# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

07 Nov 2026

## The effect of chamomile extract stick on the severity of headache in patients with migraine headache.

## Protocol summary

**Study aim**
Determining the effect of chamomile aqueous extract stick on headache severity in patients with migraine headaches

**Design**
his study was a triple-blind randomized controlled clinical trial

**Settings and conduct**
At the beginning of the study, the MIDAS Questionnaire will be completed by the patients. Then, a chamomile essential oil stick will be provided to the intervention group, while a placebo stick will be provided to the control group. Participants will be instructed to apply the stick to the forehead and temporal areas for 30–40 minutes at the onset of headache and before taking any analgesic medication. Pain intensity during each attack will be recorded using the Numeric Rating Scale (NRS). After three months, the MIDAS questionnaire will be completed again.

**Participants/Inclusion and exclusion criteria**
efinitive diagnosis of migraine based on the International Headache Society (IHS) criteria Having at least 5 migraine headache attacks Duration of each attack between 4 and 72 hours Presence of at least two of the following characteristics: Unilateral pain Pulsating quality Moderate to severe intensity Aggravation by physical activity Presence of at least one of the following symptoms: Nausea or vomiting Photophobia Phonophobia Age between 18 and 65 years History of migraine for at least one year Willingness to participate in the study and completion of written informed consen

**Intervention groups**
In this study, the intervention group consists of migraine patients who, during an attack, apply a chamomile extract stick topically. Headache severity and associated symptoms are assessed using standard questionnaires after application. The control group includes similar patients who use a placebo stick (without active chamomile extract), allowing a clear comparison between chamomile treatment and no active intervention.

**Main outcome variables**
Severity of migraine headache in patients

## General information

**Reason for update**

**Acronym**

**IRCT registration information**
IRCT registration number: **IRCT20251109067923N1**
Registration date: **2026-06-01, 1405/03/11**
Registration timing: **retrospective**

Last update: **2026-06-01, 1405/03/11**
Update count: **0**

**Registration date**
2026-06-01, 1405/03/11

**Registrant information**

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**Recruitment status**
**Recruitment complete**

**Funding source**

**Expected recruitment start date**
2026-01-05, 1404/10/15

**Expected recruitment end date**
2026-05-05, 1405/02/15

**Actual recruitment start date**
2026-01-05, 1404/10/15

**Actual recruitment end date**
2026-05-05, 1405/02/15
**Trial completion date**
2026-05-05, 1405/02/15

**Scientific title**
The effect of chamomile extract stick on the severity of headache in patients with migraine headache.

**Public title**
The effect of chamomile extract stick on the severity of headache in patients with migraine headache.
**Purpose**
Supportive
**Inclusion/Exclusion criteria**
**Inclusion criteria:**
At least 5 headache attacks.Duration of each attack lasting 4–72 hours. At least 2 of the following characteristics: unilateral location pulsating quality moderate to severe intensity aggravation by routine physical activity. At least 1 of the following associated symptoms: nausea vomiting phonophobia photophobia Symptoms not attributable to another disorder. Age between 18 and 65 years. History of migraine headaches for at least one year .Onset of the first headache attack before the age of 50 years
**Exclusion criteria:**
Presence of serious acute or chronic medical conditions, such as abnormal neurological examination findings blood pressure higher than 140/90 mmHg History of skin lesions , eczema, any type of allergic reaction in the temporal and forehead regions. Severe headache unresponsive to at least three types of analgesic medications experiencing headache on more than 15 days per month for 3 months or longer. Breastfeeding pregnancy inability to read (required for completing headache diary forms) Patients at risk of suicide those diagnosed with psychiatric disorders
**Age**
From **18 years** old to **65 years** old
**Gender**
Both

