Clinical Trial Protocol
Iranian Registry of Clinical Trials

08 Nov 2026

Development and clinical evaluation of a Myrtus communis mucoadhesive buccal tablet for minor recurrent aphthous stomatitis: a randomized controlled trial

Protocol summary

Study aim

Comparison of the efficacy and safety of a Myrtus communis mucoadhesive buccal tablet versus 2% amitriptyline gel and 0.01% dexamethasone mouthwash in treating minor recurrent aphthous stomatitis.

Design

In this single-center, randomized, active-controlled phase 2/3 trial, 81 patients were allocated to three parallel arms (27/28/26) using computer-generated blocks of 6 with sealed, opaque allocation concealment. Outcome assessors and the statistician were blinded; participants were not, due to different dosage forms (tablet, gel, mouthwash). No placebo group was included.

Settings and conduct

Single-center study at Kerman University of Medical Sciences. Block randomization; allocation concealment with sealed envelopes. Outcome assessor and statistician blinded; participants not blinded. No placebo. Treatment for 10 days; assessments on days 0, 1, 4, 6, and 10.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Age 18–65 years; active minor aphthous lesion; ≥3 recurrent aphthous stomatitis episodes per year; written informed consent. Exclusion criteria: Hypersensitivity to study components; acute infectious disease; pregnancy or lactation; systemic corticosteroids or immunosuppressants within 3 months; oral lesions due to systemic conditions; systemic antibiotics within 14 days; topical oral ulcer treatment within 72 hours; active cancer; orthodontic appliances or removable partial dentures; participation in another clinical trial; inability or unwillingness to comply with the protocol.

Intervention groups

Three parallel active-treatment groups (all three times daily for 10 days; no eating, drinking, or rinsing for 30 minutes afterward): Group A: Topical 2% amitriptyline gel Group B: Myrtus communis mucoadhesive buccal tablet Group C: 0.01% dexamethasone mouthwash

Main outcome variables

Change in aphthous ulcer diameter (mm) from baseline to day 10

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20260912071020N1**
Registration date: **2026-09-17, 1405/06/26**
Registration timing: **retrospective**

Last update: **2026-09-17, 1405/06/26**
Update count: **0**

Registration date

2026-09-17, 1405/06/26

Registrant information

Name

Morteza Barkam

Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2026-04-04, 1405/01/15

Expected recruitment end date

2026-09-11, 1405/06/20

Actual recruitment start date
2026-04-04, 1405/01/15
Actual recruitment end date
2026-09-11, 1405/06/20
Trial completion date
2026-09-11, 1405/06/20

Scientific title
Development and clinical evaluation of a Myrtus communis mucoadhesive buccal tablet for minor recurrent aphthous stomatitis: a randomized controlled trial

Public title
Evaluation of the Effect of Myrtus communis Mucoadhesive Buccal Tablet in the Treatment of Recurrent Aphthous Stomatitis
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Age between 18 and 65 years Presence of an active minor recurrent aphthous stomatitis lesion on non-keratinized oral mucosa (labial or buccal mucosa) History of at least three recurrent aphthous stomatitis episodes per year Provision of written informed consent
Exclusion criteria:
Known hypersensitivity to study components Acute infectious disease Pregnancy or lactation Systemic use of corticosteroids or immunosuppressants within the past 3 months Oral lesions secondary to systemic conditions (e.g., ulcerative colitis, Crohn's disease, Behçet's syndrome, or severe anemia) Systemic antibiotic use within the past 14 days Topical oral ulcer treatment within the past 72 hours Diagnosis of active cancer Orthodontic appliances or removable partial dentures Concurrent participation in another clinical trial Inability or unwillingness to comply with study protocols
Age
From **18 years** old to **65 years** old
Gender
Both

