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Effectiveness of an oral nutrition supplementation enriched with HMB and UC-II® combined with exercise training in older adults with knee osteoarthritis

Submission date
22/03/2024

Recruitment status
No longer recruiting

Registration date
17/04/2024

Overall study status
Completed

Last Edited
20/06/2025

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Osteoarthritis (OA) is the most common type of joint disease which affects mainly the knee and hip joints. Improvement of OA-related symptoms is crucial before it progress to irreversible structural damage. Dietary interventions such as protein supplementation in the form of oral nutrition supplements (ONS) and exercise training have been incorporated into the management of OA. Hydroxymethylbutyrate (HMB) and undenatured type II collagen (UC-II®) have been widely studied for their potential benefits in maintaining joint health. However, little is known about the effectiveness of ONS supplemented with HMB and UC-II® and a combination of exercise training on the improvement of OA in older adults. Therefore, this study aims to determine the effectiveness of ONS enriched with HMB and UC-II® combined with exercise training OA-related symptoms, OA-related biomarkers, body composition and morphological change of OA condition as well as gene expression profile among adults with knee OA.

Who can participate?
Adults aged 50 to 75 years with knee OA

What does the study involve?
Participants are randomly allocated into three groups: an intervention group receiving the nutrition supplement and exercise training (ONS+ET), an intervention group receiving exercise training (ET) only, and a control group receiving usual care (UC). The ONS+ET intervention group will receive an oral nutrition supplement enriched with HMB and UC-II®. Both ONS+ET and ET groups will receive exercise training. The control group will receive routine care. Participants will be interviewed about personal and social information, medical history, lifestyle factors and dietary history. Body measurements, OA-related symptoms, pain, blood profiles, inflammatory biomarkers, gene expression profiles, physical fitness, quality of life, nutritional status, disability and psychological status will be assessed throughout the study period. A subsample of

participants from each group will be randomly chosen for magnetic resonance imaging (MRI scan), performed by a trained radiographer to assess the skeletal muscle and morphological changes of the knee.

What are the possible benefits and risks of participating?
As current treatments for OA such as over-the-counter analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs) and intra-articular joint injections are only meant to relieve severe pain. Therefore, the findings of this study could offer healthcare professionals valuable perspectives on an alternative method in the symptomatic management of knee OA. No risks are known as the procedures involved are part of standard procedures. The results of the data obtained will be reported in a collective manner with no reference to any specific individual. The data from each individual will remain confidential. Participants will be told their results only.

Where is the study run from?
The National University of Malaysia (Universiti Kebangsaan Malaysia) (Malaysia)

When is the study starting and how long is it expected to run for?
December 2023 to December 2025

Who is funding the study?
Powerlife (M) Sdn. Bhd. (Malaysia)

Who is the main contact?
1. Dr Yee Xing You, youyeexing@ukm.edu.my
2. Ms Anastasia Xin Wei Yap, anastasiayxw@gmail.com

Contact information

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Additional identifiers

Protocol serial number
NN-2023-017

Study information

Scientific Title
Efficacy of Oral Nutritional Supplementation Enriched with HMB and UC-II® Combined with Exercise Training on Osteoarthritis-related Outcomes among Adults with Knee Osteoarthritis

Study objectives
Current study hypothesis as of 22/11/2024:

12 weeks of oral nutrition supplementation enriched with HMB and UC-II® combined with exercise training can reduce OA-related symptoms, improve OA-related biomarkers, body composition, morphological changes of OA condition as well as gene expression profile among adults with knee OA.

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Previous study hypothesis:

1. Oral nutrition supplementation enriched with HMB and UC-II® can improve body composition among older adults with knee osteoarthritis (OA).
2. Oral nutrition supplementation enriched with HMB and UC-II® can improve inflammatory biomarkers among older adults with knee OA.
3. Oral nutrition supplementation enriched with HMB and UC-II® can reduce pain, stiffness and physical function among older adults with knee OA.
4. Oral nutrition supplementation enriched with HMB and UC-II® can improve morphological change of OA condition using magnetic resonance imaging among older adults with knee OA.
5. Oral nutrition supplementation enriched with HMB and UC-II® can sustain its positive impact on body composition, OA-related symptoms, inflammatory biomarkers and morphological change of OA condition among older adults with knee OA after 12 weeks of post-intervention.
6. Oral nutrition supplementation enriched with HMB and UC-II® will cause changes to the metabolic-associated gene expression profile and pathways among older adults with knee OA.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 28/05/2024, Medical Research Ethics Committee of the National University of Malaysia (Universiti Kebangsaan Malaysia) (Universiti Kebangsaan Malaysia Research Ethics Secretariat, 1st Floor, Clinical Block, Chancellor Tuanku Muhriz Hospital, UKM Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, Kuala Lumpur, 56000, Malaysia; +60 391455046; sepukm@ukm.edu.my), ref: JEP-2024-264

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Quality of life, Screening, Efficacy

Health condition(s) or problem(s) studied
Knee osteoarthritis

Interventions
Current interventions as of 22/11/2024:

There will be two interventional groups in this study, which are the study group receiving the oral nutritional supplementation combined with exercise training (ONS+ET) and the study group receiving exercise training (ET) only. The control group will be receiving usual care (UC). As this is

a randomized controlled trial, a computerised software will be used to randomize the participants. Group allocation of participants will be based on gender and ethnicity by block randomisation method using an online randomiser.

