Clinical Trial Protocol
Iranian Registry of Clinical Trials

08 Nov 2026

Evaluation of the effects of a topical gel based on Nanostructured Lipid Carriers (NLC) loaded with Omega-3 compared to placebo on knee pain and inflammation in patients with knee osteoarthritis

Protocol summary

Study aim

To evaluate and compare the clinical efficacy in pain reduction and local safety of a topical omega 3 nanostructured lipid carrier gel versus a placebo gel in patients with mild to moderate knee osteoarthritis

Design

A phase 2, double blind, randomized, placebo controlled clinical trial with a parallel within person split body design on 30 patients using permuted block randomization and opaque sealed envelopes for allocation concealment

Settings and conduct

Eligible patients will be selected by an orthopedist at Shohada Hospital affiliated with Tabriz University of Medical Sciences. After obtaining informed consent, 30 patients will receive identical tubes with blinded codes؛ patients, the outcome assessor, and the data analyst will be blinded to the allocation.

Participants/Inclusion and exclusion criteria

Inclusion criteria include patients aged greater than or equal to 50 years with mild to moderate knee osteoarthritis and baseline pain score 2 to 7؛ Exclusion criteria include severe osteoarthritis, fish oil hypersensitivity, recent anti inflammatory or omega 3 use, recent knee injection or physical therapy, local skin disease, and body mass index greater than 30

Intervention groups

Intervention group: applies omega 3 nanostructured lipid carrier gel twice daily for four weeks on the assigned knee؛ Control group: applies placebo gel concurrently twice daily for four weeks on the contralateral knee

Main outcome variables

Change in knee pain intensity; change in knee inflammation severity

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20130313012810N103**
Registration date: **2026-06-11, 1405/03/21**
Registration timing: **registered_while_recruiting**

Last update: **2026-06-11, 1405/03/21**
Update count: **0**

Registration date

2026-06-11, 1405/03/21

Registrant information

Name

Hamed Hamishehkar

Name of organization / entity

Drug Applied Research Center, Tabriz University of Medical Sciences

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2026-06-11, 1405/03/21

Expected recruitment end date

2026-07-12, 1405/04/21

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date
empty

Scientific title
Evaluation of the effects of a topical gel based on Nanostructured Lipid Carriers (NLC) loaded with Omega-3 compared to placebo on knee pain and inflammation in patients with knee osteoarthritis

Public title
Evaluation of a topical omega-3 gel for the reduction of pain and improvement of knee osteoarthritis

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Age greater than or equal to 50 years Confirmed diagnosis of knee osteoarthritis based on the American College of Rheumatology (ACR) clinical criteria Baseline pain score between 2 and 7 on the Visual Analog Scale (VAS) despite receiving standard care Radiographic evidence of knee osteoarthritis with Kellgren-Lawrence grade 1 to 3 Physical ability to apply the topical gel twice daily and attend all follow-up sessions Willingness to provide written informed consent and comply with study protocols

Exclusion criteria:
Presence of severe knee osteoarthritis with Kellgren-Lawrence grade 4 History of hypersensitivity or intolerance to fish oil, omega-3, or any component of the gel formulation Severe systemic comorbidities including uncontrolled diabetes (HbA1c greater than 9 percent), recent cardiovascular events, renal or hepatic impairment, or active malignancy Use of systemic anti-inflammatory drugs (NSAIDs, corticosteroids, biologics) or omega-3 supplements within the past 4 weeks Active skin diseases, open wounds, severe inflammation, redness, or extreme local warmth at the knee site preventing topical application Pregnancy, lactation, or planning to become pregnant during the study period Inability to ambulate without assistance or inability to complete assessments due to severe cognitive impairment History of intra-articular knee injections within the past 3 months Receipt of physical therapy or hydrotherapy for the knee within the past 3 months Presence of lower extremity radiculopathy, neuropathy, or other neurogenic conditions such as polio Concomitant pain in the hip or ankle joints that confounds the assessment of knee pain Body Mass Index (BMI) greater than 30 kilograms per square meter Secondary knee osteoarthritis resulting from previous bone fractures or trauma Requirement for concurrent treatment with regular systemic NSAIDs (except for a maximum of 10 tablets of 500 mg acetaminophen without codeine per month) Participation in any other clinical trial within the past 30 days

Age
From **50 years** old

Gender
Both

Phase
2

Groups that have been masked

- Participant
- Outcome assessor
- Data analyser

Sample size
Target sample size: **30**
More than 1 sample in each individual
Number of samples in each individual: **2**
Two evaluation units (left and right knees) will be assessed per participant; one knee serves as the intervention unit (receiving the Omega-3 nanostructured lipid carrier gel) and the contralateral knee serves as the control unit (receiving the placebo gel) for concurrent comparison.