Phase
3
Groups that have been masked
No information
Sample size
Target sample size: **75**
Actual sample size reached: **81**
Randomization (investigator's opinion)
Randomized
Randomization description
This study used block randomization with a block size of 6. The unit of randomization was individual patients. The random sequence was generated in a 1:1:1 ratio for the three groups (2% amitriptyline gel, Myrtus communis mucoadhesive tablet, and dexamethasone mouthwash) by an independent statistician using computer-generated random numbers. No stratification was applied. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes, so allocation was revealed only after patient enrollment. Treatments were dispensed in identical coded containers. Outcome assessors and the statistician were blinded to group assignment. Complete participant blinding was not feasible due to the distinct physical forms of the interventions (tablet, gel, mouthwash). No quasi-random methods (e.g., day of visit, odd/even) were used.
Blinding (investigator's opinion)
Not blinded
Blinding description
Placebo
Not used
Assignment
Parallel
Other design features
This study had a two-phase design: Phase 1 involved the development and physicochemical characterization of a mucoadhesive buccal tablet containing Myrtus communis essential oil; Phase 2 was a randomized, parallel-group, active-controlled, three-arm clinical trial. In the clinical phase, patients were allocated in a 1:1:1 ratio to receive either 2% amitriptyline gel, the Myrtus communis mucoadhesive tablet, or 0.01% dexamethasone mouthwash. The study had no placebo group and used active comparators. Participant blinding was not feasible because of the distinct dosage forms (tablet, gel, and mouthwash); however, outcome assessors and the statistician were blinded. Randomization was performed using block randomization with a block size of 6, and allocation concealment was achieved with sequentially numbered, opaque, sealed envelopes. The primary outcome was change in ulcer diameter, and secondary outcomes included pain intensity (VAS), erythema, and exudate, assessed at baseline and on days 1, 4, 6, and 10. Due to baseline imbalance in erythema and exudate scores among the groups, analyses were conducted using mixed-effects models adjusted for baseline values. The study was single-center and limited to patients with minor recurrent aphthous stomatitis (RAS).

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethics committee of Kerman University of Medical Sciences
Street address
Kerman University of Medical Sciences Campus, Beginning of Haft Bagh Alavi Road, Kerman
City
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Province
Kerman
Postal code
7616910002
Approval date
2026-08-29, 1405/06/07

Ethics committee reference number
IR.KMU.AH.REC.1405.084

Health conditions studied

1

Description of health condition studied
Minor recurrent aphthous stomatitis (MiRAS)
ICD-10 code
K12.0
ICD-10 code description
Recurrent oral aphthae

Primary outcomes

1

Description
The primary outcome variable was the change in minor recurrent aphthous ulcer diameter (mm) from baseline (day 0) to day 10. Ulcer diameter was measured using a calibrated UNC-15 periodontal probe; the largest and perpendicular diameters were recorded, and their mean was used as the ulcer diameter. Measurements were performed on days 0, 1, 4, 6, and 10. The primary endpoint was the difference in ulcer diameter at day 10 compared with day 0. The sample size was calculated to detect a 2.0 mm difference in ulcer diameter with SD = 2.5 mm, 80% power, and $\alpha = 0.05$.
Timepoint
Ulcer diameter was measured at baseline (Day 0, before intervention) and on Days 1, 4, 6, and 10 after treatment initiation. The primary outcome was the change in ulcer diameter from Day 0 to Day 10.
Method of measurement
Ulcer diameter was measured using a calibrated UNC-15 periodontal probe. The largest diameter of the ulcer and its perpendicular diameter were recorded, and the mean of the two was considered as the ulcer diameter.

Secondary outcomes

1

Description
Oral pain intensity experienced by the patient was measured using a Visual Analogue Scale from 0 to 10, where 0 indicated no pain and 10 indicated the worst imaginable pain.
Timepoint
At baseline (Day 0, before intervention) and on Days 1, 4, 6, and 10 after treatment initiation.
Method of measurement
Visual Analogue Scale with a range of 0 to 10; patient-reported.

2

Description
The degree of redness (erythema) of the oral mucosa surrounding the aphthous ulcer was assessed by a clinician using a 4-point scale: 0 = none (normal mucosal color), 1 = mild (faint or light pink halo), 2 = moderate (distinct red halo), 3 = severe (intense, deep red or violaceous halo).
Timepoint
Erythema score was measured at baseline (Day 0, before intervention) and on Days 1, 4, 6, and 10 after treatment initiation.
Method of measurement
Erythema score was measured using a standardized 4-point scale through clinical examination by the assessing clinician.

