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Beneficial potential of a nutraceutical formulation containing abscisic acid in patients with type 2 diabetes

Submission date
24/06/2022

Recruitment status
No longer recruiting

Registration date
26/07/2022

Overall study status
Completed

Last Edited
06/08/2024

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Diabetes is a metabolic disease that has reached epidemic proportions, with type 2 diabetes mellitus (T2DM) as the most prevalent form, affecting 90–95% of diabetic subjects. The use of therapeutic strategies aimed to contrast hyperglycaemia is essential, especially to avoid diabetes-related microvascular and macrovascular complications. Among bioactive molecules with hypoglycaemic potential, abscisic acid (ABA) has gained great interest in the scientific literature in the last decades. ABA is produced and released by pancreatic β-cells in response to high glucose concentrations. As a result, this molecule would promote stimulation of insulin release and the uptake of peripheral glucose, overall contributing to the reduction of plasma glucose levels. Additionally, a reduced release of ABA has been reported after a glucose load in patients with T2DM or gestational diabetes, further supporting this molecule as key actor in the control of diabetic pathology. Our scientific interest in thinned unripe fruits arose from the observation that ABA is not only produced by humans after glucose stimulation, but also represents a historically known phytohormone, whose content reaches the highest concentration in a specific stage of immaturity in plants. Interestingly, it is in this phase that crops may be subjected to fruit thinning, a typical agronomical practice carried out to improve fruit size and quality in harvest management. In this scenario, the large number of unripe fruits discarded every year due to this process turns out to represent innovative and high-value resources of abscisic acid, in line with the concepts of food waste revaluation and environmental sustainability. Therefore, this study aims to evaluate the beneficial contribution to the control of glucose homeostasis by a nutraceutical formulation based on thinned nectarines in patients with T2DM.

Who can participate?
Patients with T2DM aged 18–83 years.

What does the study involve?
Partecipants are randomly allocated to three intervention groups: placebo (PL) group (500 mg of maltodextrins three times/day), low dose of TN (LD) group (500 mg of TN three times/day, lyophilized), or high dose of TN (HD) group (750 mg of TN three times/day, lyophilized). Both

placebo and TN treatments were self-administered as tablets.
For the evaluation of primary and secondary outcomes, blood samples will be taken at 0 and 12 weeks. Body measurements will be also taken at the start and end of the study.

What are the possible benefits and risks of participating?
Participants taking part in this study should benefit from the synergistic effects of ABA and polyphenols present in the nutraceutical formulation. This may include a positive influence on markers of glycemic control. There are no known risks to participants taking part in this study.

Where is the study run from?
1. Samnium Medical Cooperative (Italy)
2. Department of Pharmacy, University of Naples “Federico II” (Italy)

When is the study starting and how long is it expected to run for?
May 2019 to December 2019

Who is funding the study?
1. Samnium Medical Cooperative (Italy)
2. Department of Pharmacy, University of Naples “Federico II” (Italy)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
n°28 of 15/05/2017

Study information

Scientific Title
Beneficial contribution on glucose homeostasis by an agro-food waste product rich in abscisic acid: result from a three-month, three-arm, parallel-group randomized controlled trial conducted on sixty-one patients with type 2 diabetes

Study objectives
The hypoglycemic hormone abscisic acid (ABA) has gained great interest in the scientific literature in the last decades. The high ABA concentration in thinned nectarines (TN) led us to test these food matrices for their potential in diabetes management. Therefore, the aims of this study are:
1. To evaluate the effects on glycemic control after supplementation with two different doses of a TN-based nutraceutical formulation.
2. To evaluate the correlation between glycemia and ABA plasmatic levels of patients undergoing the clinical trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/07/2027, Scientific Ethics Committee of AO Rummo Hospital (Via dell'Angelo 1, 82100, Benevento, Italy; +39 0824571111; comitatoeticoav@gmail.com), ref: 70128

Study design
Monocentric interventional double-blind parallel-group randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