Randomization (investigator's opinion)
Randomized

Randomization description
Randomization will be performed at the patient level to determine the treatment sequence for the knees (left vs. right) using a permuted block randomization method (with block sizes of 2 and 4). Each patient will be allocated to one of two sequences: Sequence A (Left knee: Omega-3 NLC gel; Right knee: Placebo gel) or Sequence B (Left knee: Placebo gel; Right knee: Omega-3 NLC gel). The unit of randomization is the individual patient. The allocation sequence will be generated using statistical software by an independent statistician who is not involved in clinical assessments. To ensure allocation concealment, sequentially numbered, opaque, sealed envelopes will be utilized. Upon enrollment of an eligible patient, the corresponding envelope will be opened in numerical order to determine which knee receives the active intervention and which receives the placebo.

Blinding (investigator's opinion)
Double blinded

Blinding description
The investigational products (Omega-3 NLC gel and placebo gel) will be identical in all physical characteristics, including color, odor, consistency, and packaging in identical tubes. The formulations will be prepared and labeled with unique codes (e.g., Gel A and Gel B) by the principal investigator (the formulation pharmacist), who is aware of the assignments but will have no role in the clinical enrollment, management, or evaluation of the patients. The participants (patients) will be fully blinded to which knee receives the active or placebo gel throughout the study. The outcome assessor (the clinician responsible for measuring and recording the VAS pain scores at baseline and at the end of the study) will also be completely blinded to the identity of the gels. Furthermore, the compiled data will be provided to the data analyst (statistician) in a coded format, and unblinding of the treatment codes will only occur after the statistical analysis has been fully completed.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee of Tabriz University of Medical Sciences

Street address
Tabriz University of Medical Sciences, Daneshgah Street, Tabriz

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Tabriz

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East Azarbaijan

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5165665811

Approval date
2026-05-24, 1405/03/03

Ethics committee reference number
IR.TBZMED.REC.1405.116

Health conditions studied

1

Description of health condition studied
Knee Osteoarthritis

ICD-10 code
M17

ICD-10 code description
Osteoarthritis of knee

Primary outcomes

1

Description
The severity of knee joint pain intensity in patients with mild to moderate osteoarthritis

Timepoint
At baseline before the intervention and four weeks after the start of the treatment

Method of measurement
Using the zero to ten centimeter visual analog scale questionnaire

2

Description
The severity of local inflammation and swelling in the knee joint area

Timepoint
At baseline before the intervention and four weeks after the start of the treatment

Method of measurement
Through local physical examination and knee joint palpation by an orthopedist specialist

Secondary outcomes

1

Description
The requirement and consumption amount of rescue analgesic medication by the patient during the study period

Timepoint
At baseline, two and four weeks after the start of the trial

Method of measurement
By counting the number of consumed acetaminophen tablets recorded in the patient daily diary log

Intervention groups

1

Description
Intervention group: 30 patients with bilateral knee osteoarthritis will topically apply an omega 3 nanostructured lipid carrier gel formulation twice daily (morning and evening) to the randomly assigned knee for a duration of one month (30 days). For each application, 1 gram of the gel will be applied topically to the affected knee areas. The formulation is prepared under standard laboratory conditions at the Drug Applied Research Center, Tabriz University of Medical Sciences, and packaged into identically coded tubes. The chemical composition of the gel consists of a lipid phase (omega 3 fatty acids, Precirol ATO 5, and gamma oryzanol), an aqueous surfactant phase (Tween 80 and Poloxamer), and a gel base matrix (Carbopol 940, triethanolamine, and distilled water). All participants will receive standardized education regarding proper topical application techniques and daily adherence protocols before initiating the trial.

Category
Treatment - Drugs

2

Description
Control group: The same patients will topically apply the placebo gel formulation twice daily (morning and evening) to the contralateral knee (opposite to the intervention knee) for a duration of one month (30 days). For each application, 1 gram of the gel will be applied topically to the affected knee areas. The formulation is prepared under standard laboratory conditions at the Drug Applied Research Center, Tabriz University of Medical Sciences, and packaged into coded tubes identical to the active gel. The chemical composition of the placebo gel is identical to the intervention gel except that Miglyol oil replaces the omega 3 fatty acids in the lipid phase (consisting of Miglyol, Precirol ATO 5, and gamma oryzanol)؛ while the aqueous surfactant phase (Tween 80 and Poloxamer) and the gel base matrix (Carbopol 940, triethanolamine, and distilled water) remain the exact same. All participants will receive standardized education regarding proper topical application techniques and daily adherence protocols

before initiating the trial.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Shohada Hospital

Full name of responsible person

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Sponsors / Funding sources

1

Sponsor

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Grant name

A student thesis with registration code 77481

Grant code / Reference number

77481

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Tabriz University of Medical Sciences

Proportion provided by this source

100

Public or private sector

Public

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Academic

Person responsible for general inquiries

Contact

Name of organization / entity

Tabriz University of Medical Sciences

Full name of responsible person

Hamed Hamishehkar

Position

Professor

Latest degree

Ph.D.

Other areas of specialty/work

Medical Pharmacy

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Undecided - It is not yet known if there will be a plan to make this available

Study Protocol

No - There is not a plan to make this available

Statistical Analysis Plan

No - There is not a plan to make this available

Informed Consent Form

No - There is not a plan to make this available

Clinical Study Report

No - There is not a plan to make this available

Analytic Code

No - There is not a plan to make this available

Data Dictionary

No - There is not a plan to make this available