Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

Formulation and Evaluation of the Efficacy of Peppermint Gel in Reducing Pain and Improving Knee Joint Function in Patients with Osteoarthritis compared to diclofenac gel

Protocol summary

Study aim
Evaluating the effectiveness of a topical peppermint product in improving pain in early knee osteoarthritis compared to topical diclofenac

Design
This study is a randomized, double-blind, controlled clinical trial with a parallel design.

Settings and conduct
Patients are enrolled in the study after an initial visit by an orthopedic specialist and a diagnosis of early osteoarthritis based on the clinical criteria of the American College of Rheumatology [1] including knee pain + osteophytes on radiographs + at least 1 of the following 3 criteria: age over 50 years, morning stiffness less than 30 minutes, and crepitus, and review of entry and exit criteria. Then, a demographic questionnaire is completed to record personal information, as well as an initial assessment to determine the level of pain based on VAS and pain, physical activity, and quality of life of patients based on the KOOS questionnaire.

Participants/Inclusion and exclusion criteria
Entry: 1 -Age between 50 and 80 years. 2 - Osteophyte severity grade 1 to 3 according to the Kolgren-Allernes classification 3- VAS score ≥ 4 < 8 Exclusion criteria: 1 - Attendance at another clinical study in the past 6 months 2- Cognitive or psychiatric disorder 3- Use of oral and intra-articular corticosteroids in the past two months 4- People with a history of allergy to herbal medicines

Intervention groups
After entering the study, patients in the intervention group will be given a product containing peppermint and diclofenac gel to be applied topically around the knee three times a day for 4 weeks. Patients will be visited three times, at the beginning of treatment, after 4 weeks of treatment, and 4 weeks after stopping treatment. KOOS and VAS questionnaires will also be completed.

Main outcome variables
VAS; koos score

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20211215053418N1**
Registration date: **2025-12-16, 1404/09/25**
Registration timing: **prospective**

Last update: **2025-12-16, 1404/09/25**
Update count: **0**

Registration date
2025-12-16, 1404/09/25

Registrant information

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Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
recruiting

Funding source

Expected recruitment start date
2026-01-10, 1404/10/20

Expected recruitment end date
2027-01-10, 1405/10/20

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
Formulation and Evaluation of the Efficacy of Peppermint Gel in Reducing Pain and Improving Knee Joint Function in Patients with Osteoarthritis compared to diclofenac gel

Public title
Formulation and Evaluation of the Efficacy of Peppermint Gel in Reducing Pain and Improving Knee Joint Function

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
1 - Age between 50 and 80 years. 2 - Osteophyte severity grade 1 to 3 according to the Kellgren-Allerance classification 3 - VAS score ≥4 & <8

Exclusion criteria:
1 - Participation in another clinical study in the past 6 months 2 - Cognitive or psychiatric disorder 3 - Use of oral and intra-articular corticosteroids in the past two months 4 - People with a history of allergy to herbal medicines 5 - Skin disease at the joint site 6 - Patients with acute arthritis, osteoarthritis secondary to rheumatological diseases such as rheumatoid arthritis and gout, arthritisInfection, metabolic arthritis, traumatic arthritis, uncontrolled diabetes, known heart, liver, cancer 7 - Joint replacement surgery 8 - Fibromyalgia, radiculopathy and neuropathy 9 - Those who are unable to tolerate the study and complete the treatment and follow-up period 10 - Patients who are taking glucosamine, chondroitin sulfate and muscle relaxants at the same time

Age
From **50 years** old to **80 years** old

Gender
Both

Phase
3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size
Target sample size: **72**

Randomization (investigator's opinion)
Randomized

Randomization description
Randomization and Concealment of Treatment Allocation Process (Randomization and Concealment): Randomization will be performed using the permuted block randomization method. The block size is 4, and the ratio of the intervention group (peppermint gel) to the control (diclofenac gel) in each group is equal to (1:1). In each block, random sequences of four combinations (two allocations to the intervention group and two allocations to the control group) will be created in order to maintain balance in the allocation of groups. The generation of the random sequence will be performed by the project methodologist. In order to conceal the treatment process, the boxes containing the products (peppermint gel and diclofenac gel) will be labeled with random codes. After the product is allocated to each patient, the corresponding code will be recorded in the patient file. The codes will be opened after the study is completed and data collection is completed. In the event of serious adverse events, the patient's product code will be opened for review.