The oral nutrition supplementation enriched with HMB and UC-II® used in ONS+ET group is a complete nutrition sponsored by Powerlife (M) Sdn. Bhd. The name of the intervention product is known as Metabolic + Energold.

As per dietitian's recommendation, participants in the intervention group will be asked to consume two servings of Metabolic + Energold daily, with each serving containing 60 g of Metabolic + Energold powder in sachet form and it is to be diluted in 200 ml of room temperature water. By taking two servings of the oral nutrition supplement daily, each participant will be getting 518 kcal and 20.8 g of protein.

All participants from both the intervention groups will receive home-based exercise programmes by trained physiotherapists. An exercise manual with pictorial representations and written descriptions of each exercise will be given. All participants are encouraged to perform the exercises on a daily basis (approximately 30 minutes each time) for 12 weeks. All participants are required to attend the follow ups at Week 6 and Week 12. Depending on the outcomes of the individual assessments by the physiotherapist at each visit, the selection of exercises and the appropriate level of difficulty for each exercise and ankle weights will be prescribed. The exercises are derived from a Self-Management Education Programme for knee OA developed by Kamsan et al. (2024), which comprises stretching exercises, non-resistance exercises, strengthening exercises and functional exercises for lower limbs.

In addition, participants from the two intervention groups will also receive two sessions of nutrition education by dietitians, each on the baseline visit and the follow up on Week 6.

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Previous interventions:

As this is a randomized controlled trial, a computerised software will be used to randomize the participants. Group allocation of participants will be based on gender and ethnicity by block randomisation method using an online randomiser.

Participants in the intervention group will be administered with an oral nutrition supplementation enriched with HMB and UC-II® and exercise training, whereas participants in the control group will receive routine care and exercise training. Both groups will receive the same exercise training routines.

The oral nutrition supplementation enriched with HMB and UC-II® used in the intervention group of this study is a complete nutrition sponsored by Powerlife (M) Sdn. Bhd. The name of the intervention product is known as Metabolic + Energold.

As per dietitian's recommendation, participants in the intervention group will be asked to consume two servings of Metabolic + Energold daily, with each serving containing 60 g of Metabolic + Energold powder in sachet form and it is to be diluted in 200 ml of room temperature water. By taking two servings of the oral nutrition supplement daily, each participant will be getting 518 kcal and 20.8 g of protein.

All participants from both the intervention group and control group will receive home-based exercise programmes by trained physiotherapists. An exercise manual with pictorial representations and written descriptions of each exercise will be given. All participants are encouraged to perform the exercise programmes three times per week (approximately 30 minutes each time) for 12 weeks. All participants are required to attend the monthly follow-up for 12 weeks. Depending on the outcomes of the individual assessments by the physiotherapist at each visit, the selection of exercises and the appropriate level of difficulty for each exercise and ankle weights will be prescribed. The Otago exercise programme (OEP) will be utilised in this study which comprises strengthening exercises with graded levels of difficulty.

Intervention Type
Supplement

Primary outcome(s)
Current primary outcome measure as of 22/11/2024:

1. OA-related symptoms (or the severity of OA symptoms) measured using the Knee Injury and Osteoarthritis Outcome Score (KOOS) at baseline, week 6 and week 12
2. Inflammatory biomarkers (osteoarthritis-related biomarkers) such as cytokines (interleukin-1β), tumour necrosis factor-α (TNF-α), tumour growth factor-β (TGF-β), matrix metalloproteinase-13 (MMP-13), C-telopeptide of crosslinked
collagen type I and type II (CTX-I and CTX-II), and osteocalcin measured using conventional ELISA assay of blood serum at baseline and week 12

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Previous primary outcome measure:

1. OA-related symptoms (or the severity of OA symptoms) measured using the Knee Injury and Osteoarthritis Outcome Score (KOOS) at baseline, week 6, week 12 and week 24
2. Pain intensity measured using the visual analogue scale (VAS) at baseline, week 6, week 12 and week 24
3. Inflammatory biomarkers (osteoarthritis-related biomarkers) such as cytokines (interleukin-1β), tumour necrosis factor-α (TNF-α), radical oxygen species, advanced glycation end products (AGEs) and prostaglandins measured using multiplex ELISA assay of blood serum at baseline, week 12 and week 24

Key secondary outcome(s)
Current secondary outcome measures as of 22/11/2024:

