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The beneficial effect of two varieties of apples, such as Golden Delicious and Canadian White Renetta, on the improvement of normal lipid and glucose metabolism in insulin-resistant subjects with and without a diagnosis of non-alcoholic fatty liver disease

Submission date 27/08/2025	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 24/09/2025	**Overall study status** Completed	
Last Edited 05/10/2026	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Insulin resistance is a key risk factor for metabolic syndrome (MS), which includes conditions like high blood pressure, abnormal cholesterol, high blood sugar, and increased waist size. MS is common, especially in people with type 2 diabetes, and often comes with changes in body fat and fatty liver disease. Non-Alcoholic Fatty Liver Disease (NAFLD), affecting around 25% of the global population, involves fat buildup in the liver and can progress to serious conditions like NASH, cirrhosis, and liver cancer. NAFLD is closely linked to MS and insulin resistance. Because MS and NAFLD raise the risk of heart disease, diabetes, and liver damage, it's important to find dietary strategies to help prevent them. Apples, rich in beneficial compounds like quercetin and anthocyanins, have shown positive effects on heart health and metabolism. This study aims to show that eating Golden Delicious and Renetta apples as part of a balanced diet can improve blood sugar and fat levels in people with insulin resistance, with or without NAFLD.

Who can participate?
Patients between the ages of 18 and 75, diagnosed with MS with or without NAFLD

What does the study involve?
The study includes six groups of participants treated for 9 months with either Golden Delicious or Renetta apples, alongside a controlled diet.

Group breakdown:
Group A1: MS only, diet only (control)
Group A2: MS only, diet + Golden Delicious apple
Group A3: MS only, diet + Renetta apple

Group B1: MS + NAFLD, diet only (control)
Group B2: MS + NAFLD, diet + Golden Delicious apple
Group B3: MS + NAFLD, diet + Renetta apple

All participants will be asked to fill in a food diary to verify compliance with treatments. The total duration of the study will be approximately 12 months, with 1 month for enrolment, approximately 9 months for the conduct of the study, considering the timing for the last subject enrolled. After that, the analysis of the results will follow. The study will begin after a positive opinion of the Ethics Committee, and will end after the last subject has been enrolled and the last analyzes have been performed.

What are the possible benefits and risks of participating?
An improvement in the parameters evaluated as indicators of glucose and lipid metabolism and liver markers, and non-alcoholic fatty liver disease is hypothesized for the enrolled subjects, after taking active treatment. However, no benefit may be achieved. In the event of changes in plasma parameters that, in the opinion of the attending physician, require a pharmacological intervention or adverse effects, the subject will need to exit the study.

Where is the study run from?
COMEGEN Soc. Coop. Sociale, Italy

When is the study starting and how long is it expected to run for?
April 2025 to October 2026

Who is funding the study?
Consorzio Melinda SCA, Italy

Who is the main contact?
Dr Matteo Laringe, alessandra.baldi.alimenti@gmail.com

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Additional identifiers

Protocol serial number
ME25_01

Study information

Scientific Title
Study of the efficacy of the intake of two varieties of apple (Malus domestica (Suckow) Borkh.) such as Golden Delicious apple and Canadian White Renetta apple, as part of a correct and balanced diet, on the improvement of normal lipid and carbohydrate metabolism in insulin-resistant subjects with and without a diagnosis of non-alcoholic fatty liver disease (NAFLD): single-center, controlled, randomized, open clinical study

Acronym
ME25

Study objectives
The study will aim to evaluate the efficacy of of the consumption of an apple a day of two varieties of apples such as Golden Delicious Apple DOP and Canadian White Renetta Apple DOP, known to be rich in micronutients and polyphenols, for the improvement of normal lipid and carbohydrate metabolism, through the reduction of blood levels of lipids and glucose, in insulin-resistant subjects with and without a diagnosis of non-alcoholic fatty liver disease (NAFLD).

