

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

12 Jul 2026

### Assesment of the effects of coffee main constituents (caffeine and chlorogenic acid) supplementation on inflammatory, metabolic factors, hepatic steatosis and fibrosis in none- alcoholic fatty liver patients with type 2 diabetes

#### Protocol summary

##### Summary

In this randomized, double blind, placebo controlled trial with parallel design, 100 patients suffering from NAFLD and type 2 diabetes will be selected among patients referring to Gastroenterology and endocrinology Clinic of Shariati Hospital in Tehran. Participants will be randomly assigned to one of the following interventions or control group based on the blocked randomization method. In this study neither the patient nor the clinical and laboratory investigators will be aware of the treatment assignment. 1) Group I: will receive caffeine (200 mg) 1 capsule/d plus chlorogenic acid (200 mg) 1 capsule/d for 6 months. 2) Group II: will receive caffeine (200 mg) 1 capsule/d plus placebo (200 mg) 1 capsule/d for 6 months. 3) Group III: will receive placebo (200 mg) 1 capsule/d plus chlorogenic acid (200 mg) 1 capsule/d for 6 months. 4) Group IV: will receive placebo (200 mg) 1 capsule/d plus placebo (200 mg) 1 capsule/d for 6 months. So supplementation will be daily and will supervise for 6 months. After a 10- to 12-h fasting, blood samples will be taken at baseline and at 6th month of the intervention. Fatty liver will be diagnosed by documented laboratory data and FibroScan. The initial clinical visit will be 2 weeks after the introduction of treatment in arms. The follow-up interval will be every 4 weeks. Measurements will be taken on the day treatment begins (day 0) and 6 months after the treatment begins (day 180), including laboratory examinations (liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT]), lipid profile, blood glucose, inflammatory and oxidative stress biomarkers, and insulin resistance) and body composition, blood pressure, hepatic steatosis and fibrosis, anthropometric measurement, and self-administered questionnaires to evaluate subjective symptoms, lifestyle factors, menopausal status and postmenopausal, and medication

use). Compliance with treatment will be assessed at each visit (monthly) by interview. To assess potential changes in daily food consumption and physical activity during the 6-month intervention, participants will keep a completely food intake record for a 72-h period at home and a record of their physical activity at baseline and at 6th month of the intervention. All participants will be advised a balanced diet for the duration of trial.

#### General information

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT201707024010N21**  
Registration date: **2017-09-15, 1396/06/24**  
Registration timing: **prospective**

Last update:

Update count: **0**

##### Registration date

2017-09-15, 1396/06/24

##### Registrant information

##### Name

Azita Hekmatdoost

##### Name of organization / entity

Shahid Beheshti University of Medical Sciences,  
National Institute of Nutrition Research

##### Country

Iran (Islamic Republic of)