1. Body composition measured using bioelectric impedance analyzer (InBody 270) at baseline, week 6 and week 12
2. Blood profiles such as full blood count, blood sugar profile, lipid profile, liver function test and renal profile analysed at the medical laboratory (Innoquest Pathology Sdn. Bhd.) at baseline and week 12
3. Physical fitness assessed using the Functional Fitness MOT (FFMOT) and International Physical Activity Questionnaire (IPAQ) at baseline, week 6 and week 12
4. Quality of life measured using Control, Autonomy, Self-realisation and Pleasure questionnaire (CASP-12) at baseline, week 6 and week 12
5. Diet intake assessed using a dietary history questionnaire (DHQ) at baseline, week 6 and week

12
6. Morphological changes of knee determined using magnetic resonance imaging (MRI) at baseline and week 12
7. Nutritional status assessed using Patient-Generated Subjective Global Assessment (PG-SGA) at baseline, week 6 and week 12
8. Disability assessed using the World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0) questionnaire at baseline, week 6 and week 12
9. Psychological status evaluated using the Depression, Anxiety and Stress Scale (DASS21) at baseline, week 6 and week 12
10. Gene expression profile analysed using qPCR from total RNA extracted using Blood/Cell RNA Mini Kit with DNase (Geneaid) at baseline and week 12

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Previous secondary outcome measures:

1. Body composition measured using bioelectric impedance analyzer (InBody 270) at baseline, week 6, week 12 and week 24
2. Blood profiles such as full blood count, blood sugar profile, lipid profile, liver function test and renal profile analysed at the medical laboratory (Pathlab Malaysia Sdn. Bhd.) at baseline and week 12
3. Physical fitness measured using the Senior Fitness test (modified-SFT) and International Physical Activity Questionnaire (IPAQ) at baseline, week 6, week 12 and week 24
4. Quality of life measured using Control, Autonomy, Self-realisation and Pleasure questionnaire (CASP-12) at baseline, week 6, week 12 and week 24
5. Diet intake assessed using a dietary history questionnaire (DHQ) at baseline, week 6, week 12 and week 24
6. Morphological changes of knee determined using magnetic resonance imaging (MRI) at baseline, week 12 and week 24
7. Instrumental activities of daily living (IADL) measured using an IADL questionnaire at baseline
8. Nutritional status assessed using Patient-Generated Subjective Global Assessment (PG-SGA) at baseline
9. Disability assessed using the World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0) questionnaire at baseline, week 6, week 12 and week 24
10. Psychological status evaluated using depression, anxiety and stress scale (DASS21) at baseline, week 6, week 12 and week 24
11. Metabolic gene expression profile and pathway analysis analysed using Blood/Cell RNA Mini Kit with DNase (Geneaid) at baseline, week 12 and week 24

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Malaysians aged >=50 years old with at least mild osteoarthritis as diagnosed by a physician or clinical radiologist and do not suffer from diseases as mentioned in the exclusion criteria (see participant exclusion criteria)
2. Able to communicate in Malay or English language
3. Able to eat and drink safely without modified texture diets

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
50 Years

Upper age limit
75 Years

Sex
All

Key exclusion criteria
1. Receiving enteral tube feeding (ETF), parenteral nutrition or consuming ONS (or those who had consumed ONS in the past 4 weeks prior to the study)
2. Institutionalised older adults, bedridden or having severe health problems
3. Suffering from chronic kidney disease, dementia, liver failure, malignancy, gastrointestinal diseases, thyroid disorders, palliative care for terminal disease, stroke
4. Suffering from other type of arthritis; rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, post-meniscectomy OA, femoro-patellar OA, Genuvarum/valgum
5. Suffering from major psychiatric illness
6. Consuming medications that could affect muscle mass and/or function (e.g., HMG-CoA reductase inhibitors, steroids) within 1 year before enrolling in the study
7. Physical disabilities (unable to walk even with a walking aid)
8. Currently participating in other clinical trials
9. Participants with claustrophobia (for participants selected to undergo MRI)
10. Participants with metallic implants, such as prostheses, shrapnel or aneurysm clips, or electric implants, such as cardiac pacemakers (for participants selected to undergo MRI)

Date of first enrolment
01/06/2024

Date of final enrolment
30/11/2024

Locations

Countries of recruitment
Malaysia

Study participating centre
Orthopedics & Traumatology Department, Hospital Canselor Tuanku Muhriz Universiti Kebangsaan Malaysia

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Sponsor information

Organisation
Powerlife (M) Sdn. Bhd.

Funder(s)

Funder type
Industry

Funder Name
Powerlife (M) Sdn. Bhd

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Yee Xing You (youyeexing@ukm.edu.my). Only statistical data will be provided after obtaining consent from the participants.
The type of data that will be shared: Data in the published manuscript.
Dates of availability: June 2025.
Whether consent from participants was required and obtained: Yes.
Comments on data anonymization: All patients' data will be confidential.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		19/06/2025	20/06/2025	Yes	No