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Effect of oleocanthal- and oleacein-rich extra virgin olive oil on blood glucose and metabolic control in people with type 2 diabetes

Submission date
14/05/2026

Recruitment status
Recruiting

Registration date
27/05/2026

Overall study status
Ongoing

Last Edited
21/10/2026

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Type 2 diabetes mellitus is a common long-term condition that affects blood sugar levels and increases the risk of cardiovascular disease and other health complications. Chronic inflammation and oxidative stress are believed to play an important role in the progression of the disease. Extra virgin olive oil (EVOO), a key component of the Mediterranean diet, contains natural phenolic compounds with potential anti-inflammatory and antioxidant effects. Among these compounds, oleocanthal and oleacein may help improve glucose metabolism and overall metabolic health. The aim of this study is to evaluate whether regular consumption of EVOO rich in oleocanthal and oleacein improves glycaemic control and metabolic health in people with type 2 diabetes.

Who can participate?
Men and women aged 40 to 70 years with established type 2 diabetes mellitus and excess body fat may participate in the study if they have stable diabetes treatment and meet the study eligibility criteria.

What does the study involve?
Participants will be randomly assigned to one of two groups for 12 weeks. One group will receive an EVOO with a high content of oleocanthal and oleacein, while the other group will receive a control EVOO with low phenolic compound content. Participants will be asked to replace their usual culinary oil with the study oil for all home cooking and raw consumption. Approximately 1 litre of olive oil per week will be provided. Four study visits will take place at the hospital. Participants will undergo blood tests, anthropometric measurements, blood pressure assessment, continuous glucose monitoring, and collection of urine and stool samples. Questionnaires assessing diet, physical activity, emotional well-being, and cognitive function will also be completed.

What are the possible benefits and risks of participating?
Participants may benefit from close monitoring of their diabetes and metabolic health during the study. The information obtained may also contribute to improving knowledge about

nutritional approaches for type 2 diabetes management. The risks associated with participation are considered low because the intervention involves a commonly consumed food product. Possible inconveniences include blood sampling, wearing the glucose monitoring sensor, and mild gastrointestinal discomfort related to olive oil consumption.

Where is the study run from?
The study is coordinated from the Hospital Regional Universitario de Málaga, with participant recruitment through primary care centres in the Málaga-Guadalhorce Health District.

When is the study starting and how long is it expected to run for?
Recruitment is expected to begin in June 2026 and finish in June 2027. The study is expected to be completed in December 2027.

Who is funding the study?
The study is funded by the Instituto de Salud Carlos III (ISCIII), Spain.

Who is the main contact?
Dr Francisco-Javier Bermudez-Silva, Principal Investigator of the DiAOVE study at the Hospital Regional Universitario de Málaga, javier.bermudez@ibima.eu.

Contact information

Type(s)
Principal investigator, Scientific, Public

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Additional identifiers

Instituto de Salud Carlos III (ISCIII), Spain, grant number
PI23/01785

Study information

Scientific Title
DiAOVE: a monocentric randomized double-blind controlled nutritional intervention trial assessing the effects of oleocanthal- and oleacein-rich extra virgin olive oil on glycaemic control,

continuous glucose monitoring metrics and metabolic outcomes in adults with type 2 diabetes mellitus

Acronym
DiAOVE

Study objectives
To evaluate the effect of a nutritional intervention with extra virgin olive oil rich in oleocanthal and oleacein on glycemic control and metabolic profile in individuals with type 2 diabetes mellitus.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 30/03/2026, CEIm Provincial de Málaga (Avda. Carlos de Haya 84, Pabellón A, 7º planta, Málaga, 29010, Spain; 34951291977; eticainvestiga.hch.sspa@juntadeandalucia.es), ref: SICEIA-2026-001097

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Type 2 diabetes

Interventions
Participants with type 2 diabetes mellitus will be randomly assigned in a 1:1 ratio to one of two parallel intervention groups for 12 weeks. Randomisation will be stratified by sex and baseline HbA1c level (<8% vs ≥8%) using computer-generated random allocation with permuted blocks of variable size. The study is double-blind, and both participants and investigators will remain masked to treatment allocation throughout the study. The intervention products will be packaged and labelled identically using alphanumeric codes to ensure blinding.