##### Phone

+98 21 2293 0824

##### Email address

hekmat@sina.tums.ac.ir

##### Recruitment status

**Recruitment complete**

##### Funding source

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |                                                                                      |          |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--------------------------------------------------------------------------------------|----------|
| NNFTRI, SBMU                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  | Assignment                                                                           | Parallel |
| <b>Expected recruitment start date</b><br>2017-10-02, 1396/07/10                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  | <b>Other design features</b>                                                         |          |
| <b>Expected recruitment end date</b><br>2018-10-02, 1397/07/10                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |  | <b>Secondary Ids</b><br>empty                                                        |          |
| <b>Actual recruitment start date</b><br>empty                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |  | <b>Ethics committees</b>                                                             |          |
| <b>Actual recruitment end date</b><br>empty                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |  | <b>1</b>                                                                             |          |
| <b>Trial completion date</b><br>empty                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |  | <b>Ethics committee</b>                                                              |          |
| <b>Scientific title</b><br>Assesment of the effects of coffee main constituents (caffeine and chlorogenic acid) supplementation on inflammatory, metabolic factors, hepatic steatosis and fibrosis in none- alcoholic fatty liver patients with type 2 diabetes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | <b>Name of ethics committee</b><br>NNFTRI, SBMU                                      |          |
| <b>Public title</b><br>Assesment of the effects of coffee main constituents in none- alcoholic fatty liver patients with type 2 diabetes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |  | <b>Street address</b><br>46, Hafezi St., Farahzadi Blvd., Shahrak QODS, Tehran, Iran |          |
| <b>Purpose</b><br>Treatment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |  | <b>City</b><br>Tehran                                                                |          |
| <b>Inclusion/Exclusion criteria</b><br>Inclusion Criteria: Patient diagnosed with type 2 diabetes based on American Diabetes Association (ADA) definition or who only take oral antidiabetic drug. CAPscore >263<br>Exclusion Criteria: Taking any kind of antibiotics two weeks before recruitment; History of alcohol consumption ; pregnancy or lactation; Professional athletes; Other liver disease (viral/etc); High dose synthetic estrogens, methotrexate , amiodarone, steroids, chloroquine, immunosuppressive drugs; A history of Cardiovascular disease; Renal disease, Celiac disease, Cirrhosis; History of Upper Gastrointestinal surgery ; A history of hypothyroidism or Cushing's syndrome; History of drug dependence; Body mass index (BMI) $\geq 35$ kg/m <sup>2</sup> ; A restrictive diet or weight change $\geq 5$ kg during the 3 months prior to study; Any change in treatment with oral hypoglycemic; anti hypertensive and antilipid agents during the study; Use of weight loss medications |  | <b>Postal code</b><br>Approval date<br>2017-07-18, 1396/04/27                        |          |
| <b>Age</b><br>From <b>30 years</b> old to <b>50 years</b> old                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |  | <b>Ethics committee reference number</b><br>1396.145                                 |          |
| <b>Gender</b><br>Both                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |  | <b>Health conditions studied</b>                                                     |          |
| <b>Phase</b><br>3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |  | <b>1</b>                                                                             |          |
| <b>Groups that have been masked</b><br>No information                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |  | <b>Description of health condition studied</b><br>NAFLD                              |          |
| <b>Sample size</b><br>Target sample size: <b>100</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  | <b>ICD-10 code</b><br>k76.0                                                          |          |
| <b>Randomization (investigator's opinion)</b><br>Randomized                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |  | <b>ICD-10 code description</b><br>(Nonalcoholic fatty liver disease (NAFLD           |          |
| <b>Randomization description</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  | <b>Primary outcomes</b>                                                              |          |
| <b>Blinding (investigator's opinion)</b><br>Double blinded                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  | <b>1</b>                                                                             |          |
| <b>Blinding description</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |  | <b>Description</b><br>ALT                                                            |          |
| <b>Placebo</b><br>Used                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |  | <b>Timepoint</b><br>Before and 24 weekes after the intervention                      |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | <b>Method of measurement</b><br>U/L                                                  |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | <b>2</b>                                                                             |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | <b>Description</b><br>Liver Steatosis                                                |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | <b>Timepoint</b><br>Before and 6 weekes after the intervention                       |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | <b>Method of measurement</b><br>ultrasonography                                      |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | <b>3</b>                                                                             |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | <b>Description</b><br>Liver fibrosis                                                 |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | <b>Timepoint</b>                                                                     |          |

