# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

07 Nov 2026

# A Randomized Controlled Trial to Evaluate the Effect of a Topical Cream Containing Achillea millefolium and Tanacetum Oils on Musculoskeletal Pain in Adults: Comparison with Placebo

## Protocol summary

**Study aim**

Evaluation of the effect of a cream containing Achillea millefolium (yarrow) and Tanacetum (tansy) oils on reducing musculoskeletal pain, improving motor function, and assessing its safety and anti-inflammatory effects.

**Design**

This study is a phase2–3randomized, double-blind, parallel-group clinical trial conducted on100patients with mild to moderate musculoskeletal pain. Participants will be randomly assigned to 2 groups: Treatment and, Placebo groups.

**Settings and conduct**

This study is conducted in the clinic of a physical medicine specialist and follows a randomized design. Participants are instructed to apply the topical cream once or twice daily for a duration of one to two months, depending on pain severity. The participants, outcome assessor, and data analyst are all blinded to the group assignments.

**Participants/Inclusion and exclusion criteria**

Inclusion: Stable mild to moderate musculoskeletal pain, written informed consent, no recent use of analgesic drugs or supplements, ability to comply with study procedures, no allergy to herbs or topical products. Exclusion: Allergy to herbs or essential oils, skin disease at the cream application site, recent use of analgesic drugs, systemic disease affecting pain, pregnancy or breastfeeding, use of drugs affecting pain or mood, inability to comply with the study protocol, recent participation in another clinical trial.

**Intervention groups**

1. Treatment group: recipients of a topical cream containing therapeutic oils of Achillea millefolium and Tanacetum. 2. Placebo group: recipients of a cream without active herbal ingredients, with similar appearance and texture.

**Main outcome variables**

pain intensity (measured by VAS), motor function (assessed using standard questionnaires), patient satisfaction with treatment, and the occurrence of possible side effects

## General information

**Reason for update**

**Acronym**

AMTO-Pain

**IRCT registration information**

IRCT registration number: **IRCT20250720066574N1**
Registration date: **2025-08-28, 1404/06/06**
Registration timing: **prospective**

Last update: **2025-08-28, 1404/06/06**
Update count: **0**

**Registration date**

2025-08-28, 1404/06/06

**Registrant information**

**Name**

Ali Aghababai-Beni

**Name of organization / entity**

**Country**

Iran (Islamic Republic of)

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**Recruitment status**

**Recruitment complete**

**Funding source**

**Expected recruitment start date**

2025-10-23, 1404/08/01

**Expected recruitment end date**

2026-04-21, 1405/02/01

**Actual recruitment start date**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

A Randomized Controlled Trial to Evaluate the Effect of a Topical Cream Containing Achillea millefolium and Tanacetum Oils on Musculoskeletal Pain in Adults: Comparison with Placebo

**Public title**

Investigation of the Effect of Achillea millefolium and Tanacetum Oils in Cream Form on Musculoskeletal Pain

**Purpose**

Treatment

**Inclusion/Exclusion criteria**

**Inclusion criteria:**

Having mild to moderate musculoskeletal pain (involving areas such as the lower back, neck, knee, shoulder, joints, or muscles), with a pain score between 3 and 7 on the Visual Analog Scale (VAS) Stable musculoskeletal pain for at least the past two weeks No use of topical or oral analgesic medications or supplements within the past 72 hours Written informed consent to participate in the study Ability to comply with study procedures (completing forms, regular use of the cream, and attending follow-up visits) No known hypersensitivity or history of allergy to herbal components or topical products

**Exclusion criteria:**

Known allergy or hypersensitivity to medicinal herbs or essential oils Presence of dermatological conditions at the site of cream application Use of topical analgesic or anti-inflammatory products at the pain site within the past 72 hours Use of topical analgesic or anti-inflammatory products at the site of pain within the past 72 hours Presence of systemic diseases affecting pain Pregnancy or breastfeeding Concurrent use of medications affecting pain perception or mood Inability to comply with the study protocol or complete assessment forms Participation in another clinical trial within the past month