The intervention consists of the complete replacement of the participant's usual culinary oil with a specifically characterised extra virgin olive oil (EVOO). Participants allocated to the intervention group will receive EVOO with a high content of phenolic compounds, particularly oleocanthal and oleacein (AOVE-T), while the control group will receive a low-phenolic control EVOO obtained by phenolic extraction ("washed" EVOO) while preserving the lipid matrix (AOVE-C). Participants will be instructed to use exclusively the assigned oil both raw and for home cooking and to avoid other culinary oils or fats during the intervention period. Approximately 1 litre of EVOO per week will be supplied to each participant. No additional structured dietary modifications or caloric restriction will be prescribed. Glycaemic control will be assessed using glycated haemoglobin (HbA1c) and two 10-day periods of continuous glucose monitoring performed before and at the end of the intervention.

Intervention Type
Supplement

Primary outcome(s)
1. Fasting venous blood glycated haemoglobin (HbA1c) measured using standard clinical laboratory biochemical assays (%) at baseline (Visit 2) and 12 weeks (Visit 4)

Key secondary outcome(s)
1. Continuous glucose monitoring metrics, including mean glucose, glucose management indicator (GMI), coefficient of variation (CV), time in range (70–180 mg/dL), time below range, time above range and ambulatory glucose profile (AGP), measured using continuous interstitial glucose monitoring systems according to international consensus recommendations at baseline and 12 weeks

2. Glucose metabolism and insulin resistance, assessed via fasting plasma glucose (mg/dL), fasting insulin levels (µU/mL), HOMA-IR and HOMA2-IR indices, in fasting venous blood samples measured using standard clinical laboratory biochemical assays at baseline and 12 weeks

3. Lipid profile, assessed via total cholesterol (mg/dL), LDL cholesterol (mg/dL), HDL cholesterol (mg/dL), and triglycerides (mg/dL), in fasting venous blood samples measured using standard clinical laboratory biochemical assays at baseline and 12 weeks

4. Anthropometric and clinical parameters, including body mass index (BMI) (kg/m²), waist circumference (cm), waist-to-hip ratio, waist-to-height ratio, fat mass estimated by bioimpedance analysis (BIA), hydration and nutritional status assessed by bioelectrical impedance vector analysis (BIVA), and systolic and diastolic blood pressure (mmHg), measured using standardized anthropometric procedures, bioelectrical impedance analysis and automated blood pressure measurement devices at baseline and 12 weeks

5. inflammatory markers, including high-sensitivity C-reactive protein (hs-CRP) (mg/L), interleukin-6 (IL-6) (pg/mL), tumor necrosis factor alpha (TNF-α) (pg/mL), interleukin-1β (IL-1β) (pg/mL), interferon gamma (IFN-γ) (pg/mL), and other inflammatory markers included in commercial multiplex panels, in plasma samples measured using commercially available multiplex assays, ELISA and standardized laboratory biochemical methods at baseline and 12 weeks

6. oxidative stress markers, including glutathione reductase (GR) (U/L), total thiols (TT) (µM), lipid peroxidation hydro derivatives (LOOH) (µM), lipid peroxidation organic derivatives (LOOH)

(μM), total antioxidant status (TAS) (mmol/L), and other oxidative stress markers, in plasma samples measured using laboratory biochemical assays and standardized oxidative stress analytical methods at baseline and 12 weeks

7. Symptoms of anxiety measured using the total score and/or anxiety subscales of the Brief Symptom Inventory 48 (BSI-48) questionnaire at baseline and 12 weeks

8. 8. Symptoms of depression measured using the total score and/or depression subscales of the Patient Health Questionnaire (PHQ-9) at baseline and 12 weeks

9. Cognitive performance, including global cognition and executive function/attention measured using the Montreal Cognitive Assessment (MoCA), Trail Making Test (TMT) Parts A and B, the Stroop test, and the Symbol Digit Modalities Test (SDMT) at baseline and 12 weeks