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 10/06/2025, Campania Territorial Ethics Committee 1 (Comitato Etico Territoriale Campania 1) (Via Mariano Semmola, 52, INT "Fondazione Giovanni Pascale", Naples, 80131, Italy; +39 081/ 17770131 - 132 - 130; comitatoetico@istitutotumori.na.it), ref: 7/25

Primary study design
Interventional

Study design
Single-center randomized controlled open-label clinical trial

Study type(s)
Efficacy, Prevention, Quality of life

Health condition(s) or problem(s) studied
Insulin-resistant subjects with and without a diagnosis of non-alcoholic fatty liver disease (NAFLD)

Interventions
The randomization sequence was generated by a statistician using STATA 16 software (Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC), and subjects were assigned to each of the two treatment groups in a random and unpredictable manner by means of simple randomization. This procedure minimizes the “selection bias”, i.e. systematic differences between the baseline characteristics of the groups being compared (prognostic and treatment response imbalance).

The concealment of the randomization list protects the allocation sequence until assignment and is stored in an inviolable place in the experimental center. Both the generation of the allocation sequence and the randomization list are separated through the use of sealed envelopes. These envelopes were prepared by a person not clinically involved in the trial, must be opaque, sealed, stapled and numbered in order consistent with that of the randomization list, and then stored in a sealed cabinet. The experimenter who enrolled the subjects, and who gave them one of the three treatments to be compared by opening the next envelope each time, remained unaware of the randomization list.

The design includes 6 experimental groups with a treatment period of 9 months, with the products under study such as Golden Delicious Apple DOP and White Renetta Apple of Canada DOP. The clinical study involves six arms, grouped into two main groups:
Group A: subjects with metabolic syndrome (MS);
Group B: subjects with MS and NAFLD.

The experimental groups will be the following:
GROUP A1 (22 subjects): subjects with MS who will have to follow the isocaloric diet (MS control group);
GROUP A2 (22 subjects): subjects with MS who will have to take one Golden Delicious Apple DOP per day in combination with an isocaloric diet (Golden MS treated group);
GROUP A3 (22 subjects): subjects with MS who will have to take one DOP Renetta Apple per day in combination with an isocaloric diet (Renetta MS treated group);

GROUP B1 (22 subjects): subjects with MS and NAFLD who will have to follow the isocaloric diet (control group MS+NAFLD);
GROUP B2 (22 subjects): subjects with MS and NAFLD who will have to take one Golden Delicious Apple DOP per day in combination with an isocaloric diet (Golden MS+NAFLD treated group);
GROUP B3 (22 subjects): subjects with MS and NAFLD who will have to take one Renet Apple per day in combination with an isocaloric diet (treated group Renetta MS+NAFLD).
All subjects are asked for the entire duration of the study to fill in a food diary to verify compliance with treatments.
Each subject of each experimental group, after taking the Golden Delicious Apple DOP or the Renetta Apple DOP in combination with the isocaloric diet (treated groups) or the isocaloric diet alone (control group), will undergo the analyses, as reported in the study layout.

Intervention Type
Supplement

Primary outcome(s)
Lipid and carbohydrate metabolism will be assessed through the reduction of blood lipid and glucose levels, respectively, using the following methods at baseline (t0), 90 days (t1), 180 days (t2), and 270 days (t3) of treatment:
Determination of blood levels measured using standard blood tests of:
1. Total cholesterol (TC)
2. LDL cholesterol (LDL-C)
3. HDL cholesterol (HDL-C)
4. Triglycerides (TG)
5. Glycated hemoglobin (HbA1c)
6. Glycemia

