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# Understanding the impact of different doses of Reducose® mulberry leaf extract on blood glucose and insulin responses after eating a complex meal

**Submission date**
30/05/2022

**Recruitment status**
No longer recruiting

**Registration date**
08/06/2022

**Overall study status**
Completed

**Last Edited**
19/07/2024

**Condition category**
Nutritional, Metabolic, Endocrine

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

## Plain English summary of protocol

Background and study aims
Reducose mulberry leaf extract can be used to lower the body's glucose (sugar) response after eating foods containing carbohydrates. It has been developed for use as both a food ingredient and for use in dietary supplements. The sponsor has successfully completed four clinical trials with Reducose which evaluated the effects of Reducose® in lowering the glycaemic index of common carbohydrates in a healthy Indian population; the effects of Reducose® in lowering the glycaemic index of common carbohydrates in a healthy Chinese population; the effects of three different doses of Reducose® versus placebo on the blood glucose and insulin response in healthy individuals following a starch challenge; and the effects of Reducose® versus placebo on the blood glucose and insulin response in healthy individuals following a sugar challenge. This study aims to evaluate the effects of three different doses of a dietary supplement (capsule) containing Reducose® on the blood glucose and insulin response of healthy volunteers after a complex meal. As proteins and fats are known to impact gastric (stomach) emptying and blood glucose response, a meal containing fats, proteins and carbohydrates will be used. Three dose levels are included to better understand the dose-response of Reducose®.

Who can participate?
Healthy volunteers aged 18-60 years with a body mass index (BMI) of 20 - 29.9 kg/m²

What does the study involve?
Participants will be recruited to attend four study visits, at least 48 hours apart, in order to test either three different doses of Reducose dietary supplement capsules or a matching placebo (dummy supplement). The test product or placebo will be taken before eating a meal that matches the composition of a typical Western diet. This process will be replicated in each of the four study visits. The test products are packaged in opaque capsules that have been matched for size, weight, and colour, and neither participants nor the study team will be aware of the order

that the test products are given until all of the tests have been completed. Blood will be drawn from finger pricks at regular intervals over 180 minutes. Changes in blood glucose and insulin levels will be measured in the blood samples.

What are the possible benefits and risks of participating?
Mulberry extract has an excellent safety profile and is widely consumed in Asia and is available as a dietary supplement around the world. Previous clinical trials have shown that Reducose does not have any reported adverse reactions. Participants will have multiple finger pricks to test for blood glucose and insulin levels, therefore there will be a risk of discomfort and bruising and a small risk of inflammation/infection at the site. Local infection control/procedures will be followed during each study visit.

Where is the study run from?
Oxford Brookes Centre for Nutrition and Health, Oxford Brookes University (UK)

When is the study starting and how long is it expected to run for?
August 2019 to May 2021

Who is funding the study?
Phynova Group Ltd (UK)

Who is the main contact?
Andrew Gallagher
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# Contact information

### Type(s)
Scientific

### Contact name
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# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
REDUCE 1.1

# Study information

### Scientific Title
A double-blind, placebo-controlled, four-arm, single-dose, cross over, dose-ranging trial to investigate the effects of Reducose mulberry leaf extract on postprandial glucose and insulin after consuming a complex meal

