# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

07 Nov 2026

## Therapeutic Efficacy of Urtica dioica and Evening Primrose in Patients with Rheumatoid Arthritis: A Randomized Double-Blind, Placebo-Controlled Clinical Trial

## Protocol summary

**Study aim**

Study of anti-inflammatory and anti-arthritis effect of nettle and evening primrose on total plasma antioxidant capacity and clinical signs in patients with rheumatoid arthritis

**Design**

In this phase 2 Randomized Double-Blind, Placebo-Controlled Clinical Trial, 90 patients with rheumatoid arthritis are divided into three groups: nettle, evening primrose, and placebo by simple randomization method.

**Settings and conduct**

This study is performed in the office of rheumatology. Patients are classified into intervention groups after being informed about the study and obtaining informed consent. Medicines have no name and only numbers and are given to the patient. Tests and examinations are performed and compared before and after the intervention. Researchers, rheumatologists, and patients are unaware of the allocation of study groups.

**Participants/Inclusion and exclusion criteria**

Inclusion criteria: 1- Willingness to participate in the study and signing a written consent 2- Rheumatoid arthritis Exclusion criteria: 1- History of allergy to nettle or evening primrose

**Intervention groups**

In this study, to evaluate the anti-inflammatory and anti-arthritic effects of nettle and evening primrose, patients with rheumatoid arthritis were randomly divided into three groups: nettle, evening primrose, and placebo (to compare results) and consume three times a day for three months.

**Main outcome variables**

Measurement of inflammatory factors ESR, CRP, RF, Anti-CCP, cytokine IL-17 and total antioxidant capacity of TAC in serum and calculation of DAS28 in rheumatoid arthritis patients before and after interference

## General information

**Reason for update**

**Acronym**

**IRCT registration information**

IRCT registration number: **IRCT20201001048897N1**
Registration date: **2021-01-02, 1399/10/13**
Registration timing: **prospective**

Last update: **2021-01-02, 1399/10/13**
Update count: **0**

**Registration date**

2021-01-02, 1399/10/13

**Registrant information**

**Name**

Bahareh Abd-Nikfarjam

**Name of organization / entity**

**Country**

Iran (Islamic Republic of)

**Phone**

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**Email address**

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**Recruitment status**

**Recruitment complete**

**Funding source**

**Expected recruitment start date**

2021-01-09, 1399/10/20

**Expected recruitment end date**

2021-08-11, 1400/05/20

**Actual recruitment start date**

2021-01-09, 1399/10/20

**Actual recruitment end date**

2021-01-19, 1399/10/30

**Trial completion date**

2021-08-21, 1400/05/30

**Scientific title**
Therapeutic Efficacy of Urtica dioica and Evening Primrose in Patients with Rheumatoid Arthritis: A Randomized Double-Blind, Placebo-Controlled Clinical Trial

**Public title**
Therapeutic Efficacy of Urtica dioica and Evening Primrose in Patients with Rheumatoid Arthritis

**Purpose**
Treatment

**Inclusion/Exclusion criteria**
**Inclusion criteria:**
RA was diagnosed according to the revised 2010 American College of Rheumatology (ACR) criteria
**Exclusion criteria:**
Patients with cardiovascular disease Patients with respiratory diseases Patients with renal disease Patients with liver disease Patients under sex hormone therapy Use supplements before the intervention Changing the treatment of RA patients Allergy to nettle Patients with other inflammatory diseases

**Age**
No age limit

**Gender**
Both

**Phase**
2

**Groups that have been masked**

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

**Sample size**
Target sample size: **90**
Actual sample size reached: **90**

**Randomization (investigator's opinion)**
Randomized

**Randomization description**
- Simple randomization, shuffling cards - Unit of Randomization: individual - Tools used in randomization: cards shuffling - How to make a random sequence: In this method, a number of cards selected by the researcher as the first group and the same number of cards for the next groups are considered; Then, by merging the cards together (cards shuffling), a card is removed and its allocation is recorded, and that card is returned to all other cards after the new card is removed. The cards are then shuffled and another card is issued. This process is followed by reaching a random sequence according to the sample size continues. - Concealment: Herbal medicines and placebo are provided to patients with exactly the same packaging.

