Clinical Trial Protocol
Iranian Registry of Clinical Trials

20 Nov 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 Aminoteransferas 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
Aminoteransferase 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

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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 silymarine in the priod 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, organs 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
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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 aminoteransferase 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
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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 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
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