Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

The effect of theobromine supplementation on anthropometric indices, glycemic indices, cardiovascular risk factors, and genes expression of PPARα and Sirt1 in subjects with metabolic syndrome.

Protocol summary

Study aim

Determining the effect of theobromine supplementation on anthropometric indices, glycemic indices, cardiovascular risk factors, and genes expression of PPARα and Sirt1 in subjects with metabolic syndrome.

Design

A 12-week triple-blid, randomized parallel clinical trial on 80 overweight and obese subjects with metabolic syndrome

Settings and conduct

After the approval of the proposal study subjects were selected from those who refer to the health centers affiliated to Kermanshah University of Medical Sciences. Eligible individuals will be interviewed and the goals, methods and importance of conducting the study will be explained in detail to each of them After providing written consent, they will be divided into 2 groups of Theobromine and placebo by Stratified Blocked Randomization. Subjects will be asked to take a 450 mg / day theobromine capsule for 12 weeks.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Overweight or subjects aged 40 to 55 years with metabolic syndrome. Exclusion criteria: having Diabetes, cancer, hepatitis, cardiovascular disease, hematological, neurological, renal, thyroid and gastrointestinal disorders. Consumption of medications or supplements that affect appetite, weight or metabolism, and having any weight loss diet or heavy exercise program in the past 6 months. Patients treated with statins and antihypertensive drugs will only be included in the study if they are treated for more than 3 months for statins and more than 6 months for high blood pressure.

Intervention groups

Intervention group: 450 mg/d theobromine capsule in breakfast meal for 12 weeks. Control group: 450 mg/d placebo capsule in breakfast meal for 12 weeks.

Main outcome variables

weight, waist circumference, hip circumference, fasting blood sugar, fasting insulin, HOMA-IR, lipid profile, HDL2-c, HDL3-c, HDL2-c/HDL3-c, and blood pressure.

General information

Reason for update

Considering the association of HDL-c subclasses (HDL2-c, HDL3-c and HDL2-c/HDL3-c) with metabolic syndrome and cardiovascular diseases (CVD), assessing these variables can provide a more precise result on the effect of theobromine on CVD risk factors. Additionally, HDL-c function can be determined via assessing these factors. Therefore, we aim to include these variables in our study.

Acronym

IRCT registration information

IRCT registration number: **IRCT20091114002709N59**
Registration date: **2022-03-05, 1400/12/14**
Registration timing: **registered_while_recruiting**

Last update: **2023-12-12, 1402/09/21**
Update count: **1**

Registration date

2022-03-05, 1400/12/14

Registrant information

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Name of organization / entity

Iran University of Medical Sciences

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Recruitment status
Recruitment complete
Funding source

Expected recruitment start date
2022-01-19, 1400/10/29
Expected recruitment end date
2022-05-19, 1401/02/29
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
The effect of theobromine supplementation on anthropometric indices, glycemic indices, cardiovascular risk factors, and genes expression of PPARα and Sirt1 in subjects with metabolic syndrome.

Public title
The effect of Theobromine supplementation on anthropometric indices, glycemic indices, cardiovascular risk factors, and genes expression of PPARα and Sirt1 in subjects with metabolic syndrome.
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Overweight or obese (25 ≤BMI≤ 35 kg/m^2) men and women aged 40 to 55 years . Having metabolic syndrome according to IDF definition (Waist circumference greater than 94 cm for men and 80 cm for women, Triglyceride ≥ 150mg/dl, HDL-c ≤ 40mg/dl for men and HDL-c ≤ 50mg/dl for women or medication, Systolic blood pressure ≥ 130mmHg and DBP≥ 85 mmHg or medication, Fasting blood sugar≥ 100mg/dl or medication) Tendency to participate in the study
Exclusion criteria:
Smoking Subjects with diabetes, cancer, hepatitis, cardiovascular diseases, hematological disorders, Neurological disorders, renal disorders, gastrointestinal and thyroid disorders Insulin therapy, use hypoglycemic and weight reduction medication, vasodilators, hormone therapy, corticosteroids, non steroid anti inflammatory drugs, antihistamines, Selective serotonin reuptake inhibitors, anti gout and psychotics medication. Use of any vitamin and mineral supplement, antioxidants and omega3. Pregnancy, lactation and adherence to a specific diet People treated with statins and antihypertensive drugs will only be included in the study if they are treated for more than 3 months for statins and more than 6 months for high blood pressure.
Age
From **40 years** old to **55 years** old
Gender
Both

Phase
3
Groups that have been masked
- Participant
- Investigator
- Data analyser