**Age**

No age limit

**Gender**

Both

**Phase**

2-3

**Groups that have been masked**

- Participant
- Investigator
- Outcome assessor
- Data analyser

**Sample size**

Target sample size: **120**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

In this study, randomization will be performed using permuted block randomization with variable block sizes (4 and 6) to maintain balance in the number of participants allocated to the two groups: the intervention group (topical cream containing Achillea millefolium and Melissa officinalis oils) and the control group (placebo cream). Unit of randomization: Individual (each participant will be independently assigned to one of the two groups). Stratification: Randomization will be stratified by sex (male/female) and pain status (acute/chronic) to ensure balanced distribution of these variables between groups. Random sequence generation tool: The allocation sequence will be generated by an independent statistician using statistical software (e.g., R or Stata). Within each stratum, blocks of variable sizes will be randomly arranged. Sequence generation and storage: The final allocation sequence will be stored in an encrypted file and managed by a person not involved in participant recruitment or outcome assessment (statistician or study pharmacist). Allocation concealment: To prevent selection bias, Sequentially Numbered, Opaque, Sealed Envelopes (SNOSE) or a centralized randomization system will be used. The recruiter will open the next envelope or obtain the allocation code from the system only after confirming eligibility of the participant. Blinding: The intervention and placebo creams will be identical in appearance, packaging, labeling, and texture, and will only be distinguished by code. Thus, participants, clinical investigators, and outcome assessors will remain blinded to group allocation. Code breaking (Unblinding): Unblinding will only be permissible in case of a medical emergency and must be fully documented. After data collection is completed and the database is locked, codes will be released by the independent statistician. Quasi-randomization: No quasi-random methods (such as allocation by date of birth or order of recruitment) will be used in this study.

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

This study will be conducted as a double-blind randomized controlled trial. Both participants and investigators responsible for administering the intervention and assessing outcomes will be blinded to group allocation. The creams for intervention and placebo will be identical in appearance, texture, and packaging to maintain blinding. Data analysts will also be blinded during data analysis to prevent bias. Allocation concealment will be ensured using sealed, opaque envelopes. The Data Safety Monitoring Board, if involved, will have access to unblinded data only when necessary for safety assessments

**Placebo**

Used

**Assignment**

Parallel

**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**
**Name of ethics committee**
Research Ethics Committee of Islamic Azad University-Shahrekord Branch
**Street address**
Rahmatiyeh
**City**
Shahrekord
**Province**
Chahar-Mahal-va-Bakhtiari
**Postal code**
8813733395
**Approval date**
2025-06-25, 1404/04/04
**Ethics committee reference number**
IR.IAU.SHK.REC.1404.081

## Health conditions studied

### 1

**Description of health condition studied**
Myositis
**ICD-10 code**
M60
**ICD-10 code description**
Myositis

### 2

**Description of health condition studied**
Polyarthrosis
**ICD-10 code**
M15
**ICD-10 code description**
Polyosteoarthritis

### 3

**Description of health condition studied**
Coxarthrosis [arthrosis of hip]
**ICD-10 code**
M16
**ICD-10 code description**
Osteoarthritis of hip

### 4

**Description of health condition studied**
Osteoarthritis of knee
**ICD-10 code**
M17
**ICD-10 code description**
Osteoarthritis of knee

### 5

**Description of health condition studied**
Osteoarthritis of first carpometacarpal joint
**ICD-10 code**
M18
**ICD-10 code description**
Osteoarthritis of first carpometacarpal joint

### 6

**Description of health condition studied**
Other and unspecified osteoarthritis
**ICD-10 code**
M19
**ICD-10 code description**
Other and unspecified osteoarthritis

### 7

**Description of health condition studied**
Calcification and ossification of muscle
**ICD-10 code**
M61
**ICD-10 code description**
Calcification and ossification of muscle

### 8

**Description of health condition studied**
Other disorders of muscle
**ICD-10 code**
M62
**ICD-10 code description**
Other disorders of muscle

### 9

**Description of health condition studied**
Disorders of muscle in diseases classified elsewhere
**ICD-10 code**
M63
**ICD-10 code description**
Disorders of muscle in diseases classified elsewhere

### 10

**Description of health condition studied**
Rheumatoid arthritis with rheumatoid factor
**ICD-10 code**
M05
**ICD-10 code description**
Rheumatoid arthritis with rheumatoid factor

### 11

**Description of health condition studied**
Other rheumatoid arthritis
**ICD-10 code**
M06
**ICD-10 code description**
Other rheumatoid arthritis

**12**

**Description of health condition studied**
Enteropathic arthropathies
**ICD-10 code**
M07
**ICD-10 code description**
Enteropathic arthropathies

**13**

**Description of health condition studied**
Juvenile arthritis
**ICD-10 code**
M08
**ICD-10 code description**
Juvenile arthritis

**14**

**Description of health condition studied**
Gout
**ICD-10 code**
M10
**ICD-10 code description**
Gout

**15**

**Description of health condition studied**
Other crystal arthropathies
**ICD-10 code**
M11
**ICD-10 code description**
Other crystal arthropathies

**16**

**Description of health condition studied**
Other and unspecified arthropathy
**ICD-10 code**
M12
**ICD-10 code description**
Other and unspecified arthropathy

**17**

**Description of health condition studied**
Other arthritis
**ICD-10 code**
M13
**ICD-10 code description**
Other arthritis

