Clinical Trial Protocol
Iranian Registry of Clinical Trials

31 May 2026

The effect of Bromelain supplementation alone and in combination with Curcumin on disease symptoms and severity, inflammatory markers and oxidative stress in patients with Rheumatoid Arthritis

Protocol summary

Study aim

The effect of Bromelain supplementation alone and in combination with Curcumin on disease symptoms and severity, inflammatory markers and oxidative stress in patients with Rheumatoid Arthritis

Design

A phase 3, randomized, triple-blind, controlled clinical trial conducted on 75 patients.

Settings and conduct

Blood samples will be collected twice from Rheumatoid Arthritis (RA) patients visiting Firoozgar Hospital who meet the inclusion criteria: once at baseline and once after the intervention, to assess the targeted factors.

Participants/Inclusion and exclusion criteria

Inclusion Criteria: 1. Willingness to participate and signing the informed consent form. 2. Age between 18 and 65 years. 3. Diagnosis of Rheumatoid Arthritis (RA) based on the American College of Rheumatology (ACR) criteria 4. Disease duration of at least two years. 5. No intake of dietary supplements (antioxidants, omega-3, etc.) in the past two months, except for routine supplements prescribed for Rheumatoid Arthritis (Vitamin D, Calcium, Vitamin A). 6. No history of diabetes, hypertension, acute cardiovascular diseases, thyroid disorders, kidney failure, or liver dysfunction based on the patient's medical history. 7. Stable medication regimen for at least one month before the study. 8. Not pregnant or breastfeeding 9. No use of contraceptive drugs. 10. No substance abuse. 11. Exclusion of individuals with allergies to pineapple, carrot, or fennel. 12. Exclusion of individuals taking anticoagulant medications.

Intervention groups

Three groups of 25 RA patients: Bromelain (200 mg), Bromelain + Curcumin (200 mg + 300 mg), and Placebo (Maltodextrin).

Main outcome variables

TAC, MDA, CRP, ESR, TNF-α, IFN-γ, IL-17, disease severity, number of painful joints, number of inflamed joints, number of joints with tenderness, pain level, DAS28, joint stiffness

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20120415009472N29**
Registration date: **2025-03-15, 1403/12/25**
Registration timing: **prospective**

Last update: **2025-03-15, 1403/12/25**
Update count: **0**

Registration date

2025-03-15, 1403/12/25

Registrant information

Name

Naheed Aryaeian

Name of organization / entity

Iran University of Medical Sciences

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2025-04-21, 1404/02/01

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
The effect of Bromelain supplementation alone and in combination with Curcumin on disease symptoms and severity, inflammatory markers and oxidative stress in patients with Rheumatoid Arthritis

Public title
The effect of bromelain and curcumin on rheumatoid arthritis
Purpose
Supportive
Inclusion/Exclusion criteria
Inclusion criteria:
Diagnosis of Rheumatoid Arthritis Based on American College of Rheumatology (ACR) Criteria(If there are at least four criteria for six weeks of the criteria 1- Morning dryness for at least one hour in three joints or more 2- Arthritis of three joint areas or more 3- Arthritis of the hand joints 4- Symmetric arthritis 5- Rheumatoid nodules 6- Positive rheumatoid factor 7- Typical radiographic changes in the wrist and hand) The duration of the disease should be at least two years. The patient expresses his / her consent to participate in the study
Exclusion criteria:
Taking supplements (omega 3, antioxidants, etc.) in the last two months Having any of the diseases of diabetes, hypertension, thyroid disorder and kidney failure and Liver dysfunction Changes in the amount of medication taken in the past month Pregnancy and lactation Taking contraceptives People who are allergic to pineapple, carrots, and fennel. People who take anticoagulant medications. Substance abuse
Age
From **18 years** old to **65 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size
Target sample size: **75**
Randomization (investigator's opinion)
Randomized
Randomization description
In this study, samples will be selected based on availability, and randomization will be performed for group allocation. For randomization, a random list for three groups, each with a sample size of 25 participants, was generated using web-based software. The letters A, B, and C will be assigned to the numbers 1 to 3 using random number generation. The numbers 1 to 3 correspond to the three groups: Group 1 (Bromelain), Group 2 (Bromelain + Curcumin), and Group 3 (Placebo). Based on the order of patient visits, the type of intervention, represented by letters A, B, and C, will be assigned to each patient according to the sequential list generated by the random number software. Patient selection will initially be based on their visits, making it a convenience sample, but drug allocation will be randomized.
Blinding (investigator's opinion)
Triple blinded
Blinding description
This study is a triple-blind, placebo-controlled randomized clinical trial, meaning that the patient, the researcher, and the analysts performing the statistical analyses will remain unaware of the type of intervention until the analysis is completed. The pharmacist will attach labels A, B, and C to the medication packages, which will be provided to patients visiting the therapist according to the sequential list generated by the random number program. After the completion of the analysis and the review of the results, the pharmacist will be contacted to disclose the label assignments. This information will then be used in the preparation of the report and the manuscript, particularly in the findings, discussion, and conclusion sections.
Placebo
Used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Research Ethics Committees of Iran University of Medical Sciences
Street address
Iran University of Medical Sciences Hemat Highway, Between Sheikh Fazlollah Nouri Highway and Shahid Chamran Highway, Next to Milad Tower, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1449614535
Approval date
2025-02-23, 1403/12/05
Ethics committee reference number
IR.IUMS.REC.1403.1051

