

Clinical Trial Protocol

Iranian Registry of Clinical Trials

21 Jul 2026

The effect of non-caloric sweeteners compared with sucrose on the gut microbiome, cardiovascular risk factors, and sex hormones in women with obesity

Protocol summary

Study aim

This study aimed to investigate the effect of non-caloric sweeteners compared with sucrose on the gut microbiome, cardiovascular risk factors, and sex hormones in women with obesity.

Design

A 4-arm triple-blind, randomized parallel controlled clinical trial. A total of 160 eligible participants will be assigned to four intervention groups (n=40) using block randomization.

Settings and conduct

This study will be conducted in the Nutrition and Food Security research center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. The intervention period will last 3 months. The four tested beverages will be provided in the same sweetness, shape, color, and appearance and will be packed in the same bottles. All bottles will be labeled with four codes (A, B, C, and D) by a person who is not aware of the study objectives. Therefore, participants and administrators will be blinded to the content of the bottles until data analyses. Physical activity assessment, three-day weighted food record, anthropometric and blood pressure measurements will be conducted at the baseline, mid-intervention, and the end of the intervention period, and blood samples, 24-hour urine samples, and stool samples will also be collected from participants at the start and the end of each intervention period.

Participants/Inclusion and exclusion criteria

Women with obesity who are experiencing menopausal transition (aged 42-52 years) without any other chronic diseases who do not smoke or drink alcohol, experience infection or antibiotic use, and give consent to enter the study

Intervention groups

After a 4-week run-in period, 160 eligible women will be randomly assigned to four groups (n=40) in which they

will receive daily a 500mL bottle containing sucrose (50 g), or aspartame (268 mg), or saccharin (125 mg), or steviol glucosides (200 mg).

Main outcome variables

Gut microbiome, Cardiometabolic markers, Sex hormones

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20130223012571N7**

Registration date: **2021-03-08, 1399/12/18**

Registration timing: **prospective**

Last update: **2021-03-08, 1399/12/18**

Update count: **0**

Registration date

2021-03-08, 1399/12/18

Registrant information

Name

Amin Salehi-Abargouei

Name of organization / entity

Shahid Sadoughi University of Medical Sciences

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2021-06-22, 1400/04/01

Expected recruitment end date

2022-04-20, 1401/01/31

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The effect of non-caloric sweeteners compared with sucrose on the gut microbiome, cardiovascular risk factors, and sex hormones in women with obesity

Public title

Non-caloric sweeteners, microbiome, and cardiometabolic risk - a randomized clinical trial of Iranian women

Purpose

Basic science

Inclusion/Exclusion criteria**Inclusion criteria:**

Women between 42 and 52 years old BMI ≥ 30 kg/m²
Stable weight (weight change ≤ 3 kg in the past 3 months)
Presence of an intact uterus and at least one ovary
Report of a menstrual cycle in the three months before screening
Absence of pregnancy, lactation, or use of oral contraceptives or hormone therapy
Willing to participate in the study.

Exclusion criteria:

History or diagnosis of thyroid disease (unless controlled by medication), type 1 or 2 diabetes mellitus, kidney disease, liver disease, cardiovascular disease, and chronic gastrointestinal disease
History of recent infection and antibiotic use
Smoking
Consuming alcoholic drinks
Taking medications that may affect body weight and composition, lipid profile and blood glucose control (including metformin, glibenclamide, atorvastatin, aspirin or other non-steroidal anti-inflammatory drugs), cholestyramine, colestipol, niacin, clofibrate, gemfibrozil, probucol, or 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase inhibitors, Being on a specific diet

Age

From **42 years** old to **52 years** old

Gender

Female

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size

Target sample size: **160**

Randomization (investigator's opinion)

Randomized

Randomization description

An independent statistician will use a statistical software

[statistical package for social sciences (SPSS)] which generates random numbers to block-randomize participants into one of the four trial groups (labeled as A, B, C, and D), ensuring that all the subjects will receive treatments in a balanced and random order. Each label will be assigned to one of the four sweeteners used as treatment (aspartame, saccharine, steviol glycosides, and sucrose).