3

Description
The amount of fibrinous coating (exudate) on the ulcer base was assessed by a clinician using a 4-point scale: 0 = none (clean ulcer base), 1 = mild (thin, patchy white/yellow layer covering less than 25% of the ulcer base), 2 = moderate (moderate fibrinous layer covering 25% to 75% of the ulcer base), 3 = severe (thick, continuous layer covering more than 75% of the ulcer base).
Timepoint
Exudate score was measured at baseline (Day 0, before intervention) and on Days 1, 4, 6, and 10 after treatment initiation.
Method of measurement
Exudate score was measured using a standardized 4-point scale through clinical examination by the assessing clinician.

Intervention groups

1

Description
Intervention group: Dexamethasone sodium phosphate mouthwash was prepared at a concentration of 0.01% w/v (equivalent to 0.5 mg per 5 mL). The solution was prepared by dissolving dexamethasone sodium phosphate with sodium monophosphate and sodium diphosphate in distilled water. Patients rinsed with 5 mL of the mouthwash for 30 seconds and then spat it out, three times daily for 10 consecutive days. Participants were advised to refrain from eating, drinking, or rinsing for 30 minutes after application.
Category
Treatment - Drugs

2

Description
Intervention group: Topical amitriptyline hydrochloride gel was prepared at a concentration of 2% w/w. The gel was formulated using hydroxypropyl methylcellulose as the gelling agent and preserved with methylparaben (0.1%) and propylparaben (0.01%). Patients applied a small amount of the gel sufficient to cover the ulcer three times daily for 10 consecutive days. Participants were advised to refrain from eating, drinking, or rinsing

for 30 minutes after application.

Category

Treatment - Drugs

3

Description

Intervention group: A mucoadhesive buccal tablet containing 25 mg of Myrtus communis essential oil (equivalent to 12.5% w/w) per 200 mg tablet. The essential oil was extracted by hydrodistillation from dried, authenticated Myrtus communis leaves. Each tablet was formulated with polymeric excipients including carbomer, alginate, microcrystalline cellulose (Avicel), polyethylene glycol 6000, and magnesium stearate (Formulation F2). Patients placed one tablet directly onto the ulcer three times daily (every 8 hours), allowing it to adhere and dissolve in situ, for 10 consecutive days. Participants were advised to refrain from eating, drinking, or rinsing for 30 minutes after application.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Kerman University of Medical Sciences, School of Dentistry

Full name of responsible person

Morteza Barkam

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Sponsors / Funding sources

1

Sponsor

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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

Kerman 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

Kerman University of Medical Sciences

Full name of responsible person

Morteza Barkam

Position

Non-faculty pharmacist

Latest degree

Medical doctor

Other areas of specialty/work

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Position

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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available
Study Protocol
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
No - There is not a plan to make this available
Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available
Clinical Study Report
Undecided - It is not yet known if there will be 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
De-identified individual participant data (without any identifying information) and the study protocol are available upon reasonable request from the corresponding author. Access will be granted to researchers with a clearly defined and approved research objective. The raw data include demographic information, ulcer diameter, pain scores, erythema, and exudate scores at different time points. No sensitive or personally identifiable data will be publicly released.
When the data will become available and for how long
Access will begin 6 months after publication of the study results and will remain available for 5 years.
To whom data/document is available
Researchers affiliated with academic and scientific institutions are permitted to access the de-identified data and study documents after submitting a written request with a clearly defined research objective and obtaining approval from the corresponding author and the ethics committee. Access for commercial or industrial purposes is not permitted without a separate agreement.
Under which criteria data/document could be used
Data and documents may be used solely for academic and scientific research purposes, including re-analysis, meta-analysis, verification of results, and secondary research related to minor recurrent aphthous stomatitis and topical therapies. Commercial, legal, or patent-related use is not permitted.
From where data/document is obtainable
Requests for access to de-identified data and study documents should be directed primarily to the corresponding author.
What processes are involved for a request to access data/document
The applicant must complete the following steps: Submit a written request Ethics committee approval Sign a data sharing agreement Data preparation Data/document delivery Estimated total process time: 6 to 8 weeks from initial request submission to data receipt.
Comments