**Phase**
N/A
**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

**Sample size**
Target sample size: **96**
Actual sample size reached: **96**
**Randomization (investigator's opinion)**
Randomized
**Randomization description**
This study is a randomized, controlled, triple-blind clinical trial. Block randomization with a 1:1 allocation ratio was used to ensure balanced group sizes throughout the study. Variable block sizes were applied to reduce predictability of allocation sequences. The unit of randomization was individual; each eligible participant was independently assigned to either the intervention or control group. Stratified randomization was not applied in this study. Randomization Tools • Computer-generated random number software • Allocation sequence prepared by an independent investigator (supervisor) • Sequentially Numbered, Opaque, Sealed Envelopes (SNOSE) The allocation sequence was generated using computer-based random number software according to predetermined block sizes. The sequence was accessible only to the independent investigator responsible for allocation and was concealed from the clinical and research team. To prevent selection bias, allocation concealment was rigorously implemented: • Opaque, light-proof, sealed envelopes • Sequentially numbered according to the random allocation list • Each envelope contained either a chamomile-containing patch (intervention group) or an identical placebo patch (control group) • After enrollment, envelopes were opened sequentially without knowledge of content • Data were coded prior to statistical analysis to ensure that the statistician remained blinded Thus, triple blinding (participants, treating physician/research team, and statistician) was maintained throughout all stages of the study.
**Blinding (investigator's opinion)**
Triple blinded
**Blinding description**
This study is a randomized controlled clinical trial with a triple-blind design. Blinding has been implemented as follows: Participants: After receiving a full explanation of the study objectives and procedures and providing written informed consent, participants are enrolled in the trial. They are unaware of the type of patch received (chamomile-containing patch or placebo). Both patches are identical in appearance, size, color, smell, texture, and packaging. Participants are fully aware of their participation in a clinical trial; blinding applies only to the type of intervention. Treating physicians and healthcare personnel: Physicians and any healthcare staff involved in patient care are blinded to group allocation. The intervention packages contain no identifying marks indicating group assignment. Outcome assessors and data collectors: The researcher responsible for follow-up assessments and data collection is blinded to group allocation. All data are recorded using participant codes without reference to intervention type. Statistician: Data are analyzed in a coded format (Group A and Group B). The statistician remains blinded to the actual group allocation until completion of the analysis. Random allocation is performed by an independent individual not involved in clinical assessment, data collection, or statistical analysis, using computer-generated random numbers. Allocation concealment is ensured through sequentially numbered, opaque, sealed envelopes. Neither the principal investigator nor the research team has access to the allocation sequence. Therefore, participants, care providers, outcome assessors, and the statistician are all blinded to the intervention assignment, and allocation concealment is fully maintained throughout the study
**Placebo**

Used

**Assignment**

Parallel

**Other design features**

First-time design and development of a chamomile stick

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**

**Name of ethics committee**

Research Ethics Committees of Shahid Sadoughi University of Medical Sciences

**Street address**

Termeh Ave

**City**

yazd

**Province**

Yazd

**Postal code**

8915313783

**Approval date**

2025-10-12, 1404/07/20

**Ethics committee reference number**

IR.SSU.REC.1404.106

## Health conditions studied

### 1

**Description of health condition studied**

migraine headache

**ICD-10 code**

G43.111

**ICD-10 code description**

Migraine with aura, intractable, with status migrainosus

## Primary outcomes

### 1

**Description**

Severity and disability of migraine headaches

**Timepoint**

Three months before the intervention and three months after the intervention

**Method of measurement**

Migraine disability assessment score

## Secondary outcomes

### 1

**Description**

The number of migraine attacks, the duration of the attacks, the amount of medication taken due to headaches, the duration of the disease and the accompanying symptoms