Blinding (investigator's opinion)
Double blinded

Blinding description
Blinding: Peppermint gel and diclofenac gel will be prepared in a single form, with the same label, and with the same smell and color (with the addition of color and essential oil) by a pharmaceutical specialist in the Medicinal Plants Laboratory of the Iranian Medicine Faculty of Babol. The only person who knows the nature of the drugs is the pharmacist who makes the drugs.

Placebo
Not used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

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

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Babol University of Medical sciences, Sargord Ghasemi avenue, Babol

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Province
Mazandaran

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4718647745

Approval date
2025-10-15, 1404/07/23

Ethics committee reference number
IR.MUBABOL.REC.1404.123

Health conditions studied

1

Description of health condition studied
Early osteoarthritis of the knee

ICD-10 code
M17

ICD-10 code description
Osteoarthritis of knee

Primary outcomes

1

Description

The primary outcome of pain will be assessed using the VAS and KOOS questionnaires, and the secondary outcomes of joint symptoms, physical activity, exercise, and quality of life in patients will be measured using the KOOS questionnaire.

Timepoint

Patients will be visited three times, at the beginning of treatment, 4 weeks after the start of treatment, and 4 weeks after stopping treatment.

Method of measurement

KOOS: A valid, reliable, and responsive self-report instrument used for short-term and long-term follow-up of various knee injuries, including osteoarthritis, and was developed to expand the WOMAC index.[30] This relatively new, well-designed, and simple self-report instrument has good reliability, validity, and responsiveness in various populations with various knee problems [31].It can be used to assess the patient's opinion about knee problems in short-term and long-term follow-up periods ranging from one week to one decade, as well as in young and middle-aged people with osteoarthritis following trauma.The original version of the questionnaire has remained unchanged, although some small improvements have been made. The content of this questionnaire consists of 42 items, which are classified into 5 subgroups or arms:1. Pain intensity and frequency during physical activities [1]2. Symptoms such as knee stiffness or swelling and limited range of motion, clicking sound [2]3. Difficulty experiencing daily activities [3]4. Difficulty performing sports and recreational activities [4]5. Lifestyle changes and knee-related quality of life [5]Each question is scored between 0 and 4. The criterion for answering the questions is the patient's condition in the past week. After summing the items in each subgroup, the resulting number is obtained based on a specific formula in the form of scores between 0 and 100. Where 0 indicates a severe knee problem and 100 indicates a problem-free condition. Obtaining an overall score from the KOOS questionnaire is of no value and is not recommended [32]. Normalization of the scores of each subscale is performed using the following formulas [33].VAS: Visual analogue scale (VAS) is used to measure pain in patients.It has high validity and reliability [34, 35].The visual analogue scale for measuring pain intensity is a 10 cm ruler with the word no pain written on the left end and the word most severe pain written on the right end.The pain intensity is reported by the patient using a visual analogue scale (VAS) that has been standardized for measuring pain and recorded by the researcher. The visual analogue scale is divided from zero to ten as follows:0-1: no pain2-3: little pain4-5: a lot of pain,6-7: very bad pain8-9: maximum pain10: pain

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group: After entering the study, patients will be randomly assigned to one of the drug groups (intervention with peppermint gel) or control (diclofenac gel). The intervention group will be given a product containing peppermint to be applied topically around the knee three times a day for 4 weeks. Patients will be visited three times, at the beginning of treatment, after 4 weeks of treatment, and 4 weeks after discontinuation of treatment, and a review of drug use as well as possible side effects such as skin burning and itching and allergic symptoms will be recorded in the drug side effects checklist at follow-up times. KOOS and VAS questionnaires will also be completed.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Babol 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

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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
Yes - There is a plan to make this available
Statistical Analysis Plan
Yes - There is a plan to make this available
Informed Consent Form
Yes - There is a plan to make this available
Clinical Study Report
Yes - There is a plan to make this available
Analytic Code
Undecided - It is not yet known if there will be a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available
Title and more details about the data/document
-

When the data will become available and for how long

-

To whom data/document is available

-

Under which criteria data/document could be used

-

From where data/document is obtainable

-

What processes are involved for a request to access data/document

-

Comments