Sample size
Target sample size: **80**
Randomization (investigator's opinion)
Randomized
Randomization description
Randomization is done by Stratified Blocked Randomization with the volume 4. Stratification will be done based on participants BMI (25-30 and 30-35). Considering the sample size of 40 in each strata, 10 blocks with volume 4 will be produced in each strata and subjects in each strata will be assigned to treatment or placebo group based on a random list produced by PASS 11 statistical software . The random list containing 3-digit codes for each patient that identifies the relevant treatment will be provided to the researcher and will be inserted on the labels of 80 drug bottles. Only the study project executive expert is aware of the designed codes. Randomization and blinding of the study are performed to maintain concealment.
Blinding (investigator's opinion)
Triple blinded
Blinding description
Researchers, participants and data analyzer will be blinded in this study. so that the patient does not know which treatment group he or she belongs to, because both the placebo and supplement groups are prepared in exactly the same form and package. By following a random list containing codes 1 to 80, The researchers also do not know which treatment group was assigned to each patient. Because the random list will be prepared by the project executive expert (Personal except researcher and data analyst) and only the patient code will be recorded on each drug package. Thus, none of the participants, researchers and data analysts of the study type They do not know the dedicated treatment and the study will be triple-blind.
Placebo
Used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethic Committee of Iran University of Medical Sciences
Street address
Hemmat Highway, Iran University of Medical Sciences
City
Tehran
Province

Tehran

Postal code

1449614535

Approval date

2021-11-20, 1400/08/29

Ethics committee reference number

IR.IUMS.REC.1400.761

Health conditions studied

1

Description of health condition studied

Metabolic syndrome

ICD-10 code

ICD-10 code description

Primary outcomes

1

Description

Weight

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Seca scale

2

Description

Body mass index(BMI)

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Weight (kg) divided by height squared (square meters)

3

Description

Waist circumference

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Measuring tape

4

Description

Hip circumference

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Measuring tape

5

Description

Systolic blood pressure

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Sphygmomanometer

6

Description

Triglyceride

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Colorimetri

7

Description

Total cholesterol

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Colorimetri

8

Description

LDL-c

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Colorimetri

9

Description

HDL-c

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Colorimetri

10

Description

Fasting insulin

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

ELIZA kit

11

Description

Fasting blood sugar

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

Enzymatic

12

Description

HDL2-C Subclass

Timepoint

At the beginning of the study and at the end of week 12

Method of measurement

ELISA (enzyme-linked immunosorbent assay)

13

Description
HDL3-C Subclass
Timepoint
At the beginning of the study and at the end of week 12
Method of measurement
ELISA (enzyme-linked immunosorbent assay)

14

Description
HDL2-C/HDL3-C
Timepoint
At the beginning of the study and at the end of week 12
Method of measurement
Dividing HDL2-C to HDL3-C values

Secondary outcomes

1

Description
Sirtuin 1 gene expression
Timepoint
At the beginning of the study and at the end of week 12
Method of measurement
Real Time PCR

2

Description
PPARα gene expression
Timepoint
At the beginning of the study and at the end of week 12
Method of measurement
Real Time PCR

Intervention groups

1

Description
Intervention group: Daily intake of a 450 mg theobromine capsule (made by BulkSupplement company; USA) in breakfast meal for 12 weeks.
Category
Treatment - Other

2

Description
Control group: Daily intake of a 450 mg maltodextrin capsule (made by Karen Pharmaceuticals and Dietary Supplements Company; Iran) in breakfast meal for 12 weeks.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
All health centers affiliated to Kermanshah University of Medical Sciences
Full name of responsible person
Ebrahim Shakiba
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Bahar street, healyh deputy of kermanshah universiyu of medical sciences
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Kermanshah
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Iran University of Medical Sciences
Full name of responsible person
Hossein Keyvani, deputy head of Research and technology, Iran university of medical sci
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research-m@iums.ac.ir
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Iran 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
Iran University of Medical Sciences
Full name of responsible person
Farzad Shidfar
Position
Full professor
Latest degree
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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
اطلاعات بیشتری وجود ندارد
Study Protocol
Yes - There is a plan to make this available
Statistical Analysis Plan
Yes - There is a plan to make this available
Informed Consent Form
Yes - There is a plan to make this available
Clinical Study Report
Yes - There is a plan to make this available
Analytic Code
Yes - There is a plan to make this available
Data Dictionary
Yes - There is a plan to make this available
Title and more details about the data/document
Information on the main implications can be shared at the end of the study.
When the data will become available and for how long
The access period will be 6 months after the results are published.
To whom data/document is available
The data from this study will be available only to researchers working in academic and scientific institutions.
Under which criteria data/document could be used
6 months after the publication of the articles obtained from the data of this project, at the request of the person in charge of the project and his consent, the study data can be made available to researchers.
From where data/document is obtainable
Applicants can contact the responsible author via email or the following mailing address to obtain the required data. Postal address: Tehran-Hemmat Highway-Iran University of Medical Sciences-Faculty of Health-Department of Nutrition. Contact number: 00982188622755. Email: shidfar.f@iums.ac.ir
What processes are involved for a request to access data/document
Applicants will be able to access the study data by sending an email to the responsible author within a

maximum of one week.

Comments