Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Investigating the Effect of Nanomicellar Silymarin on Immunological Indicators in Patients with Rheumatoid Arthritis.

Protocol summary

Study aim

Evaluating effect of nanomicellar silymarin on clinical and immunological indicators in rheumatoid arthritis

Design

A randomized, triple-blind, superiority, parallel group trial with three arms (intervention, placebo, control). Sample size: 45 patients (15 per group). Randomization: block randomization (block size 4) using computer-generated random sequence from www.randomization.com with allocation concealment by sequentially numbered, opaque, sealed envelopes. Single center (Ghaem Hospital, Mashhad, Iran). Phase 3.

Settings and conduct

Single-center trial in Mashhad. 45 RA patients randomized to 3 groups: silymarin+DMARDs, placebo+DMARDs, DMARDs alone. 8 weeks. Triple-blind (patient, assessor, analyst). Independent person seals allocation.

Participants/Inclusion and exclusion criteria

Inclusion: Active RA (ACR/EULAR 2010, score≥6); age 18-60y; disease duration 1-2y; on standard DMARDs (MTX≤10mg/wk + prednisolone≤5mg/d); no biologics. Exclusion: Malignancy; diabetes/CKD/heart failure; pregnancy/breastfeeding; BMI≥35; K/L grade≥4; unwillingness.

Intervention groups

Group1 (Intervention): Standard DMARDs + nanomicellar silymarin (SinaLiv) 70mg, 1 cap/day, 8 weeks. Group 2 (Placebo): Standard DMARDs + identical placebo (gelatin capsule with corn starch), 1 cap/day, 8 weeks. Group 3 (Control): Standard DMARDs only.

Main outcome variables

Primary outcomes (measured at baseline and week 8): 1. Gene expression changes of 22 immune-related genes including IL-1, IL-4, IL-10, IL-17, IL-18, IL-22, IL-23, TGF-β, IFN-γ, CCL2, CCL5, CXCL8, NLRP3, P2XR, BCMA, APRIL, TACI, BAFF, T-bet, GATA3, ROR-γt, and FOXP3 measured by real-time PCR. 2. Serum levels of CRP, RF, and Anti-CCP. Secondary outcomes (measured at baseline and week 8): 1. DAS28-ESR score (clinical disease activity index). 2. VAS score (pain assessment).

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20151028024760N7**
Registration date: **2026-05-11, 1405/02/21**
Registration timing: **prospective**

Last update: **2026-05-11, 1405/02/21**
Update count: **0**

Registration date

2026-05-11, 1405/02/21

Registrant information

Name
Mojgan Mohammadi
Name of organization / entity
Mashhad University of Medical Sciences
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Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-09-21, 1405/06/30

Expected recruitment end date

2028-09-20, 1407/06/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Investigating the Effect of Nanomicellar Silymarin on Immunological Indicators in Patients with Rheumatoid Arthritis.

Public title

Effect of Nanomicellar Silymarin in Rheumatoid Arthritis

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Active rheumatoid arthritis based on ACR/EULAR 2010 criteria with score of 6 or higher Age between 18 and 60 years At least one year and maximum two years have passed since disease diagnosis Receiving standard DMARDs regimen including Methotrexate up to 10 mg/week and Prednisolone up to 5 mg/day No prior use of biologic drugs

Exclusion criteria:

History of malignancy History of diabetes, chronic kidney disease or heart failure Pregnancy or breastfeeding Body mass index of 35 or higher Kellgren-Lawrence grade 4 or higher Unwillingness to continue participation in the study

Age

From **18 years** old to **60 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Outcome assessor
- Data analyser

Sample size

Target sample size: **45**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization method: Block randomization (stratified block randomization). Unit of randomization: Individual patient. Randomization strata: Patients will be stratified based on age (18-40 years and 41-60 years) and disease duration (1-1.5 years and 1.5-2 years) to ensure balance between groups. Tools used: The random sequence will be generated using www.randomization.com website with a table of random numbers. Block size of 4 will be used with 8 blocks total. How the random sequence will be built: A computer-generated random allocation sequence will be created by an independent statistician who will not be involved in patient enrollment or outcome assessment. Block sizes of 4 will be used to ensure equal allocation to three groups (intervention, placebo, control) with 15 patients per group. Allocation concealment: Yes, allocation concealment will be performed using sequentially numbered, opaque, sealed envelopes. The envelopes will be prepared by a person not involved in clinical assessments or data analysis. The randomization code will remain sealed and will be kept by this independent person until final data analysis is completed. The key to the code will not be accessible to patients, clinicians, or outcome assessors until the study is unblinded after final analysis

Blinding (investigator's opinion)

Triple blinded

Blinding description

This is a triple-blind trial. Blinding will be implemented as follows: - Participants: Patients will not know their group allocation. Intervention and placebo capsules are identical in color, size, and packaging. - Principal investigator: The PI will be blinded and will not be involved in preparation or distribution of the study medications. - Healthcare providers: Routine care physicians (other than the outcome assessor) are not blinded because the intervention is an add-on to standard care. - Data collector: The person collecting blood samples and laboratory data will not know group allocation. - Outcome assessor: The rheumatologist performing clinical evaluations (DAS28-ESR, VAS) will be blinded to group assignment. - Data analyst: The statistician will receive a de-identified dataset with coded groups (e.g., A, B, C) and will remain blinded until all analyses are completed. - DSMB: Not applicable for this pilot trial. Blinding method: An independent person not involved in patient care, assessment, or analysis will prepare sequentially numbered, opaque, sealed envelopes containing the allocation code. This person will package and code the identical capsules. The allocation key will remain sealed until final data analysis. Emergency unblinding is possible according to protocol and will be documented. Blinding will be checked by asking blinded personnel about their guesses at the end of the study.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Mashhad University of Medical Sciences