### Acronym
REDUCE

### Study objectives
The primary hypothesis is that a dietary supplement tablet containing mulberry leaf extract (Reducose®) when co-administered with mixed macronutrient meal will reduce the incremental area under the curve for plasma glucose concentration over 120 minutes in normoglycaemic adults when compared to co-administration with a placebo in a dose-dependent manner. The secondary hypothesis is that the dietary supplement when co-administered with a meal will not disproportionately increase the incremental area under the curve for plasma insulin concentration over 120 minutes in normoglycaemic adults compared to co-administration with placebo.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
1. Approved 07/03/2014, University Research Ethics Committee (UREC) at Oxford Brookes University (Research & Business Development Office, Directorate of Finance & Legal Services, Oxford Brookes University, Headington Campus, Gipsy Lane, Oxford, OX3 0BP, UK; +44 (0) 1865 48 4445; ethics@brookes.ac.uk), ref: 140806 (for glycaemic response),
2. Approved 24/01/2012, University Research Ethics Committee (UREC) at Oxford Brookes University (Research & Business Development Office, Directorate of Finance & Legal Services, Oxford Brookes University, Headington Campus, Gipsy Lane, Oxford, OX3 0BP, UK; +44 (0) 1865 48 4445; ethics@brookes.ac.uk), ref: 110594 (for insulinaemic response)

### Study design
Double-blind placebo-controlled randomized repeat measure cross over dose-ranging trial

### Primary study design
Interventional

### Secondary study design
Randomised cross over trial

## Study setting(s)
Other

## Study type(s)
Prevention

## Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

## Health condition(s) or problem(s) studied
Postprandial glycaemic control

## Interventions
The trial has a randomised cross over design and so each subject would act as their own control. Subjects are randomized to the trial using a 4x4 Latin Square block randomization, randomizing participants to one of three active doses or placebo in a block-wise manner. Researchers recruiting the participants are unaware of the allocation sequence (concealed allocation). Participants are assigned to a participant number according to their chronological order of enrolment in the study. The allocated participant number is used to identify the participants and their corresponding intervention sequence.

Participants are recruited to attend four study visits, with at least 48-hour washout period between visits. The study will evaluate three different doses of Reducose mulberry leaf extract (200 mg, 225 mg or 250 mg) against matched placebo. Reducose mulberry leaf extract is standardized to contain 5% 1-deoxynojorimycin (w/w). The test product is individually encapsulated in identical, opaque capsules (CapsuGel V-Caps Plus, Swedish Orange colour), and individually blistered and packed into cardboard boxes. The placebo contains microcrystalline cellulose and is matched for size, weight and colour.

At T -10 minutes subjects will take either the test product or placebo product with a little water.

At T=0 minutes subjects should consume the entire test meal within 10 minutes. The test meal consisted of 150 g Hovis White Bread Thick Slice and 50g Tesco Egg Mayo filler providing a macronutrient composition of 60.9% carbohydrate, 16.6% protein and 20.4% fat.

Blood samples are taken at -5 min, 0 min (baseline taken as mean of -5 min and 0 min), 15, 30, 45, 60, 90, 120, 150 and 180 min. Glycaemic response is measured using the method described by Brous et al. and carried out in accordance with ISO 26642 (2010). Blood drawn at the above time points is used to measure blood glucose and blood insulin. 300µL of capillary blood is required for insulin analysis. Sufficient blood should be drawn to enable two sets of analysis at every time point to reduce the likelihood of missing data.

## Intervention Type
Supplement

## Primary outcome measure
1. Blood glucose concentrations measured from capillary blood using HemoGue Glucose 201 DM analyser (units = mmol/L), measured at -5 min, 0 min, 15 min, 30 min, 45 min, 60 min, 90 min, 120 min, 150 min, 180 min
2. Blood glucose incremental area under curve (iAUC) calculated from blood glucose

concentrations using the trapezoid rule (units = mmol/L/min), measured at 60, 90, 120, 150 and 180 min
3. Peak blood glucose calculated from blood glucose curves (see above) (units = mmol/L)
4. Time of peak blood glucose calculated from blood glucose curves (see above) (units = minutes)

### Secondary outcome measures
1. Plasma insulin concentration measured from capillary blood using electrochemiluminescence immunoassay using automated analyzer (Cobas E411) (units = µU/mL) at -5 min, 0 min, 15 min, 30 min, 45 min, 60 min, 90 min, 120 min, 150 min, 180 min
2. Plasma insulin iAUC calculated from plasma insulin concentrations using the trapezoid rule (units = µU/mL/min), measured at 60, 90, 120, 150, and 180 min