Before and 24 weeks after the intervention

**Method of measurement**

fiberscan

**4**

**Description**

glucose

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

mg/dl

**5**

**Description**

weight

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

kg

**6**

**Description**

AST

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

U/L

**7**

**Description**

GGT

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

U/L

**Secondary outcomes**

**1**

**Description**

TG

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

mg/dl

**2**

**Description**

TC

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

mg/dl

**3**

**Description**

LDL-C

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

mg/dl

**4**

**Description**

HDL-C

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

mg/dl

**5**

**Description**

TNF- $\alpha$

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

pg/ml

**6**

**Description**

Insulin

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

$\mu$ U/mL

**7**

**Description**

c-peptide

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

ng /ml

**8**

**Description**

CRP

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

mg/l

**9**

**Description**

HbA1C

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

%

**10**

**Description**

TAC

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

µg/l

**11****Description**

Cytokeratin 18

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

u/l

**12****Description**

NFK-B

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

-

**13****Description**

α2-Macroglobulin

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

mg/l

**14****Description**

Adiponectin

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

µg/ml

**15****Description**

leptin

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

ng /ml

**16****Description**

IFN-g

**Timepoint**

Before and 24 weeks after the intervention

**Method of measurement**

pg/ml

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

caffeine (200 mg) 1 capsule/d plus placebo (200 mg) 1 capsule/d

**Category**

Treatment - Other

**2****Description**

placebo (200 mg) 1 capsule/d plus chlorogenic acid (200 mg) 1 capsule/

**Category**

Treatment - Other

**3****Description**

caffeine (200 mg) 1 capsule/d plus chlorogenic acid (200 mg) 1 capsule/d

**Category**

Treatment - Other

**4****Description**

placebo (200 mg) 1 capsule/d plus placebo (200 mg) 1 capsule/d

**Category**

Placebo

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

Endocrinology & Metabolism Institute, Tehran  
University of Medical Sciences

**Full name of responsible person**

Mohammad Reza Mohajeri- Tehrani

**Street address**

Endocrinology & Metabolism Research Institute, 5th  
floor, Shariati Hospital, North Kargar Avenue, Tehran

**City**

Tehran

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

NIMAD

**Full name of responsible person**

Azita Hekmatdoost

**Street address**

21, Besat St, west fatemi Ave, Tehran, IRAN

**City**

Tehran

**Grant name****Grant code / Reference number**

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

Yes

**Title of funding source**

NIMAD

**Proportion provided by this source**

**Public or private sector**

empty

**Domestic or foreign origin**

empty

**Category of foreign source of funding**

empty

**Country of origin**

**Type of organization providing the funding**

empty

**2**

**Sponsor**

**Name of organization / entity**

DDRI

**Full name of responsible person**

Azita Hekmatdoost

**Street address**

Shariati Hospital, North Kargar Ave

**City**

Tehran

**Grant name**

**Grant code / Reference number**

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

Yes

**Title of funding source**

DDRI

**Proportion provided by this source**

**Public or private sector**

empty

**Domestic or foreign origin**

empty

**Category of foreign source of funding**

empty

**Country of origin**

**Type of organization providing the funding**

empty

**Person responsible for general inquiries**

**Contact**

**Name of organization / entity**

Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Science

**Full name of responsible person**

Asieh Mansour

**Position**

PhD student in nutrition

**Other areas of specialty/work**

**Street address**

46, Hafezi St., Farahzadi Blvd., Shahrak QODS, Tehran, Iran

**City**

Tehran

**Postal code**

**Phone**

+98 21 8822 0071

**Fax**

**Email**

asiehmansour@yahoo.com

**Web page address**

**Person responsible for scientific inquiries**

**Contact**

**Name of organization / entity**

Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Science

**Full name of responsible person**

Azita Hekmatdoost

**Position**

MD-PhD in nutrition

**Other areas of specialty/work**

**Street address**

46, Hafezi St., Farahzadi Blvd., Shahrak QODS, Tehran, Iran

**City**

Tehran

**Postal code**

**Phone**

+98 21 2235 7483

**Fax**

**Email**

a\_hekmat2000@yahoo.com

**Web page address**

**Person responsible for updating data**

**Contact**

**Sharing plan**

**Deidentified Individual Participant Data Set (IPD)**

empty

**Study Protocol**

empty

**Statistical Analysis Plan**

empty

**Informed Consent Form**

empty

**Clinical Study Report**

empty

**Analytic Code**

empty

**Data Dictionary**

empty