Street address

Qoreishi Bulding, Daneshgah St

City

Mashhad

Province

Razavi Khorasan

Postal code

91357345

Approval date
2026-01-19, 1404/10/29
Ethics committee reference number
IR.MUMS.IRH.REC.1404.252

Health conditions studied

1

Description of health condition studied
Rheumatoid arthritis is a chronic autoimmune inflammatory disorder that primarily affects the synovial joints. It is characterized by progressive and symmetric joint inflammation, leading to cartilage destruction, bone erosion, and physical disability. The disease involves complex immunopathogenesis with key roles of inflammatory cytokines and T lymphocyte subsets. Despite available treatments including NSAIDs, glucocorticoids, and DMARDs, some patients show drug resistance or adverse effects. This study investigates the effect of nanomicellar silymarin as a potential adjunctive therapy in active RA patients.
ICD-10 code
M05
ICD-10 code description
Rheumatoid arthritis with rheumatoid factor

Primary outcomes

1

Description
Change in the expression level of the Interleukin-1 (IL-1) gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

2

Description
Change in the expression level of the Interleukin-4 (IL-4) gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

3

Description
Change in the expression level of the Interleukin-10 (IL-10) gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

4

Description
Change in the expression level of the Interleukin-17 (IL-17) gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

5

Description
Change in the expression level of the Interleukin-18 (IL-18) gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

6

Description
Change in the expression level of the Interleukin-22 (IL-22) gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

7

Description
Change in the expression level of the Interleukin-23 (IL-23) gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

8

Description
Change in the expression level of the Transforming Growth Factor-beta (TGF-β) gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

9

Description
Change in the expression level of the Interferon-gamma (IFN-γ) gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

10

Description
Change in the expression level of the CCL2 gene
Timepoint
Before intervention and 8 weeks after intervention

Method of measurement
SYBR Green-based real-time PCR assay

11

Description
Change in the expression level of the CCL5 gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

12

Description
Change in the expression level of the CXCL8 gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

13

Description
Change in the expression level of the NLRP3 gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

14

Description
Change in the expression level of the P2XR gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

15

Description
Change in the expression level of the BCMA gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

16

Description
Change in the expression level of the APRIL gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

17

Description
Change in the expression level of the TACI gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

18

Description
Change in the expression level of the BAFF gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

19

Description
Change in the expression level of the T-bet gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

20

Description
Change in the expression level of the GATA3 gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

21

Description
Change in the expression level of the ROR-γt gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

22

Description
Change in the expression level of the FOXP3 gene
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
SYBR Green-based real-time PCR assay

23

Description
C-reactive protein (CRP)
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
Latex agglutination test

24

Description
Rheumatoid factor (RF)
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
Latex agglutination test

25

Description
Anti-cyclic citrullinated peptide (anti-CCP)
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
ELISA test

Secondary outcomes

1

Description
Disease activity score 28-joint count-erythrocyte sedimentation rate (DAS28-ESR)
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
Clinical and laboratory findings

2

Description
Visual analog scale (VAS) to assess the level of joint pain
Timepoint
Before intervention and 8 weeks after intervention
Method of measurement
The amount of pain that a patient feels

Intervention groups

1

Description
Group 1 (Intervention): Standard DMARDs regimen + Nanomicellar silymarin capsule (SinaLiv, Exir Nanosina Company) 70 mg, one capsule daily for 8 weeks.Group 2 (Placebo): Standard DMARDs regimen + Identical placebo capsule (gelatin capsule containing corn starch), one capsule daily for 8 weeks.Group 3 (Control): Standard DMARDs regimen only (no additional intervention).
Category
Treatment - Other

Recruitment centers

1

Recruitment center
Name of recruitment center
Ghaem Hospital
Full name of responsible person
Masoumeh Salari
Street address
Ahmadabad Blvd
City
Mashhad
Province
Razavi Khorasan
Postal code
91766-99199
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+98 51 3840 0001
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B.ghaem@mums.ac.ir

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Mashhad University of Medical Sciences
Full name of responsible person
Mohsen Tafaghodi
Street address
Daneshgah Street, Ghoreishi Building, Third Floor, Vice Chancellery for Research and Technology
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9138813944
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TafaghodiM@mums.ac.ir
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Mashhad 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
Mashhad University of Medical Sciences
Full name of responsible person
Mojgan Mohammadi
Position
Professor
Latest degree
Ph.D.
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)
No - There is not a plan to make this available
Justification/reason for indecision/not sharing IPD
The current study protocol does not include a plan for public sharing of individual participant data (IPD). Summary results will be published in a peer-reviewed journal."
Study Protocol
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
Undecided - It is not yet known if there will be 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