Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Evaluation of the effect of L-theanine in patients with hyperthyroidism treated with methimazole: A two-group randomized placebo-controlled clinical trial

Protocol summary

Study aim
To evaluate the effects of L-theanine supplementation alongside methimazole on anxiety, sleep quality, fatigue, thyroid hormones, cortisol, and clinical and laboratory parameters in patients with

Design
A randomized, placebo-controlled, parallel-group clinical trial involving 60 participants equally allocated to two groups using block randomization. Participants and outcome assessors will be blinded

Settings and conduct
Patients will be recruited consecutively from an endocrinology clinic in Dezful. Following eligibility assessment and methimazole stabilization, participants will receive a four-week intervention, with assessments at baseline and post-intervention

Participants/Inclusion and exclusion criteria
Patients aged 18–60 years with hyperthyroidism receiving methimazole for at least four weeks, with informed consent and no recent L-theanine or sedative use. Withdrawal criteria include serious adverse events, pregnancy, severe hepatic, renal or cardiac disease, adherence below 80%, and voluntary withdrawal

Intervention groups
Intervention group (n=30): Oral L-theanine 200 mg daily plus methimazole for four weeks. Control group (n=30): Matching placebo plus methimazole for four weeks

Main outcome variables
Change in anxiety score measured using the GAD-7 questionnaire at baseline and after four weeks

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20250502065563N2**
Registration date: **2026-10-15, 1405/07/23**
Registration timing: **prospective**

Last update: **2026-10-15, 1405/07/23**
Update count: **0**

Registration date
2026-10-15, 1405/07/23

Registrant information

Name
Ali Akbar Oroojan
Name of organization / entity
Country
Iran (Islamic Republic of)
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Recruitment status
Not yet recruiting

Funding source

Expected recruitment start date
2026-12-22, 1405/10/01

Expected recruitment end date
2027-12-22, 1406/10/01

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
Evaluation of the effect of L-theanine in patients with hyperthyroidism treated with methimazole: A two-group randomized placebo-controlled clinical trial

Public title

Evaluation of the effect of L-theanine in patients with hyperthyroidism

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Age 18 to 60 years Definitive diagnosis of hyperthyroidism based on American Thyroid Association (ATA) clinical and laboratory criteria Treatment with methimazole at a dosage of 10 to 20 mg/day At least four weeks of methimazole treatment prior to the start of the intervention No use of amino acid supplements containing L-theanine within the last four weeks No regular use of sedatives, hypnotics, or medications affecting the central nervous system Ability to complete the study questionnaires Written informed consent to participate in the study

Exclusion criteria:

Pregnancy Suffering from severe liver, kidney, or heart disease Use of drugs affecting the central nervous system Reluctance to take supplements

Age

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

Gender

Both

Phase

N/A

Groups that have been masked

- Participant
- Care provider
- Outcome assessor
- Data analyser

Sample size

Target sample size: **60**

More than 1 sample in each individual

Number of samples in each individual: **2**

Collection of 5 cc of blood at two time points: upon entry into the study and at the end of the study.

Randomization (investigator's opinion)

Randomized

Randomization description

In this study, 60 eligible patients will be randomly allocated in a 1:1 ratio to the intervention group (L-theanine plus methimazole) or the control group (placebo plus methimazole) after obtaining informed consent and completing the methimazole stabilization period. The unit of randomization will be the individual patient. Randomization will be performed using variable block sizes of 4 and 6. An independent individual, not involved in trial implementation, will generate the allocation sequence using computer-generated random numbers. Both the order of block sizes and treatment assignments within each block will be randomized. No stratification will be applied. According to the generated sequence, identical-appearing packages containing L-theanine or placebo will be prepared and sequentially numbered from 1 to 60. The principal investigator will be aware of the package contents but will not participate in patient enrollment or allocation. The research assistant responsible for enrollment and dispensing will assign the next sequentially numbered package only after confirming eligibility and obtaining informed consent. This assistant will have no access to the allocation sequence or package contents, thereby maintaining allocation concealment until assignment.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study, the principal investigator will be responsible for preparing the L-theanine supplement and the placebo, coding the packages for each group, and will be aware of the intervention type. The L-theanine supplement and placebo will be provided to a research associate in identical packages bearing specific codes, with no indication of the intervention type. This research associate will be responsible for delivering the packages to patients, collecting data, and assessing study outcomes, without knowledge of the package contents or the intervention assigned to the patients. Furthermore, the participants and the treating physician will remain unaware of whether the L-theanine supplement or the placebo is being administered. The codes corresponding to the intervention type will be retained by the principal investigator, and the allocation code will be disclosed only if medically necessary to ensure patient safety. Thus, blinding will be maintained for the participants, the treating physician, and the research associate responsible for intervention delivery, data collection, and outcome assessment, while the principal investigator remains aware of the group allocations.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of DezfulUniversity of Medical Sciences

