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Collagen supplementation for tendon health

Submission date
27/09/2023

Recruitment status
Recruiting

Registration date
06/10/2023

Overall study status
Ongoing

Last Edited
09/04/2025

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Tendons transfer the force exerted by the corresponding muscle to bones and, therefore, are vital components of human locomotion. Tendon injury is very common, both in athletes and the general population. Once injured, tendons recover very poorly, resulting in a decrease in quality of life for the patient and a substantial burden on the health care system. Therefore, interventions that can aid in the prevention or treatment of tendon injury are warranted. The growth of all tissues, including tendons, is regulated by the net difference between protein synthesis and protein breakdown rates. Protein ingestion stimulates protein synthesis. Collagen is the main protein in human connective tissues, including tendons. The amino acids glycine and proline are the main building blocks of endogenous collagen and vitamin C serves as a co-factor in the synthesis and release of novel collagen proteins. Hence, dietary collagen may be the preferred protein source to deliver high amounts of glycine and proline and, together with vitamin C, maximize collagen synthesis in the tendon. However, no evidence is available on the effect of vitamin C-enriched collagen supplementation on human tendon protein synthesis. Hence, the main objective of the current study is to assess the impact of dietary collagen supplementation on human tendon protein synthesis.

Who can participate?
Adults aged between 18 and 40 years old attending the Department of Orthopedics from the participating hospital for planned anterior cruciate ligament (ACL) reconstruction with hamstring autograft

What does the study involve?
Participants need to ingest a test drink twice daily (100 mL per dose), perform 5 minutes of low-intensity exercise twice daily, ingest deuterium oxide (20 mL) daily, and provide a saliva sample daily, for seven days.

What are the possible benefits and risks of participating?
Benefits not provided at time of registration. The burden and risks involved in participating in this experiment are limited. The ingestion of deuterium oxide has been applied in numerous published studies and is entirely safe and non-toxic in the amounts provided in the present study. Tissue collection will occur during ACL surgery, which is already planned as part of the participants' course of treatment. A graft of the hamstring tendon will be used for ACL reconstruction, and a sample will be obtained under anesthesia during the standard surgical

procedure. The tissue is extracted during the standard procedure, meaning that patients will not take on any extra burden by participating in this study. Two additional blood samples (2 x 10 mL) will be obtained before and after the experimental period.

Where is the study run from?
HAN University of Applied Sciences (The Netherlands)

When is the study starting and how long is it expected to run for?
February 2023 to July 2026

Who is funding the study?
HAN University of Applied Sciences (The Netherlands)

Who is the main contact?
Dr Jan-Willem van Dijk, JanWillem.vanDijk@han.nl (The Netherlands)

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
NL84264.096.23

Study information

Scientific Title
The effect of collagen supplementation on human tendon protein synthesis

Acronym
COL-TEN

Study objectives
The main objective of the current study is to assess the impact of dietary collagen supplementation on human tendon protein synthesis.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 30/05/2023, Medical Ethical Review Commission METC Zuyderland (Secretariaat, T3 Heerlen, Postbus 5500, Sittard, 6130 MB , Netherlands; +31 (0)88 4590129; metc@zuyderland.nl), ref: METCZ20230038

Study design
Double-blind randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital, University/medical school/dental school

Study type(s)
Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Tendon protein synthesis in otherwise healthy males and females scheduled for anterior cruciate ligament (ACL) surgery.

Interventions
The study involves two parallel groups: an intervention group and a control group:
Intervention: A vitamin C-containing collagen supplement (20 g per dose) will be ingested as a drink (100 mL of water mixed with 20 g of collagen powder) twice daily for 7 days, once at breakfast and once before sleep.
Control: A vitamin C-enriched maltodextrin will be used as an isocaloric placebo.

Using a computer random number generator, participants will be randomly allocated to the intervention group or the placebo group on a 1:1 ratio, stratified by sex. This study has a double-blind design, with both participants and researchers blinded to treatment allocation. A member of our research group will create the randomization list.
The intervention providers are an experienced lab technician with a background in chemistry and a researcher with a background in human movement sciences. The intervention is a food-grade supplement which will be provided to the participant by the researcher. Vitamin C-enriched collagen or maltodextrin supplementation will be administered at a twice daily dose of 20 g (40 g per day), as an oral supplement of 100 ml per drink. The participant mixes the dose of powder with tap water at home. After stirring the mixture for 10 seconds, the participant drinks the mixture.

Intervention occurs at the participant's home. Surgery will occur in the hospital.
Participants will be visited once at their home for baseline measurements. The second study visit will take place at the hospital before surgery.

Intervention Type
Supplement

Primary outcome measure
Tendon tissue protein synthesis rate, expressed as fractional synthesis rate (FSR, %/d), will be measured for 7 days prior to surgery. To calculate FSR, the standard precursor-product method will be used. Tendon protein synthesis rates will be calculated from:
1. Saliva 2H enrichment (i.e., precursor)
2. Tissue protein-bound enrichment 2H-alanine
3. Plasma albumin enrichment 2H-alanine

Secondary outcome measures
A ligament in muscle protein synthesis rate, expressed as fractional synthesis rate (FSR, %/d), will be measured for 7 days prior to surgery. To calculate FSR, the standard precursor-product method will be used. Tendon protein synthesis rates will be calculated from:
1. Saliva 2H enrichment (i.e., precursor)
2. Tissue protein-bound enrichment 2H-alanine
3. Plasma albumin enrichment 2H-alanine

Overall study start date
01/02/2023

Completion date
01/07/2026

Eligibility

Key inclusion criteria
1. Otherwise healthy male and female volunteers
2. Aged 18 to 40 years old
3. Recruited from patients attending the Department of Orthopedics from the participating hospital
4. Planned for ACL reconstruction with hamstring autograft
5. BMI ≥18.5 and ≤27.5 kg/m2

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
40 Years

Sex
Both

Target number of participants
30

Key exclusion criteria
1. Blood donation during the study period or during the last 2 months
2. Pregnancy
3. Third-generation oral contraceptives
4. Currently smoking
5. Consumption of >21 alcoholic beverages per week
6. Use of any medications known to affect protein metabolism (i.e. corticosteroids, non-steroidal anti-inflammatories, or prescribed acne medications)
7. Regular use of protein or other nutritional supplements (including vitamins).
8. Reported slimming or medically prescribed diet
9. Use of antibiotics in the past month
10. Current participation in another biomedical research study

Date of first enrolment
28/02/2024

Date of final enrolment
01/06/2026

Locations

Countries of recruitment
Netherlands

Study participating centre
HAN University of Applied Sciences
Heyendaalseweg 141
Nijmegen
Netherlands
6525 AJ

Study participating centre
Maxima Medical Center
Dominee Theodor Fliednerstraat 1
Eindhoven
Netherlands
5631 BM

Sponsor information

Organisation
HAN University of Applied Sciences

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Sponsor type
University/education

Website
https://www.hanuniversity.com/en/#

ROR
https://ror.org/0500gea42

Funder(s)

Funder type
University/education

Funder Name
HAN University of Applied Sciences

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/07/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request. Upon reasonable request by other researchers, raw data (Excel file) will be made available after the publication of the scientific reports. Data can be used for scientific peer review or meta-analytic procedures. Data will be fully anonymized. Access to the datasets is via JanWillem.vanDijk@han.nl.

IPD sharing plan summary
Available on request