### Overall study start date
02/08/2019

### Completion date
17/05/2021

## Eligibility

### Key inclusion criteria
1. Consent to study protocol
2. Aged 18-60 years
3. Body mass index (BMI) 20-29.9 kg/m²
4. Fasting blood glucose <6.1 mmol/l

### Participant type(s)
Healthy volunteer

### Age group
Adult

### Lower age limit
18 Years

### Upper age limit
60 Years

### Sex
Both

### Target number of participants
40

### Total final enrolment
43

### Key exclusion criteria
1. Aged< 18 or> 60 years
2. Pregnant or lactating

3. Body mass index (BMI) <18.5 or >30 kg/m²
4. Fasting blood glucose value >6.1 mmol/l
5. Any known food allergy or intolerance
6. Medical condition(s) or medication(s) known to affect glucose regulation or appetite and/or which influence digestion and absorption of nutrients (stable doses of oral contraceptives, acetylsalicylic acid, thyroxin, vitamins and mineral supplements or drugs to treat hypertension or osteoporosis are acceptable)
7. Known history of diabetes mellitus or the use of antihyperglycaemic drugs or insulin to treat diabetes and related conditions
8. Known IBS, severe liver, heart or kidney problems or blood clotting disorders
9. Major medical or surgical event requiring hospitalization within the preceding 3 months
10. Use of steroids, protease inhibitors or antipsychotics (all of which have major effects on glucose metabolism and body fat distribution)
11. High vulnerability level for COVID-19 (assessed using this tool - https://alama.org.uk/covid-19-medical-risk-assessment/)
12. Displayed any COVID-19 symptoms 14 days prior to any test session (high temperature, new continuous cough, loss or change to sense of smell or taste)

### Date of first enrolment
03/01/2020

### Date of final enrolment
07/05/2021

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
### Oxford Brookes Centre for Nutrition and Health
Oxford Brookes University
Headington Campus
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OX3 0BP

## Sponsor information

### Organisation
Phynova Group Ltd

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### Sponsor type
Industry

### Website
https://www.phynova.com

## Funder(s)

### Funder type
Industry

### Funder Name
Phynova Group Ltd

## Results and Publications

### Publication and dissemination plan
Planned publication of the trial results in a peer-reviewed academic journal. The study protocol has not been published but is adapted from the methods published in Brouns et al (Brouns F, Bjorck I, Frayn KN, Gibbs AL, Lang V, Slama G, Wolever TMS. Glycaemic index methodology. Nutr Res Rev 2005;18:145-171) and was conducted in accordance with ISO 26642:2010. The research protocol and statistical analysis plan will be available on request from info@phynova.com.

### Intention to publish date
01/12/2022

### Individual participant data (IPD) sharing plan
The datasets generated and analysed during the current study will be available to researchers upon request from Phynova Group Limited. Anonymised patient level data will be available for research purposes within six months of publishing the results of the primary endpoints, key secondary endpoints and safety data in a peer-reviewed journal. As participants only consented for their data to be used to investigate a particular health benefit of the test product, access to data will only be provided for researchers that are investigating the same or an equivalent product for the same health benefit. Data will be made available on request provided Phynova has the legal authority to provide the data; for example, if Phynova has out-licensed the data to another company then it would no longer have the legal authority to provide the data. Data will

only be made available if Phynova is able to anonymise the data without compromising the confidentiality and privacy of research participants. Data from clinical trials where the data labels and/or supporting documents are not in English will only be made available in their original format and no translations will be provided. The following information will be made available: raw dataset excluding any patient images, protocol with any amendments, analysis and reporting plan. Researchers requesting access to data should email their requests to info@phynova.com and should include a description of the intended research.

## IPD sharing plan summary

Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 29/05/2024 | 19/07/2024 | Yes | No |