Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

A comparative study on the effect of oral bromelain capsules versus placebo on pain intensity and healing time in patients with recurrent aphthous stomatitis

Protocol summary

Study aim
Determining the impact of oral Bromelain capsules on recurrent oral ulcers

Design
A phase 3 clinical trial with a control group, parallel groups, double-blind, randomized, involving 20 patients. Coin tossing will be used for randomization.

Settings and conduct
This study is a randomized clinical trial conducted among patients with minor recurrent aphthous ulcers who refer to the Faculty of Dentistry, Babol University of Medical Sciences. Each participant will receive oral bromelain treatment during one episode of aphthous ulceration and a placebo treatment during another episode. The study will be performed in a double-blind manner, so that neither the patients nor the dentist will be aware of whether bromelain or placebo is being administered.

Participants/Inclusion and exclusion criteria
Inclusion criteria:Presence of minor recurrent aphthous ulcers located on the labial or buccal mucosa, occurring at least four times per year. Exclusion criteria: Patients with a history of any systemic disease associated with oral ulcerations such as gastrointestinal disorders (Crohn’s disease, ulcerative colitis), Behçet’s syndrome, Reiter’s syndrome, hematologic diseases, malnutrition, or allergic conditions; patients with a history of receiving chemotherapy, immunosuppressive drugs, or corticosteroids within the past year; patients presenting with other oral mucosal lesions

Intervention groups
Intervention Group: Participants in this group will receive oral bromelain capsules, two 500 mg capsules daily. Control Group: Participants in this group will receive two placebo capsules daily.

Main outcome variables
Wound size, pain, duration of recovery

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20250113064371N1**
Registration date: **2025-11-14, 1404/08/23**
Registration timing: **prospective**

Last update: **2025-11-14, 1404/08/23**
Update count: **0**

Registration date
2025-11-14, 1404/08/23

Registrant information

Name
Sobhan Cholaki

Name of organization / entity

Country
Iran (Islamic Republic of)

Phone
+98 11 3219 9592

Email address
cholaki.dent@gmail.com

Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2025-12-22, 1404/10/01

Expected recruitment end date
2026-02-20, 1404/12/01

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
A comparative study on the effect of oral bromelain capsules versus placebo on pain intensity and healing time in patients with recurrent aphthous stomatitis

Public title
The effect of Bromelain on recurrent aphthous stomatitis

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
The presence of minor aphthous ulcers in the oral mucosa of the lips or cheeks for a minimum of four episodes per year

Exclusion criteria:
Systemic disease causing oral ulcers History of receiving chemotherapy, immunosuppressants, or corticosteroids within the past year Patients with other mucosal lesions Pregnant and breastfeeding women Patients undergoing treatment with anticoagulant medications Patients whose normal healing of aphthous ulcers typically occurs in less than 5 days.

Age
No age limit

Gender
Both

Phase
3

Groups that have been masked

- Participant
- Care provider

Sample size
Target sample size: **20**

Randomization (investigator's opinion)
Randomized

Randomization description
The randomization of the use of oral bromelain capsules or placebo will be alternated, such that patients will be assigned a number based on their order of enrollment in the study (from 1 to 20). Patients with odd numbers (1, 3, 5, etc.) will receive oral bromelain capsules, while those with even numbers (2, 4, 6, etc.) will receive the placebo. In the second phase, the medication not received in the first phase will be administered.

Blinding (investigator's opinion)
Double blinded

Blinding description
Patients will not be informed about their medication (oral bromelain capsules or placebo). The placebo powder will be enclosed in capsules that are identical to the oral bromelain capsules and will be administered to the patients. Both the resident and the specialist in oral diseases will also not be provided with information regarding the type of medication consumed by the patients during the first and second examinations. An external observer (one of the residents specializing in oral diseases) will randomly assign code A or B to the placebo and the oral bromelain capsules, and the patients and researchers will be informed that they belong to group A or B; however, they will not be informed about which group is the intervention group and which is the control group. Ultimately, after the completion of the study and the interpretation of results by the statistical consultant, the external observer will disclose to which group each name belonged.

Placebo
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

Street address
Babol University of Medical Sciences, Keshavarz Boulavard, Ganjafrouz Street, Babol

City
Babol

Province
Mazandaran

Postal code
4717647745

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

Ethics committee reference number
IR.MUBABOL.HRI.REC.1404.145

Health conditions studied

1

Description of health condition studied
Recurrent Aphthous Stomatitis

ICD-10 code
K12.0

ICD-10 code description
Recurrent oral aphthae

Primary outcomes

1

Description
Wound area

Timepoint
All patients in both periods are examined by a specialist in oral and dental diseases on the first, third, fifth, and seventh days. If healing of the lesions occurs at any time prior to these examinations, subsequent assessments will not be conducted. In the absence of healing by the seventh day, the use of the capsule or placebo will continue, and the patient will be re-examined on the tenth day.