Health conditions studied

1

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

Primary outcomes

1

Description
Tumour necrosis factor- α (TNF-α)
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Enzyme-linked immunosorbent assay (ELISA)

2

Description
Total antioxidant capacity (TAC)
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Chromatography

3

Description
Erythrocyte sedimentation rate (ESR)
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Westergren method

4

Description
Malondialdehyde (MDA)
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Chromatography

5

Description
Interferon gamma (IFN-γ)
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Enzyme-linked immunosorbent assay (ELISA)

6

Description
Interleukin-17 (IL-17)
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Enzyme-linked immunosorbent assay (ELISA)

7

Description
C-reactive protein (CRP)
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Immunoturbidometric method

8

Description
Disease activity score
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Formula DAS28

9

Description
Illness severity
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Physician global assessment

10

Description
Pain
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
Visual analogue scale

11

Description
Morning stiffness
Timepoint
Before the intervention and after the end of the intervention
Method of measurement
How long (minutes) it takes for the joint dryness to go away.

12

Description

Number of painful joints

Timepoint

Before the intervention and after the end of the intervention

Method of measurement

Doctor's examination

13

Description

Tender joint counts (TJC)

Timepoint

Before the intervention and after the end of the intervention

Method of measurement

Doctor's examination

14

Description

Swollen joint count

Timepoint

Before the intervention and after the end of the intervention

Method of measurement

Doctor's examination

Secondary outcomes

1

Description

Dosage of drugs

Timepoint

Before the intervention and after the end of the intervention

Method of measurement

Questionnaire

Intervention groups

1

Description

Intervention Group 1:A total of 25 participants in this group will receive bromelain, taking two 200 mg bromelain capsules daily (one with breakfast and one with lunch) for 12 weeks. The capsules will be provided by Salamat Parmon Amin (SPAmeda) Company.

Category

Treatment - Drugs

2

Description

Intervention Group 2:A total of 25 participants in this group will receive a combination of bromelain and curcumin, taking two capsules daily, each containing 200 mg of bromelain and 300 mg of curcumin (one with breakfast and one with lunch) for 12 weeks. The capsules will be provided by Salamat Parmon Amin (SPAmeda) Company.

Category

Treatment - Drugs

3

Description

Control Group:A total of 25 participants in this group will receive a placebo, taking two capsules daily containing maltodextrin (identical in appearance, color, smell, and taste to the intervention capsules but with no therapeutic effect), one with breakfast and one with lunch, for 12 weeks. The capsules will be provided by Salamat Parmon Amin (SPAmeda) Company.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Firoozgar hospital

Full name of responsible person

Simin Almasi

Street address

Firouzgar Hospital, Be'afarain St., Valiasr Sq.

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Iran University of Medical Sciences

Full name of responsible person

Dr. Majid Safa

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Vice-chancellor for Research, Iran University of Medical Sciences, Hammat Broadway

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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
Iran 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
Iran University of Medical Sciences
Full name of responsible person
Naheed Aryaeian
Position
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Latest degree
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Other areas of specialty/work
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Person responsible for updating data

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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
Yes - There is a plan to make this available
Data Dictionary
Yes - There is a plan to make this available
Title and more details about the data/document
Only a section of the data, such as primary outcomes

information or the like, will be shared.

When the data will become available and for how long

Access period start 5 months after results publishing.

To whom data/document is available

The obtained data from current study will be available only for working researchers in academic and scientific institutions

Under which criteria data/document could be used

5 months after the publicized papers from this study, the obtained data will be available to the researchers for further analysis.

From where data/document is obtainable

Applicants can be communicated to correspond author be e-mail or postal address to receive the requested data. Postal address: Nutrition Department, School of Public Health, Iran University of Medical Sciences, Hemat Highway, Tehran Cell phone: +982186704743 Email: n-aryaeian@sina.tums.ac.ir

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

Publishing in scientific-research journals Applicants will be given access to the obtained data from current study by sending an email to correspond author.

Comments