**Timepoint**

Three months before and after the intervention

**Method of measurement**

Migraine disability assessment score

## Intervention groups

### 1

**Description**

Intervention group:Chamomile essential oil (Matricaria chamomilla L.) is used as the active ingredient. One kilogram of dried flowers is authenticated botanically and assigned a herbarium code by the Faculty of Pharmacy. The essential oil is extracted by hydrodistillation using a Clevenger apparatus. After separation, the pure essential oil is stored in dark glass containers at 4°C until formulation.Formulation and Composition:The topical stick containing chamomile essential oil is prepared using the Heating and Congealing Molding Method. The concentration of essential oil in the final product is 1% (w/w).The excipients used belong to the GRAS (Generally Recognized as Safe) category and include petrolatum jelly, carnauba wax, cetyl alcohol, stearyl alcohol, paraffin wax, white petrolatum, and hydrogenated castor oil. The formulation is adjusted according to the physicochemical properties of the extracted essential oil.In the intervention group, the stick contains chamomile essential oil at the specified concentration, whereas in the control group, an identical stick with the same base composition but without essential oil (placebo) is produced. Both products are identical in shape, color, odor, texture, weight, size, and packaging.Dosage and Administration:Participants are instructed to apply the stick topically to the frontal and temporal areas at the onset of a headache attack, creating a uniform thin layer. The product is used at each headache episode over a period of three months.All products are provided in identical coded packages to maintain blinding.

**Category**

Treatment - Drugs

### 2

**Description**

The control group will use a placebo stick that is similar in appearance, color, and method of application to the chamomile essential oil stick but does not contain the active ingredient. The chamomile essential oil stick will be applied topically to the forehead and temporal areas and contains natural chamomile essential oil intended to reduce the severity of migraine headaches.

**Category**

Placebo

## Recruitment centers

**1**

**Recruitment center**
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Shahid Sadoughi Hospital, Yazd
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## Sponsors / Funding sources

**1**

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**Web page address**
http://http//:www.research.ssu.ac.ir
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
Yes
**Title of funding source**
Yazd 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**
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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**
No - There is not a plan to make this available
**Clinical Study Report**
Yes - There is a plan to make this available
**Analytic Code**
Not applicable
**Data Dictionary**
Yes - There is a plan to make this available
**Title and more details about the data/document**
In this study, individual participant data will be shared only after de-identification to ensure privacy. The shared dataset will include primary outcome measures such as headache severity, duration of attacks, frequency of episodes, and associated symptoms, along with standardized questionnaires (e.g., MIDAS and VAS). No personal or identifiable information will be released. Access to these data will be provided after publication of the main study results, through the corresponding author or the institutional repository of Shahid Sadoughi University of Medical Sciences, Yazd, Iran
**When the data will become available and for how long**
The de-identified study documents and datasets will be made available after completion of the trial and publication of the main results. Start of access period: 6 months after publication of the study results in peer-reviewed journals Duration of availability: Data will remain accessible for at least 5 years following publication.
**To whom data/document is available**
The de-identified data and study documents will be available only to researchers affiliated with recognized academic institutions and scientific centers. Requests must be submitted through the corresponding author or the institutional repository. Access for non-academic or industry professionals will be considered only if a formal research collaboration with the university or study team is established.
**Under which criteria data/document could be used**
Data may be used only for scientific and academic research purposes; commercial or promotional use is prohibited. Analyses must be limited to research questions related to migraine and complementary therapies. Use of data must comply with research ethics principles and regulations of Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Applicants must submit their approved research proposal or study plan along with the request. Any publication resulting from these data must include proper citation of the original study. Data will be shared only in de-identified format, excluding any personal or identifiable information. Access is subject to approval by the university's ethics committee and the corresponding author.
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**What processes are involved for a request to access data/document**
Submission of formal request: Applicants must submit a formal request including the purpose of research and an approved proposal to the corresponding author or supervisor. Initial review of request: The research team and university ethics committee will review the request within 2 weeks. Ethics committee approval: If required, the request will be referred to the university's ethics

committee. This step usually takes 2–4 weeks. Signing of data use agreement: Once approved, applicants must sign a data use agreement outlining conditions (e.g., non-commercial use, confidentiality). Delivery of data/documents: De-identified datasets or requested documents will be provided within 2 weeks after the agreement is signed. Estimated total duration: Typically 6–10 weeks from submission of request to receipt of data.

**Comments**