Method of measurement
Measurement of the wound diameter in patients will be conducted using an Iwanson gauge with an accuracy of one-tenth of a millimeter, recording both the maximum and minimum diameters. Subsequently, the area of the wound will be calculated using a mathematical formula based on the shape of the wound (circular or elliptical).

2

Description
Pain
Timepoint
All patients in both periods are examined by a specialist in oral and dental diseases on the first, third, fifth, and seventh days. If healing of the lesions occurs at any time prior to these examinations, subsequent assessments will not be conducted. In the absence of healing by the seventh day, the use of the capsule or placebo will continue, and the patient will be re-examined on the tenth day.
Method of measurement
Pain will be evaluated using the VAS (Visual Analog Scale) as a numerical measure from 0 to 10. For the patient, the number zero will be described as a state of no pain, while the number ten will represent the most severe pain experienced. In order to standardize the pain-inducing stimulus among patients, unsweetened orange juice (single-use) will be utilized.

3

Description
Duration of Recovery
Timepoint
All patients in both periods are examined by a specialist in oral and dental diseases on the first, third, fifth, and seventh days. If healing of the lesions occurs at any time prior to these examinations, subsequent assessments will not be conducted. In the absence of healing by the seventh day, the use of the capsule or placebo will continue, and the patient will be re-examined on the tenth day.
Method of measurement
The duration of recovery will be recorded in the patient's file for each period based on pain relief (0=VAS), wound healing, and the absence of any pseudo-membrane, expressed as the number of days.

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group: Patients suffering from minor aphthous oral ulcers will be instructed to take one capsule every 12 hours (two capsules per day) on an empty stomach until their oral ulcers have healed. They will also be instructed not to use any alternative methods for alleviation and to avoid consuming irritant foods. All patients will be examined by a specialist in oral and dental diseases on the first, third, fifth, and seventh days. If healing of the ulcers occurs at any time prior to these examinations, subsequent assessments will not be conducted. Conversely, should healing not be observed by the seventh day, the use of capsules will continue, and the patient will be re-examined on the tenth day.
Category
Treatment - Drugs

2

Description
Control group: Patients with minor aphthous oral ulcers will be instructed to take one placebo capsule every twelve hours (two capsules per day) on an empty stomach until the healing of their oral ulcers occurs. Additionally, they will be advised to refrain from using other methods for symptom relief and to avoid the consumption of irritant foods. All patients will be examined by a dental specialist on the first, third, fifth, and seventh days, and if complete healing of the ulcers occurs prior to any of these examinations, subsequent examinations will be omitted. In the event that healing has not occurred by the seventh day, the use of the placebo will continue and the patient will be re-evaluated on the tenth day.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Faculty of Dentistry, Babol University of Medical Sciences
Full name of responsible person
Sobhan Cholaki
Street address
Babol University of Medical Sciences, Keshavarz Boulavard, Ganjafrouz Street, Babol
City
Babol
Province
Mazandaran
Postal code
4717647745
Phone
+98 918 745 9574
Email
cholaki.dent@gmail.com

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Babol University of Medical Sciences

Full name of responsible person
Sobhan Cholaki
Street address
Babol University of Medical Sciences, No. 1, Keshavarz Boulevard, Ganjafrouz street, Babol
City
Babol
Province
Mazandaran
Postal code
4717647745
Phone
+98 918 745 9574
Email
cholaki.dent@gmail.com
Web page address
https://pajouhan.mubabol.ac.ir/webdocument/load.action?webdocument_code=8000&masterCode=11009548

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

Contact
Name of organization / entity
Babol University of Medical Sciences
Full name of responsible person
Sobhan Cholaki
Position
Student
Latest degree
Medical doctor
Other areas of specialty/work
Dentistry
Street address
Babol University of Medical Sciences, Keshavarz Boulavard, Ganjafrouz Street, Babol
City
Babol
Province
Mazandaran
Postal code
4717647745
Phone
+98 11 3219 9592
Fax
Email
cholaki.dent@gmail.com
Web page address
https://pajouhan.mubabol.ac.ir/webdocument/load.action?webdocument_code=8000&masterCode=11009548

Person responsible for scientific inquiries

Contact
Name of organization / entity
Babol University of Medical Sciences
Full name of responsible person
Sobhan Cholaki
Position
Student
Latest degree
Medical doctor
Other areas of specialty/work
Dentistry
Street address
Babol University of Medical Sciences, Keshavarz Boulavard, Ganjafrouz Street, Babol
City
Babol
Province
Mazandaran
Postal code
4717647745
Phone
+98 11 3219 9592
Fax
Email
cholaki.dent@gmail.com

Person responsible for updating data

Contact
Name of organization / entity
Babol University of Medical Sciences
Full name of responsible person
Sobhan Cholaki
Position
Student
Latest degree
Medical doctor
Other areas of specialty/work
Dentistry
Street address
Babol University of Medical Sciences, Keshavarz Boulavard, Ganjafrouz Street, Babol
City
Babol
Province
Mazandaran
Postal code
4717647745
Phone
+98 11 3219 9592
Fax

Email
cholaki.dent@gmail.com

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
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
Not applicable
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