

Clinical Trial Protocol

Iranian Registry of Clinical Trials

11 Jun 2026

Effects of Naringenin on Aminotransferase Level, Insulin Resistance, Cardiovascular Risk Factors, and Adiponectin and Neuregulin-4 levels in Overweight or Obese Patients with Non-alcoholic Fatty Liver Disease: A Randomized Controlled trial

Protocol summary

Study aim

Effects of naringenin supplement on Aminotransferase levels, insulin resistance, cardiovascular risk factors, and serum levels of adiponectin and neuregulin-4 in obese or overweight Non-alcoholic fatty liver disease patients

Design

Randomized, double-blind, placebo-controlled, parallel trial with 2 arms (each arm includes 22 patients) and stratified permuted block randomization is used

Settings and conduct

Patients selection from Naft hospital, Tehran Taking 2 capsules per day for 4 weeks Blood sample collection, anthropometric analysis, sonography and filling out questionnaires before and after the intervention Blinding patients and investigators

Participants/Inclusion and exclusion criteria

Inclusion criteria: 20-65 years old, BMI range between 25-35, diagnosis of Non-alcoholic fatty liver disease based on sonography, informed consent for participating in the study; exclusion criteria: regular consumption of NSAIDs, antibiotics, corticosteroids, anti-hypertensive, lipid-lowering and weight-lowering agents, regular consumption of multivitamin-mineral, antioxidants, omega-3 and probiotic and also the consumption of herbal drinks such as silymarin, a pathological diagnosed condition affecting the liver such as viral hepatitis and liver transplantation, past medical history of diabetes, organs failure, gastrointestinal tract, thyroid and auto-immune disorders, kidney and severe mental diseases, cardiovascular accidents, pregnancy, intention to be pregnant, breastfeeding and menopause status, addiction and consumption of alcoholic drinks, professional exercise

Intervention groups

The intervention group should consume two capsules that each containing 100 mg naringenin, and the control

group should consume two placebo capsules

Main outcome variables

Aminotransferase levels, insulin resistance, cardiovascular risk factors, and serum levels of adiponectin and neuregulin-4

General information

Reason for update

Dosage and duration of naringenin supplementation were respectively changed from 400 mg/day and 8 weeks to 200 mg/day and 4 weeks based on the study pharmacist proposal.

Acronym

IRCT registration information

IRCT registration number: **IRCT20131125015536N12**
Registration date: **2020-08-06, 1399/05/16**
Registration timing: **prospective**

Last update: **2021-01-16, 1399/10/27**

Update count: **1**

Registration date

2020-08-06, 1399/05/16

Registrant information

Name

Mohammad Javad Hosseinzadeh

Name of organization / entity

School of Nutritional Sciences and Dietetics, TUMS

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-10-10, 1399/07/19

Expected recruitment end date

2021-06-09, 1400/03/19

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Effects of Naringenin on Aminotransferase Level, Insulin Resistance, Cardiovascular Risk Factors, and Adiponectin and Neuregulin-4 levels in Overweight or Obese Patients with Non-alcoholic Fatty Liver Disease: A Randomized Controlled trial

Public title

Effects of Naringenin Supplement on Non-alcoholic Fatty Liver Disease

Purpose

Supportive

Inclusion/Exclusion criteria

Inclusion criteria:

20 to 65 years old men and women Range of body mass index (BMI) should be between 25 to 35 Kg/m² Diagnosis of Non-alcoholic fatty liver disease based on sonography by specialist Informed consent for participating in the study

Exclusion criteria:

Regular consumption of Non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, corticosteroids, anti-hypertensive agents, lipid-lowering agents and weight-lowering agents in the period of last 3 months Regular consumption of multivitamin-minerals, antioxidants, omega3 supplement at the dosages of more than daily needs and also consumption of probiotic supplements and herbal drinks such as silymarin in the period of last 3 months Diagnosis of pathological conditions affecting the liver such as viral hepatitis and liver transplantation Past medical history of diabetes, gastrointestinal tract disorders, organ failure, thyroid disorders, kidney diseases, autoimmune diseases, severe mental diseases and several types of malignancies Past medical history of cardiovascular accidents in the period of last 3 months Pregnancy, intention to be pregnant in the next 3 months, breastfeeding and menopause status Being addict, consumption of alcoholic drinks Professional exercise