Blinding (investigator's opinion)

Triple blinded

Blinding description

The concealment will be done by putting the randomly assigned group for each participant in sealed envelopes. The allocation concealment will be conducted by an independent researcher. The four tested beverages will be provided in the same sweetness, shape, color, and appearance and will be packed in the same bottles. In addition, natural flavorings with similar color, appearance, taste, and texture will be added to all of the four treatment groups by an independent researcher from the Department of Pharmaceutics, School of Pharmacy, Shahid Sadoughi University of Medical Sciences. Participants and administrators will be unaware of the content of the bottles until data analyses. All bottles will be labeled with four codes (A, B, C, and D) by a responsible person who is not aware of the study objectives. The codes will not be released until after the statistical analyses; therefore, neither the study participants nor the personnel and the data analysts will be aware of the intervention bottles.

Placebo

Not used

Assignment

Parallel

Other design features**Secondary Ids**

empty

Ethics committees**1****Ethics committee****Name of ethics committee**

Ethics committee of Shahid Sadoughi University of Medical Sciences

Street address

Central Building of Shahid Sadoughi University of Medical Sciences, Bahrar Square, Yazd, Iran

City

Yazd

Province

Yazd

Postal code

8916978477

Approval date

2021-02-09, 1399/11/21

Ethics committee reference number

IR.SSU.REC.1399.262

Health conditions studied

1

Description of health condition studied

women with obesity

ICD-10 code

E66

ICD-10 code description

Overweight and obesity

Primary outcomes

1

Description

Gut microbiome composition

Timepoint

At baseline and the end of intervention period

Method of measurement

Sequencing the 16s rDNA extracted from the stool samples

Secondary outcomes

1

Description

Hemoglobin A1C

Timepoint

At baseline and the end of intervention period

Method of measurement

High-performance liquid chromatography method

2

Description

Fasting blood sugar

Timepoint

At baseline and the end of intervention period

Method of measurement

Laboratory kits

3

Description

Two-hour postprandial glucose

Timepoint

At baseline and the end of intervention period

Method of measurement

Laboratory kits

4

Description

Fasting serum insulin

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

5

Description

Fasting serum Triglyceride

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

6

Description

Fasting serum total cholesterol

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

7

Description

Fasting serum high-density cholesterol

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

8

Description

Fasting serum low-density cholesterol

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

9

Description

Serum alkaline phosphatase

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

10

Description

Serum gamma-glutamyl transferase

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

11

Description

Serum aspartate aminotransferase

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

12

Description

Serum alanine aminotransferase

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

13

Description

Blood urea nitrogen

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

14

Description

Serum Creatinine

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

15

Description

Serum Follicle-stimulating hormone

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

16

Description

Serum testosterone

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

17

Description

Serum estradiol

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

18

Description

Serum estriol

Timepoint

At baseline and the end of the intervention period

Method of measurement

Laboratory kits

19

Description

Weight

Timepoint

At baseline, 1 month, and the end of the intervention period

Method of measurement

Body composition analyzer

20

Description

Waist circumference

Timepoint

At baseline, 1 month, and the end of the intervention period

Method of measurement

Non-stretchable tape measure

21

Description

Hip circumference

Timepoint

At baseline, 1 month, and the end of the intervention period

Method of measurement

Non-stretchable tape measure

22

Description

Body fat mass

Timepoint

At baseline, 1 month, and the end of the intervention period

Method of measurement

Body composition analyzer

23

Description

Body lean mass

Timepoint

At baseline, 1 month, and the end of the intervention period

Method of measurement

Body composition analyzer

24

Description

Visceral fat

Timepoint

At baseline, 1 month, and the end of the intervention period

Method of measurement

Body composition analyzer

25

Description

Systolic blood pressure

Timepoint

At baseline, 1 month, and the end of the intervention period

Method of measurement

Sphygmomanometer

26**Description**

Diastolic blood pressure

Timepoint

At baseline, 1 month, and the end of the intervention period

Method of measurement

Sphygmomanometer

Intervention groups**1****Description**

Intervention group 1: Oral daily intake of a 500-milliliter beverage containing water, aspartame (268 mg), and 80 mg of para-aminobenzoic acid (PABA) once a day for 3 months

