# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

20 Jun 2026

## Study of the effects of melatonin supplementation on clinical status and metabolic profiles in patients with rheumatoid arthritis

## Protocol summary

**Study aim**

Objective: The aim of this study is to determine the effects of melatonin supplementation on clinical status and metabolic profiles in patients with rheumatoid arthritis.

**Design**

Study design: randomized double-blind placebo-controlled trial. Patients will be assigned into two groups to receive melatonin supplement (n=33) or placebo (n=33).

**Settings and conduct**

Among patients with rheumatoid arthritis referred to Beheshti Clinic, 66 patients will be selected according to inclusion and exclusion criteria. Participants, investigators or the assessors of the outcomes are unaware of the study groups. Supplements and placebos are similar in shape and size. Fasting blood samples will be taken at baseline and end of the intervention. intervention: 12 weeks.

**Participants/Inclusion and exclusion criteria**

Inclusion criteria: patients with rheumatoid arthritis.; aged 20 to 80 years. Exclusion criteria: Patients with infectious, malignant and other inflammatory diseases, those taking melatonin supplements or antioxidant supplements within 3 months prior to enrollment in the study, the night shift workers, subjects taking antibiotics medications, patients with thyroid diseases, current smokers, rheumatoid arthritis patients who were diagnosed less than 1 year before the start of the study, and unwillingness to cooperate

**Intervention groups**

Intervention group: 6 mg/day Melatonin (RAZAK, Iran), one hour before bedtime for 12 weeks. Control group: Placebo (Barij Essence, Iran), one hour before bedtime for 12 weeks.

**Main outcome variables**

Outcomes: DAS28, serum CRP and ESR (primary outcomes) and metabolic profiles, biomarkers of oxidative damage (secondary outcomes) will be quantified at study baseline and end-of-trial.

## General information

**Reason for update**

The updating process was done before publishing the paper to correct the registration information. After the initial registration of IRCT and before the start of the study and before patients recruitment, according to the project investigators, it was decided that criteria such as smoking or thyroid disease that can play a role in the rate of metabolism or exacerbation of rheumatoid arthritis should be added to exclusion criteria. Also, given that it is difficult to differentiate rheumatoid arthritis from other similar diseases at the onset of the RA because the initial manifestations may not be typical (polyarticular involvement), it was decided to exclude patients who have been diagnosed over the past year before the start of the study. In addition, since a large proportion of patients with rheumatoid arthritis mention the use of anti-inflammatory drugs such as NSAIDs in their history and the removal of a drug from the patient's drugs is not ethically correct. Also, if the patients currently using NSAIDs were excluded from the study, we lost a large part of the available samples. To solve the mentioned issue it was decided that patients in the two arms of the study be compared statistically at the end of the study in terms of drugs associated with RA to find out that is it a significant differences between the two groups or not. Regarding updating of some outcomes, before the patients entered the study, it was decided that since the clinical signs in patients with rheumatoid arthritis are very important in the diagnosis, a criterion for the severity of the disease, which includes clinical examinations of 28 important joints in this disease (DAS28-ESR) should also be included in the main outcomes, and since the ESR was required to calculate it, this variable was also added. Unfortunately, in the case of CRP, the goal was to measure quantitatively (hs-CRP) at first, but due to an error and lack of coordination with the laboratory, patients' CRP was measured qualitatively

and when the investigators realized this error, it was not possible to correct it. As a result, CRP of all patients was measured qualitatively. Also in the case of LDL, since other items in the patients' lipid profile were to be measured, LDL, which was omitted in the initial recording, was added.

**Acronym**

**IRCT registration information**

IRCT registration number: **IRCT20170513033941N67**
Registration date: **2019-11-30, 1398/09/09**
Registration timing: **registered_while_recruiting**

Last update: **2020-11-23, 1399/09/03**
Update count: **2**

**Registration date**

2019-11-30, 1398/09/09

**Registrant information**

**Name**

Mohammadreza Sharif

**Name of organization / entity**

**Country**

Iran (Islamic Republic of)

**Phone**

+98 31 5546 3378

**Email address**

ostadmohammadi-vr@kaums.ac.ir

**Recruitment status**

**Recruitment complete**

**Funding source**

**Expected recruitment start date**

2019-10-23, 1398/08/01

**Expected recruitment end date**

2019-12-21, 1398/09/30

**Actual recruitment start date**

2019-11-20, 1398/08/29

**Actual recruitment end date**

2020-02-26, 1398/12/07

**Trial completion date**

2020-05-20, 1399/02/31

**Scientific title**

Study of the effects of melatonin supplementation on clinical status and metabolic profiles in patients with rheumatoid arthritis

**Public title**

The effects of melatonin supplementation in the treatment of rheumatoid arthritis

**Purpose**

Treatment

**Inclusion/Exclusion criteria**

**Inclusion criteria:**

Patients diagnosed with rheumatoid arthritis Individuals aged 20-80 years old

**Exclusion criteria:**

Patients with infectious, malignant and other inflammatory diseases those taking melatonin supplements or antioxidant supplements within 3 months prior to enrollment in the study the night shift workers subjects taking antibiotics medications unwillingness to cooperate Patients with thyroid diseases Current smokers Rheumatoid arthritis patients who were diagnosed less than on 1 year before the start of the study

