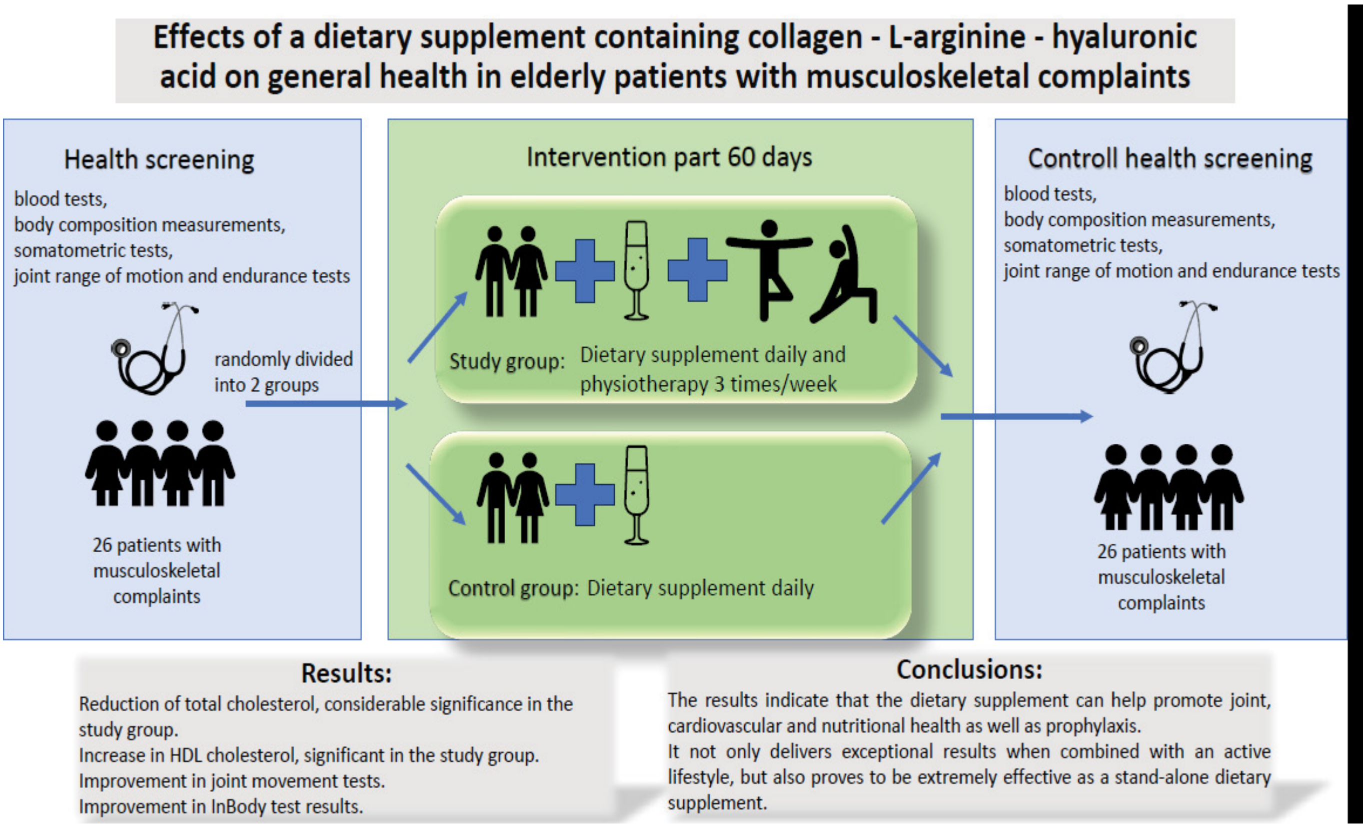
35. Campos LD, Santos JVA, Pimentel JD, et al. Collagen supplementation in skin and orthopedic diseases: A review of the literature. Helyion 9 (2023): E14961.

36. Close GL, Sale C, Baar K, et al. Nutrition for the Prevention and Treatment of Injuries in Track and Field Athletes. Int J Sport Nutr Exerc Metab 29 (2019): 189-197.

37. Ricci M, Micheloni GM, Berti M, et al. Clinical comparison of oral administration and viscosupplementation of hyaluronic acid (HA) in early knee osteoarthritis. Musculoskelet Surg 101 (2017): 45-49.

38. Serra Aguado CI, Ramos-Plá JJ, Soler C, et al. Effects of Oral Hyaluronic Acid Administration in Dogs Following Tibial Tuberosity Advancement Surgery for Cranial Cruciate Ligament Injury. Animals (Basel) 11 (2021): 1264.

39. Wu G, Meininger CJ, McNeal CJ, et al. Role of L-Arginine in Nitric Oxide Synthesis and Health in Humans. Adv Exp Med Biol 1332 (2021): 167-187.


Effects of a dietary supplement containing collagen - L-arginine - hyaluronic acid on general health in elderly patients with musculoskeletal complaints
Health screening
blood tests,
body composition measurements,
somatometric tests,
joint range of motion and endurance tests
randomly divided into 2 groups
26 patients with musculoskeletal complaints
Intervention part 60 days
Study group: Dietary supplement daily and physiotherapy 3 times/week
Control group: Dietary supplement daily
Controll health screening
blood tests,
body composition measurements,
somatometric tests,
joint range of motion and endurance tests
26 patients with musculoskeletal complaints
Results:
Reduction of total cholesterol, considerable significance in the study group.
Increase in HDL cholesterol, significant in the study group.
Improvement in joint movement tests.
Improvement in InBody test results.
Conclusions:
The results indicate that the dietary supplement can help promote joint, cardiovascular and nutritional health as well as prophylaxis.
It not only delivers exceptional results when combined with an active lifestyle, but also proves to be extremely effective as a stand-alone dietary supplement.