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

Interventions
Patients are randomly allocated to three intervention groups: placebo (PL) group (500 mg of maltodextrins three times/day), low dose of TN (LD) group (500 mg of TN three times/day, lyophilized), or high dose of TN (HD) group (750 mg of TN three times/day, lyophilized). Both placebo and TN treatments were self-administered as tablets. Treatment compliance was assessed by counting the number of tablets re-turned at the time of specified clinic visits. Throughout the study, we instructed patients to take their first dose of new medication on the day after they were given the appropriate treatments. All treatments were provided free of charge. Patients, core laboratories, clinicians, and trial staff were blind to treatment allocation. Periodic and standardized telephone interviews were performed by qualified personnel in order to verify and increase protocol compliance.

Participants were randomised by drawing of envelopes containing randomisation numbers. The random number list was generated by an investigator with no clinical involvement in the trial.

Intervention Type
Supplement

Primary outcome(s)
For the evaluation of the primary outcomes, blood samples were collected after 12 h of fasting at 0 and 12 weeks in 10-mL EDTA coated tubes, and plasma was immediately isolated by centrifugation (20 min, 2.200 g, 4˚C). All samples were stored at –80˚C until analysis.
1. Fasting plasma glucose (FPG), determined using commercially available kits (Diacron International, Italy).
2. Glycated hemoglobin (HbA1c), determined with a commercially available kit (InterMedical s.r.l, Italy).
3. Fasting plasma insulin (FPI), measured using an enzyme-linked immunosorbent (ELISA) assay commercial kit (InterMedical s.r.l, Italy).
4. Homeostatic model assessment of insulin resistance (HOMA index), calculated with the formula: FPG (mg/dl) times FPI (μUI/ml) divided by 22.5.
5. Abscisic acid (ABA) plasma levels, assessed using liquid chromatography/mass spectrometry (LC/MS) analysis of blood samples.

Key secondary outcome(s))
Unless otherwise stated, the following are assessed at 0 and 12 weeks:
1. Clinical history, assessed by interviews and analysis of previous clinical data at the baseline.
2. Nutrient intake and dietary habits, assessed using a seven-day food record validated nutritional questionnaire at the baseline and at the end of the study period.
3. Anthropometric measures, collected by measuring height, weight, and waist circumference (WC).
4. Blood pressure, assessed using a blood pressure cuff.
5. Plasma total cholesterol (TC), measured from using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International.
6. high-density lipoprotein-cholesterol (HDL-C), measured using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron

International.
7. Low-density lipoprotein-cholesterol (LDL-C), measured using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International.
8. Triglyceride levels, measured using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International.
9. Aspartate transaminase (AST), measured using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International.
10. Aspartate transaminase (AST), measured using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International.
11. Creatine levels, measured using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International.

Completion date
16/12/2019

Eligibility

Key inclusion criteria
1. Patients aged 18–83 years.
2. Clinical diagnosis of type 2 diabetes mellitus (T2DM) according to American Diabetes Association (ADA).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
61

Key exclusion criteria
1. Smokers
2. Hepatic disease
3. Renal disease
4. Heart disease
5. Type 1 diabetes mellitus (T1DM)
6. Family history of chronic diseases
7. Drug therapy or supplement intake containing polyphenols
8. Heavy physical exercise (over 10 hours per week)

9. Underweight (Body Mass Index <18.5 kg/m²)
10. Pregnant, suspected of being pregnant or hoping to become pregnant
11. Breastfeeding
12. Birch pollen allergy
13. Use of vitamin or mineral supplements 2 weeks prior to entry into the study
14. Donation of blood less than 3 months prior to the study

Date of first enrolment
13/05/2019

Date of final enrolment
10/06/2019

Locations

Countries of recruitment
Italy

Study participating centre
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Study participating centre
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Sponsor information

Organisation
Samnium Medical Cooperative (Benevento, Italy)

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Samnium Medical Cooperative

Results and Publications

Individual participant data (IPD) sharing plan
Data of individual patients will be available upon request of patient permission
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IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		31/08/2022	05/12/2022	Yes	No
Results article		03/03/2023	06/08/2024	Yes	No
Protocol file			11/07/2022	No	No