Completion date
27/12/2027

Eligibility

Key inclusion criteria
1. Men or women aged between 40 and 70 years
2. Diagnosis of type 2 diabetes mellitus established according to the criteria of the American Diabetes Association (ADA)
3. Excess body fat (preclinical or clinical obesity, according to the definition and diagnostic criteria for clinical obesity established by the 2025 Lancet Diabetes & Endocrinology Commission) determined by direct body fat measurement (DEXA scan) or fulfillment of at least two of the following criteria:
3.1. BMI ≥ 25 kg/m²
3.2. Waist circumference ≥ 102 cm for men or ≥ 88 cm for women
3.3. Waist-to-hip ratio > 0.90 for men or > 0.85 for women
3.4. Waist-to-height ratio > 0.5 for all participants
3.5. Excess body fat will be pragmatically assumed if BMI is > 40 kg/m².
4. Stable pharmacological treatment for T2DM for at least 3 or 6 months prior to inclusion, which may include:
4.1. Metformin (3 months)
4.2. DPP-4 inhibitors (3 months)
4.3. SGLT2 inhibitors (6 months)
4.4. GLP-1 receptor agonists (6 months)
5. Stable statin treatment, when indicated
6. Ability to understand the study information and provide written informed consent

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
40 Years

Upper age limit

70 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Active chronic inflammatory diseases, such as Crohn's Disease, Ulcerative Colitis, inflammatory arthritis, or other systemic inflammatory disorders
2. Chronic treatment with nonsteroidal anti-inflammatory drugs or systemic corticosteroids within the previous 6 months.
3. Habitual consumption of meals outside the home three or more times per week, which would hinder adequate control of the dietary intervention
4. Use of hormonal contraceptives, pregnancy, breastfeeding, or steroid hormone replacement therapy
5. Current diagnosis of malignant neoplasia or history of neoplasia within the year prior to inclusion
6. Active smoking or former smokers with less than 5 years of abstinence
7. Having been born and having lived for most of the first 18 years of life (more than 10 years during the first 18 years) in countries not aligned with the traditional Mediterranean diet (countries other than Spain, Italy, Greece, Southern France [Provence-Alpes-Côte d'Azur region and the departments of Hérault, Gard, Aude, and Pyrénées-Orientales in the Occitanie region], Portugal, Croatia [Dalmatian Coast], Albania, Turkey [Aegean Coast], Lebanon, Israel, Morocco, and Tunisia)
8. Objective inability to comply with study procedures, defined as the presence of significant cognitive impairment, substantial language barriers, logistical inability to attend scheduled visits, anticipated major therapeutic changes during the intervention period, or any other documented circumstance preventing adequate compliance with the intervention and data collection, as appropriately recorded in the study records

Date of first enrolment
24/08/2026

Date of final enrolment
14/06/2027

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Regional Universitario de Málaga
Spain

Sponsor information

Organisation
Fundación Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud

ROR
https://ror.org/002nw1r81

Funder(s)

Funder type

Funder Name
Instituto de Salud Carlos III

Alternative Name(s)
SaludISCIII, InstitutodeSaludCarlosIII, Instituto de Salud Carlos III | Madrid, Spain, Carlos III Institute of Health, Institute of Health Carlos III, Carlos III Health Institute, La misión del Instituto de Salud Carlos III (ISCIII), ISCIII

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Results and Publications

Individual participant data (IPD) sharing plan
Yes. De-identified individual participant data underlying the published results may be shared upon reasonable request to the principal investigator, following publication of the main study results and subject to approval of a data access agreement and applicable ethical and data protection regulations.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Other files	Consent form version 8.2	15/01/2026	15/05/2026	No	Yes
Other files	PIS biological sample donation version 8.2	15/01/2026	15/05/2026	No	Yes
Other files	Revocation modification of consent version 8.2	15/01/2026	15/05/2026	No	Yes
Participant information sheet	version 2.0	11/07/2024	15/05/2026	No	Yes
Protocol file		15/02/2026	19/05/2026	No	No
Statistical Analysis Plan		15/02/2026	19/05/2026	No	No