Street address

Azadegan Street, Dezful University of Medical Sciences, School of Medicine

City

Dezful

Province

Khouzestan

Postal code

6461653476

Approval date

2026-10-07, 1405/07/15

Ethics committee reference number

IR.DUMS.REC.1405.073

Health conditions studied

1

Description of health condition studied
Hyperthyroidism
ICD-10 code
E05
ICD-10 code description
Thyrotoxicosis [hyperthyroidism]

Primary outcomes

1

Description
Change in anxiety score measured using the Generalized Anxiety Disorder-7 (GAD-7) questionnaire
Timepoint
At baseline (before the intervention) and at the end of the fourth week after initiation of L-theanine supplementation or placebo administration.
Method of measurement
The seven-item Generalized Anxiety Disorder questionnaire, with a total score ranging from 0 to 21, where higher scores indicate greater anxiety severity.

Secondary outcomes

1

Description
Change in sleep quality score assessed using the Pittsburgh Sleep Quality Index.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Pittsburgh Sleep Quality Index questionnaire, with a total score ranging from 0 to 21; higher scores indicate poorer sleep quality.

2

Description
Change in mean fatigue severity score assessed using the Fatigue Severity Scale.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Fatigue Severity Scale consisting of nine items rated on a seven-point scale; the final score is calculated as the mean of the nine item scores.

3

Description
Change in serum cortisol concentration.
Timepoint
At baseline and at the end of the fourth week, between 7:00 and 9:00 AM.
Method of measurement
Measurement of serum cortisol in venous blood using the enzyme-linked immunosorbent assay or the standard method employed by the central laboratory.

4

Description
Change in serum thyroid-stimulating hormone concentration.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Measurement of serum thyroid-stimulating hormone concentration using the enzyme-linked immunosorbent assay.

5

Description
Change in serum free thyroxine concentration.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Measurement of serum free thyroxine concentration using the enzyme-linked immunosorbent assay.

6

Description
Change in serum triiodothyronine concentration.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Measurement of serum triiodothyronine concentration using the enzyme-linked immunosorbent assay.

7

Description
Change in systolic blood pressure measured in millimeters of mercury.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Calibrated digital blood pressure monitor after at least five minutes of seated rest; the mean of two measurements will be recorded.

8

Description
Change in diastolic blood pressure measured in millimeters of mercury.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Calibrated digital blood pressure monitor after at least

five minutes of seated rest; the mean of two measurements will be recorded.

9

Description
Change in heart rate measured in beats per minute.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Calibrated digital blood pressure monitor after at least five minutes of seated rest.

10

Description
Change in serum alanine aminotransferase level.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Measurement of alanine aminotransferase activity using a standard enzymatic colorimetric assay and an automated biochemistry analyzer.

11

Description
Change in serum aspartate aminotransferase level.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Measurement of aspartate aminotransferase activity using a standard enzymatic colorimetric assay and an automated biochemistry analyzer.

12

Description
Changes in complete blood count parameters.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Complete blood count testing using an automated hematology analyzer.

13

Description
Change in serum C-reactive protein concentration.
Timepoint
At baseline and at the end of the fourth week of intervention.
Method of measurement
Measurement of serum C-reactive protein concentration using a standard laboratory assay.

Intervention groups

1

Description
Control group: Participants in this group (n=30) will receive standard methimazole therapy at a daily dose of 10–20 mg as prescribed by their physician. They will also receive an oral placebo matched to L-theanine in appearance, color, size, and packaging, once daily, 1–2 hours before bedtime, for four consecutive weeks. Placebo administration will begin at least four weeks after initiation of methimazole treatment.
Category
Placebo

2

Description
Intervention group: Participants in this group (n=30) will receive oral L-theanine supplementation at a dose of 200 mg once daily, 1–2 hours before bedtime, for four consecutive weeks, in addition to standard methimazole therapy at a daily dose of 10–20 mg as prescribed by their physician. Supplementation will begin at least four weeks after initiation of methimazole treatment.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Private Practice of a Sub-specialist in Endocrinology and Metabolism; Faculty Member, Dezful Univers
Full name of responsible person
Hamid Karimi
Street address
1st Floor, Neshat 1 Medical Complex, Neshat Street, Taleghani Street, Dezful, Iran
City
Dezful
Province
Khouzestan
Postal code
6461796455
Phone
+98 61 4225 2840
Email
karimi.h@dums.ac.ir

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Dezfoul University of Medical Sciences
Full name of responsible person
Abbas Heidarimoghadam
Street address
Next to the Traffic Police Department, end of

Azadegan Boulevard, Dezful, Khuzestan.

City
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Province
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6461653476

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soheila.alb@gmail.com

Grant name

Grant code / Reference number

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

Title of funding source
Dezfoul 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
Dezfoul University of Medical Sciences

Full name of responsible person
Ali Akbar Oroojan

Position
Associate professor

Latest degree
Ph.D.

Other areas of specialty/work
Physiology

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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
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

Not applicable

Data Dictionary

Not applicable