Age

From 20 years old to 65 years old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Investigator

Sample size

Target sample size: 44

Randomization (investigator's opinion)

Randomized

Randomization description

In order to randomize the study groups, we will use the Stratified Permuted Block Randomization method. First, patients are stratified in terms of gender randomization, and since there will be different confounding factors in this study, a score for each individual in terms of disease risk is determined based on these confounding factors (BMI in the range of 29.9-25 = 0 and BMI in the range of 30-35=1, age in the range of 20-43 years = 0 and age in the range of 43-65 years = 1, degree of mild fatty liver disease = 0 and degree of moderate and severe fatty liver disease = 1). The sum of these scores will be at least 0 and at most 3. According to these, people who get a score of zero and one are considered as low risk and the people who get a score of two and three are considered as high risk. After that, they will be randomized separately. Block sizes: 4 4 2 6 2

Blinding (investigator's opinion)

Double blinded

Blinding description

Double-blind study (participants and researcher blinding) through naringenin and placebo supplement packaging in one shape and naming with A and B letters. The mentioned process has done by a third person, so that the researcher and the patients are not aware of the type of intervention.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Tehran University of Medical Science

Street address

Sixth floor, central Building of Tehran University of Medical Science, Ghods street, Keshavarz Blvd

City

Tehran

Province

Tehran

Postal code

1417653761

Approval date

2020-05-06, 1399/02/17

Ethics committee reference number

IR.TUMS.VCR.REC.1399.347

Health conditions studied

1

Description of health condition studied

Non-alcoholic fatty liver disease

ICD-10 code

K76.0

ICD-10 code description

Fatty (change of) liver, not elsewhere classified

Primary outcomes

1

Description

Serum aminotransferase levels

Timepoint

Before and after the intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

Blood levels through special kit

2

Description

Insulin resistance index

Timepoint

Before and after the intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

Formula

3

Description

hs-CRP

Timepoint

Before and after the intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

Blood levels through special kit

4

Description

Adiponectin

Timepoint

Before and after the intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

Blood levels through special kit

5

Description

Neuregulin-4

Timepoint

Before and after intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

Blood levels through special kit

Secondary outcomes

1

Description

Blood pressure

Timepoint

Before and after the intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

pressure indicator

2

Description

Body mass index

Timepoint

Before and after the intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

calculating according to related formula

3

Description

weight

Timepoint

Before and after the intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

Digital scale

4

Description

Height

Timepoint

Before and after the intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

Standard tape meter

5

Description

physical activity score

Timepoint

every two weeks (on the day 0, 14, 28)

Method of measurement

international physical activity questionnaire: short

6

Description

Lipid profile

Timepoint

Before and after the intervention (on the day of 0 and at the end of the next 4 weeks)

Method of measurement

Blood levels through special kit

Intervention groups

1

Description

Intervention group: Naringenin supplement (provided by Exir Nano Sina Co.) should consume before dinner and lunch at the dosages of 200 mg/day that divided into two 100 mg capsule per day for 4 weeks (method of naringenin extraction is alcoholic)

Category

Treatment - Other

2

Description

Control group: placebo (cellulose) should consume before dinner and lunch at the dosages of 200 mg/day that divided into two 100 mg capsule (provided by Exir Nano Sina Co.) per day for 4 weeks

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Naft hospital

Full name of responsible person

Mohammad Javad Hosseinzadeh Attar

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Tehran University of Medical Sciences

Full name of responsible person

Mohammad Ali Sahraeian

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Sixth Floor- Central Building of Tehran University of Medical Science, Qods St, Keshavarz Blvd

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msahrai@sina.tums.ac.ir

Grant name

Grant code / Reference number

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

Yes

Title of funding source

Tehran 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

Tehran University of Medical Sciences

Full name of responsible person

Mohammad Javad Hosseinzadeh Attar

Position

Professor

Latest degree

Ph.D.

Other areas of specialty/work

Nutrition

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Person responsible for scientific inquiries

Contact

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Position

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Latest degree

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Other areas of specialty/work

Nutrition

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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

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

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

Tehran University of Medical Sciences

Full name of responsible person

Mohammad Javad Hosseinzadeh Attar

Position

Professor

Latest degree

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Other areas of specialty/work

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