

Clinical Trial Protocol

Iranian Registry of Clinical Trials

11 Sep 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

Country

Iran (Islamic Republic of)

Phone

+98 21 8670 4750

Email address

aryaeian.n@iums.ac.ir

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

AgeFrom **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 sizeTarget 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.

City
Tehran

Province
Tehran

Postal code
1593748711

Phone
+98 21 8214 1000

Email
firoozgarhospital1@gmail.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Iran University of Medical Sciences

Full name of responsible person
Dr. Majid Safa

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

City
Tehran

Province
Tehran

Postal code
1449614535

Phone
+98 21 86701

Email
info@iums.ac.ir

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

Professor

Latest degree

Ph.D.

Other areas of specialty/work

Nutrition

Street address

Nutrition department, school of public health,
Hemmat broad way

City

Tehran

Province

Tehran

Postal code

1449614535

Phone

+98 21 8670 4750

Fax

+98 21 8862 2707

Email

aryaeian.n@iums.ac.ir

Hemmat broad way

City

Tehran

Province

Tehran

Postal code

1449614535

Phone

+98 21 8670 4750

Fax

+98 21 8862 2707

Email

aryaeian.n@iums.ac.ir

Person responsible for updating data**Contact****Name of organization / entity**

Iran University of Medical Sciences

Full name of responsible person

Naheed Aryaeian

Position

Professor

Latest degree

Ph.D.

Other areas of specialty/work

Nutrition

Street address

Nutrition department, school of public health,
Hemmat broad way

City

Tehran

Province

Tehran

Postal code

1449614535

Phone

+98 21 8670 4750

Fax

+98 21 8862 2707

Email

aryaeian.n@iums.ac.ir

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

Person responsible for scientific inquiries**Contact****Name of organization / entity**

Iran University of Medical Sciences

Full name of responsible person

Naheed Aryaeian

Position

Professor

Latest degree

Ph.D.

Other areas of specialty/work

Nutrition

Street address

Nutrition department, school of public health,

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 by 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