Category

Treatment - Other

2**Description**

Intervention group 2: Oral daily intake of a 500-milliliter bottle beverage containing water, saccharin (125 mg), and 80 mg of para-aminobenzoic acid (PABA) for 3 months

Category

Treatment - Other

3**Description**

Intervention group 3: Oral daily intake of a 500-milliliter beverage containing water, steviol glucosides (200 mg), and 80 mg of para-aminobenzoic acid (PABA) for 3 months

Category

Treatment - Other

4**Description**

Control group: Oral daily intake of a 500-milliliter beverage containing water, sucrose (50 g), and 80 mg of para-aminobenzoic acid (PABA) for 3 months

Category

Treatment - Other

Recruitment centers**1****Recruitment center****Name of recruitment center**

Nutrition and Food Security Research center, Shahid Sadoughi University of Medical Sciences, Yazd, I

Full name of responsible person

Amin Salehi-Abargouei

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Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Alem Square, Yazd, Iran

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Sponsors / Funding sources**1****Sponsor****Name of organization / entity**

Swiss National Science Foundation

Full name of responsible person

Dr. Stephanie Hoppeler

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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

Swiss National Science Foundation

Proportion provided by this source

100

Public or private sector

Public

Domestic or foreign origin

Foreign

Category of foreign source of funding

UN agencies and international organizations

Country of origin**Type of organization providing the funding**

Academic

Person responsible for general inquiries

Contact

Name of organization / entity

Yazd University of Medical Sciences

Full name of responsible person

Hamidreza Raeisi-Dehkordi

Position

MSc of Public Health Nutrition

Latest degree

Master

Other areas of specialty/work

Nutrition

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Department of Nutrition, School of Public Health,
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Person responsible for scientific inquiries

Contact

Name of organization / entity

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Full name of responsible person

Dr. Amin Salehi-Abargouei

Position

Ph.D. in Nutrition Sciences

Latest degree

Ph.D.

Other areas of specialty/work

Nutrition

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Person responsible for updating data

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Hamidreza Raeisi-Dehkordi

Position

MSc of Public Health Nutrition

Latest degree

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Yes - There is a plan to make this available

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

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

Title and more details about the data/document

We plan to register and deposit data that relates to
individual primary publications and not the whole study
database. This enables other researchers to replicate
published analyses and results as well as to re-use the
data for additional analyses such as meta-analysis.
General characteristics of participants (without the
identity of the participants) as well as baseline and after-
treatment data values of primary and secondary
outcome variables, will become available for researchers
after a request from interested investigators.

When the data will become available and for how long

Data will be available after the individual, related papers
become published.

To whom data/document is available

Data will become available for all investigators interested
in the subject.

Under which criteria data/document could be used

All efforts will be made to protect the privacy and to de-

identify the data. Therefore, data will be shared on request under the following conditions: - A meaningful study question by the requester - Outline of the planned analyses - Valid methodology - Signed data sharing agreement that contains a confidentiality agreement and approval of the study team members.

From where data/document is obtainable

The data can be obtained from principal investigators: - Principal investigator from Iran: Dr. Amin Salehi-Abargouei, MSc, Ph.D. in Nutrition. Department of Nutrition Faculty of Public Health Sahid Sadoughi University of Medical Sciences Yazd, PO Code 8915173160 Iran, Tel:+98-35-31492229, Fax:+98-35-38209119, Email: abargouei@ssu.ac.ir Alternate email: abargouei@gmail.com - Principal

investigator from Switzerland: Prof. Oscar Franco, MD, Ph.D., FESC, FFPH. Professor of Epidemiology & Public Health. University of Bern, Mittelstrasse 43, 3012 Bern, Switzerland, Tel +41316313350 Email: oscar.franco@ispm.unibe.ch

What processes are involved for a request to access data/document

The interested investigators should provide a brief description of the data needed and their reason for asking for the data by contacting principal investigators. They will assess the possibility of sharing the data and if applicable will ask for a signed data sharing agreement that contains a confidentiality agreement and approval of the study team members.

Comments