## Primary outcomes

**1**

**Description**
The primary outcome variables in this study include two measures: the intensity of pain in the affected area, assessed using the Visual Analog Scale (VAS) at the beginning and end of the intervention period, and patients' motor function, evaluated through standardized questionnaires appropriate to the affected region. These two variables are analyzed to determine the efficacy of the herbal cream in reducing musculoskeletal pain and improving physical function in affected patients.
**Timepoint**
Baseline: Before starting the use of the cream. Mid-study: Week 1 and Week 2 . End of intervention: After 2 to 4 weeks of use (depending on pain severity and prescribed duration)
**Method of measurement**
Pain Intensity: Measured using the Visual Analog Scale (VAS). This scale consists of a 10-centimeter horizontal line on which the patient marks their perceived level of pain, ranging from "no pain" (score 0) to "worst imaginable pain" (score 10). Motor Function: Assessed using standardized and validated questionnaires specific to the pain location (e.g., the Oswestry Disability Index for lower back pain, WOMAC for knee pain, or the Neck Disability Index (NDI) for neck pain).

## Secondary outcomes

empty

## Intervention groups

**1**

**Description**
Intervention group: recipients of a topical cream containing therapeutic oils extracted from Achillea millefolium (yarrow) and Tanacetum (tansy) plants.Usage: topical application on the painful area with gentle massage.Frequency: once to twice daily.Duration: at least 2 weeks and up to 4 weeks (depending on pain severity).Preparation: the cream is prepared by a licensed pharmacist in a pharmacy, free of unnecessary chemical additives, and is delivered to the patient at the clinic.
**Category**
Treatment - Drugs

**2**

**Description**
Control group: recipients of a topical cream with the same appearance, color, smell, and texture as the herbal cream but without active therapeutic ingredients (i.e., free of Achillea millefolium and Tanacetum oils).Usage, dosage, and duration are the same as the intervention group.The purpose of this group is to control for the psychological (placebo) effect of the treatment.
**Category**
Placebo

## Recruitment centers

**1**

**Recruitment center**
**Name of recruitment center**

Askarieh Hospital
**Full name of responsible person**
Dr. Modina Sadat Javadi
**Street address**
Asgariye St
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**Province**
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**Postal code**
8197133111
**Phone**
+98 31 3225 0041
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## Sponsors / Funding sources

**1**

**Sponsor**
**Name of organization / entity**
Islamic Azad University
**Full name of responsible person**
Ali Aghababai Beni
**Street address**
Rahmatiyeh
**City**
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ali.aghababai@iau.ir
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
No
**Title of funding source**
Bahar Daru Mehr Company
**Proportion provided by this source**
100
**Public or private sector**
Private
**Domestic or foreign origin**
Domestic
**Category of foreign source of funding**
*empty*
**Country of origin**
**Type of organization providing the funding**
Persons

## Person responsible for general inquiries

**Contact**
**Name of organization / entity**
Islamic Azad University
**Full name of responsible person**
Ali Aghababai Beni
**Position**
Associate professor
**Latest degree**
Ph.D.
**Other areas of specialty/work**
Medical Pharmacy
**Street address**
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## Person responsible for scientific inquiries

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**Position**
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## Person responsible for updating data

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**Email**

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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**

Yes - There is 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**

Not applicable

**Data Dictionary**

Not applicable

**Title and more details about the data/document**

The study data include de-identified participant information regarding pain intensity (based on the VAS scale), motor function (responses to standardized questionnaires), and other clinical outcome-related data. These data were collected to evaluate the efficacy of the herbal cream in reducing musculoskeletal pain and improving motor function, and will be shared as structured electronic files.

**When the data will become available and for how long**

The data will be available from the time of study publication and will remain accessible to researchers for up to 5 years thereafter. Bahar Darou Mehr Company may also request the publication of an article based on the study results.

**To whom data/document is available**

Researchers affiliated with academic, research, and other recognized scientific institutions who submit a formal request will be granted access to the data and documents. Access for individuals from industry or commercial sectors will be considered only upon ethical and scientific review and approval.

**Under which criteria data/document could be used**

The data and documents may only be used for research, educational, or secondary analysis purposes. Usage must comply with research ethics principles, participant confidentiality, and data protection regulations. Any commercial use or public dissemination without written permission from the research team is strictly prohibited. Applicants must submit a research proposal and sign a data use agreement ensuring responsible and restricted use.

**From where data/document is obtainable**

Applicants can contact the principal investigator via email or phone to request access to the study data or documents.

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

After receiving the request via email or phone, the principal investigator will review the research purpose and the applicant’s affiliation. If the request is deemed appropriate, a data-sharing agreement will be signed. Upon completion of the agreement, the requested de-identified data or documents will be provided within 2 to 4 weeks.

**Comments**