**Blinding (investigator's opinion)**
Double blinded

**Blinding description**
The results evaluator and patients did not know how to intervene.code was defined for the study groups

**Placebo**
Used

**Assignment**
Parallel

**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**
**Name of ethics committee**
Ethics Subcommittee on Biomedical Research
**Street address**
Bahonar Blvd.
**City**
Qazvin
**Province**
Qazvin
**Postal code**
34199-15315

**Approval date**
2017-03-19, 1395/12/29

**Ethics committee reference number**
IR.Qums.REC.1395.312

## Health conditions studied

### 1

**Description of health condition studied**
Therapeutic Efficacy of Urtica dioica and Evening Primrose in Patients with Rheumatoid Arthritis: A Randomized Double-Blind, Placebo-Controlled Clinical Trial

**ICD-10 code**

**ICD-10 code description**

## Primary outcomes

### 1

**Description**
DAS28 (Disease Activity Score) The DAS28 is a measure of disease activity in rheumatoid arthritis (RA). DAS stands for 'disease activity score', and the number 28 refers to the 28 joints that are examined in this assessment.

**Timepoint**
Disease Activity Score 28 is measured at the beginning of the study (before the start of the intervention) and at the end of the study (3 months after the start of herbal medicine, nettle or evening primrose, and placebo).

**Method of measurement**
The Disease Activity Score 28 is most easily calculated using a programmed calculator or a computer. Online and downloadable calculators are freely available at http://www.das-score.nl.

## Secondary outcomes

### 1

**Description**

DAS28 (Disease Activity Score) The DAS28 is a measure of disease activity in rheumatoid arthritis (RA). DAS stands for 'disease activity score', and the number 28 refers to the 28 joints that are examined in this assessment.

**Timepoint**

Disease Activity Score 28 is measured at the beginning of the study (before the start of the intervention) and at the end of the study (3 months after the start of herbal medicine, nettle or evening primrose, and placebo).

**Method of measurement**

The Disease Activity Score 28 is most easily calculated using a programmed calculator or a computer. Online and downloadable calculators are freely available at http://www.das-score.nl.

### 2

**Description**

Visual Analogue Scale (VAS) The visual analog scale is a validated, subjective measure for acute and chronic pain.

**Timepoint**

Visual Analogue Scale is measured at the beginning of the study (before the start of the intervention) and at the end of the study (3 months after the start of herbal medicine, nettle or evening primrose, and placebo).

**Method of measurement**

Visual Analogue Scale scores are recorded by making a handwritten mark on a 10-cm line that represents a continuum between “no pain” and “worst pain.”

### 3

**Description**

IL-17 cytokine has an important role in protective immunity. IL-17 plays a critical role in the parthenogenesis of various autoimmune inflammatory diseases such as rheumatoid arthritis.

**Timepoint**

IL-17 cytokine measured at the beginning of the study (before the start of the intervention) and at the end of the study (3 months after the start of herbal medicine, nettle or evening primrose, and placebo).

**Method of measurement**

Inflammatory cytokine IL-17 is measured by enzyme-linked immunosorbent assay (ELISA) technique.

### 4

**Description**

Total Antioxidant Capacity (TAC) Assay measures the total antioxidant capacity of biomolecules from a variety of samples like a human serum.

**Timepoint**

Total antioxidant capacity measured at the beginning of the study (before the start of the intervention) and at the end of the study (3 months after the start of herbal medicine, nettle or evening primrose, and placebo).

**Method of measurement**

Total antioxidant capacity is measured by enzyme-linked immunosorbent assay (ELISA) technique.

### 5

**Description**

Anti-cyclic citrullinated autoantibodies are produced by the immune system that is directed against cyclic citrullinated peptides (CCP). This test detects and measures anti-CCP antibodies in the blood. Citrulline is naturally produced in the body as part of the metabolism of the amino acid arginine.

**Timepoint**

Anti-cyclic citrirullinated peptide measured at the beginning of the study (before the start of the intervention) and at the end of the study (3 months after the start of herbal medicine, nettle or evening primrose, and placebo).

**Method of measurement**

Anti-cyclic citrirullinated peptide is measured by enzyme-linked immunosorbent assay (ELISA) technique.

### 6

**Description**

C Reactive protein (CRP) is an acute-phase protein of hepatic origin that increases following interleukin-6 secretion by macrophages and T cells.

**Timepoint**

Reactive protein C measured at the beginning of the study (before the start of the intervention) and at the end of the study (3 months after the start of herbal medicine, nettle or evening primrose, and placebo).

**Method of measurement**

The CRP latex agglutination assay is a qualitative and semi-quantitative test. The latex particles used in the CRP latex agglutination test are coated with anti-human CRP that agglutinate upon mixing with patient serum containing CRP.

### 7

**Description**

Rheumatoid factor (RF) is the autoantibody that was first found in rheumatoid arthritis. It is defined as an antibody against the Fc portion of IgG and different RFs can recognize different parts of the IgG-Fc. RF and IgG join to form immune complexes that contribute to the disease process.

**Timepoint**

Rheumatoid Factor measured at the beginning of the study (before the start of the intervention) and at the end of the study (3 months after the start of herbal medicine, nettle or evening primrose, and placebo).

**Method of measurement**

Agglutination tests: One test method mixes blood with latex beads that are covered with human antibodies. If RF is present, the latex beads clump together (agglutinate). This method is best used as a first-time screening test for rheumatoid arthritis.

**8**

**Description**
Erythrocyte sedimentation rate (ESR) is a test that indirectly measures the degree of inflammation present in the body. The test actually measures the rate of fall (sedimentation) of erythrocytes in a sample of blood that has been placed into a tall, thin, vertical tube.

**Timepoint**
Erythrocyte sedimentation rate measured at the beginning of the study (before the start of the intervention) and at the end of the study (3 months after the start of herbal medicine, nettle or evening primrose, and placebo).

**Method of measurement**
Western Green is a method for estimating the sedimentation rate of red blood cells in whole blood by mixing venous blood with an aqueous solution of sodium citrate and allowing the mixture to stand in an upright standard pipet and, after one hour, reading the millimeters the cells have descended.

## Intervention groups

**1**

**Description**
Intervention group 1: Magnolia evening primrose 400 mg capsule Intervention group 2: Nettle capsule Nettle capsule 400 mg Control group: placebo 500 mg capsule for three months three times a day Barij Essential Oil Company

**Category**
Other

## Recruitment centers

**1**

**Recruitment center**

**Name of recruitment center**
Rheumatologist's Clinic in Qazvin, Iran

**Full name of responsible person**
Bahareh Abd-Nikfarjam

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Department of Immunology, School of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran

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## Sponsors / Funding sources

**1**

**Sponsor**

**Name of organization / entity**
Metabolic Diseases Research Center, Qazvin University of Medical Sciences, Qazvin, Iran.

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**Email**
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**Web page address**
http://en.qums.ac.ir/Portal/Home/

**Grant name**

**Grant code / Reference number**

**Is the source of funding the same sponsor organization/entity?**
Yes

**Title of funding source**
Metabolic Diseases Research Center, Qazvin University of Medical Sciences, Qazvin, Iran.

**Proportion provided by this source**
100

**Public or private sector**
Private

**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**
Qazvin University of Medical Sciences

**Full name of responsible person**
Bahareh Abd-Nikfarjam

**Position**
Assistant Professor

**Latest degree**
Ph.D.

**Other areas of specialty/work**
Immunology

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## Person responsible for updating data

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**Full name of responsible person**
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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**
There is no further information
**Study Protocol**
No - There is not a plan to make this available
**Statistical Analysis Plan**
No - There is not a plan to make this available
**Informed Consent Form**
No - There is not a plan to make this available
**Clinical Study Report**
No - There is not a plan to make this available
**Analytic Code**
No - There is not a plan to make this available
**Data Dictionary**
No - There is not a plan to make this available