**Age**

From **20 years** old to **80 years** old

**Gender**

Both

**Phase**

3

**Groups that have been masked**

- Participant
- Investigator
- Outcome assessor

**Sample size**

Target sample size: **66**
Actual sample size reached: **64**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

Patients will be randomly assigned into two groups. A randomization list will be generated from 1 to 66 by a random number generator (https://stattrek.com/statistics/random-number-generator.aspx) and patients were randomly assigned into each intervention group by their numbers. The block randomization technique with 1:1 ratio will be used to achieve balanced group sizes. Supplements and placebos are in the same packaging at the Pharmaceutical company. Only the code is written on the packages. Patients and researchers do not know the type of intervention and after analyzing the data, packet codes are decoded.

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

Participants, investigators or the assessors of the outcomes are unaware of the study groups.

**Placebo**

Used

**Assignment**

Parallel

**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**

**Name of ethics committee**

Ethics committee of Kashan University of Medical Sciences

**Street address**

Ghotbe Ravandi Boulevard, Kashan

**City**

Kashan

**Province**
Isfehan
**Postal code**
8115187159
**Approval date**
2019-10-21, 1398/07/29
**Ethics committee reference number**
IR.KAUMS.MEDNT.REC.1398.078

## 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**
CRP
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Qualitative (Negative, +1, +2 and +3)

### 2

**Description**
ESR
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
mm/h

### 3

**Description**
Disease activity
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
DAS28-ESR (using a questionnaire for VAS and a checklist to note physical examination results)

## Secondary outcomes

### 1

**Description**
Malondialdehyde
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Spectrophotometry

### 2

**Description**
Glutathione peroxidase
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Spectrophotometry

### 3

**Description**
Total antioxidant capacity
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Spectrophotometry

### 4

**Description**
Triglycerides
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Enzymatic kit

### 5

**Description**
Total cholesterol
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Enzymatic kit

### 6

**Description**
HDL
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Enzymatic kit

### 7

**Description**
Insulin
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Elisa kit

**8**

**Description**
Fasting plasma glucose
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Enzymatic kit

**9**

**Description**
LDL
**Timepoint**
At the beginning of the study and after 12 weeks of intervention
**Method of measurement**
Enzymatic kit

## Intervention groups

**1**

**Description**
Intervention group: 6 mg/day Melatonin (RAZAK, Iran), one hour before bedtime for 12 weeks.
**Category**
Treatment - Drugs

**2**

**Description**
Control group: Placebo (Barij Essence, Iran), one hour before bedtime for 12 weeks.
**Category**
Placebo

## Recruitment centers

**1**

**Recruitment center**
**Name of recruitment center**
Beheshti Clinic
**Full name of responsible person**
Dr. Kamal Esalatmanesh
**Street address**
Ghotbe Ravandi Boulevard, Kashan
**City**
Kashan
**Province**
Isfehan
**Postal code**
8115187159
**Phone**
+98 31 5546 3378
**Email**
kamalesalatmanesh@kaums.ac.ir

## Sponsors / Funding sources

**1**

**Sponsor**
**Name of organization / entity**
Vice chancellor for research, Kashan University of Medical Sciences
**Full name of responsible person**
Dr. Hamidreza Banafsheh
**Street address**
Ghotbe Ravandi Boulevard, Kashan
**City**
Kashan
**Province**
Isfehan
**Postal code**
8115187159
**Phone**
+98 31 5546 3378
**Email**
banafsheh.hr@gmail.com
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
Yes
**Title of funding source**
Vice chancellor for research, Kashan 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**
Kashan University of Medical Sciences
**Full name of responsible person**
Amirhossein Loghman
**Position**
Medical Student
**Latest degree**
Medical doctor
**Other areas of specialty/work**
Internal Medicine
**Street address**
Ghotbe Ravandi Boulevard, Kashan
**City**
Kashan
**Province**
Isfehan
**Postal code**

8115187159

**Phone**
+98 31 5554 0021

**Email**
amirhosseinloghman@gmail.com

## Person responsible for scientific inquiries

**Contact**

**Name of organization / entity**
Kashan University of Medical Sciences

**Full name of responsible person**
Dr. Kamal Esalatmanesh

**Position**
Associate Professor

**Latest degree**
Subspecialist

**Other areas of specialty/work**
Internal Medicine

**Street address**
Ghotbe Ravandi Boulevard, Kashan

**City**
Kashan

**Province**
Isfehan

**Postal code**
8115187159

**Phone**
+98 31 5546 3378

**Email**
kamalesalatmanesh@kaums.ac.ir

## Person responsible for updating data

**Contact**

**Name of organization / entity**
Kashan University of Medical Sciences

**Full name of responsible person**
Dr. Kamal Esalatmanesh

**Position**
Associate Professor

**Latest degree**
Subspecialist

**Other areas of specialty/work**
Internal Medicine

**Street address**
Ghotbe Ravandi Boulevard, Kashan

**City**
Kashan

**Province**
Isfehan

**Postal code**
8115187159

**Phone**
+98 31 5546 3378

**Email**
kamalesalatmanesh@kaums.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**
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