Key secondary outcome(s)
1. Body weight measured through reduction in BMI (Body Mass Index) and abdominal circumference at baseline (t0), 180 days (t2) and 270 days (t3) of treatment
2. Blood pressure values (diastolic and systolic pressure) measured using a sphygmomanometer at baseline (t0), 90 days (t1), 180 days (t2), and 270 days (t3) of treatment
3. Levels of inflammation and pro-inflammatory cytokines measured through the determination of the blood concentration of the following biomarkers at baseline (t0), 270 days (t3) of treatment:
3.1. White blood cells (WBC)- erythrocyte sedimentation rate (ESR)- C-reactive protein (CRP)
3.2. TNF-α- IL-6
3.3. - IL-1-β
4. Specific liver markers measured through the determination of the following blood concentration of biomarkers at baseline (t0), 90 days (t1), 180 days (t2), and 270 days (t3) of treatment:
4.1. ALT (alanine aminotransferase)
4.2. AST (aspartate aminotransferase)
4.3. Bilirubina
4.4. Albumin
4.4. Total protein
5. Markers of nonalcoholic fatty liver disease (NAFLD) will be measured by LC-MS/MS-based proteomics and metabolomics analysis of serum samples at baseline (t0), 90 days (t1), 180 days (t2), and 270 days (t3)

Completion date
31/10/2026

Eligibility

Key inclusion criteria
Subjects of both sexes who have the following characteristics will be included in the study:
1. Between the ages of 18 and 75
2. Able to understand and sign the informed consent
3. Able to understand and comply with the requirements of the protocol
4. Negative HIV test
5. Negative pregnancy test
6. Diagnosis of MS (and therefore have at least three of the following risk factors:
6.1. Abdominal circumference ≥ 80 cm (women) ≥ 94 cm (men)
6.2. Triglycerides ≥ 150 mg/dl; HDL < 40 mg/dl (men); HDL < 50 mg/dl (women)
6.3. Fasting blood glucose ≥ 100 mg/dl
6.4. Blood pressure ≥ 130/85 mmHg
7. Diagnosis of NAFLD in the last 12 months before the t0 visit (if belonging to group b); the diagnosis must have been confirmed by a diagnostic imaging investigation: ultrasound and/or CT scan and/or magnetic resonance imaging of the liver
8. Who are not taking and are not taking drugs, including antidiabetics, drugs that act on the nervous system, such as antidepressants, anxiolytics, opiates
9. Who are not taking antibiotics or have not taken antibiotics in the last four weeks, or in the last 6 months, based on the intensity and duration of antibiotic treatment

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
75 Years

Sex
All

Total final enrolment
132

Key exclusion criteria
Subjects who have the following characteristics will be excluded from the study:
1. With the age < 18 and > 75 years
2. Who do not have a diagnosis of MS

3. Who do not have NAFLD (relative to group B)
4. Who have NAFLD (relative to group A)
5. Who have type 1 diabetes mellitus
6. Who has had liver diseases (cirrhosis, liver failure and hepatocarcinoma)
7. Who do not show a propensity to collaborate
8. Who have difficulty in going to the reference facility on time
9. Who are not considered suitable by the investigator due to the presence of other pathologies considered incompatible with enrollment and requiring pharmacological treatments (e.g. Active systemic diseases, diabetes, neurological and psychiatric diseases, including cognitive disorders that prevent the completion of questionnaires)
10. Suffering from HIV-acquired immunodeficiency
11. Pregnant or breastfeeding women
12. Individuals with severe visual and hearing impairments
13. With known allergies to the experimental products
14. Who use food supplements or drugs that affect lipid or carbohydrate metabolism
15. Who consume alcohol in quantities greater than 30g/day for men and 20g/day for women
16. Who use drugs of abuse
17. Who consume nicotine, caffeine and theine
18. Who have an allergy to apples or significant gastrointestinal disorders
19. Taking medication

Date of first enrolment
01/10/2025

Date of final enrolment
01/10/2025

Locations

Countries of recruitment
Italy

Study participating centre
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Sponsor information

Organisation
Consorzio Melinda SCA

Funder(s)

Funder type
Not defined

Funder Name
Consorzio Melinda SCA

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the subsequent results publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes