Dose-response effect of an apple extract on postprandial glycaemia: a randomised controlled trial.

The Glu-Pomme Study NCT02940249

July 25, 2017

INFORMATION SHEET FOR PARTICIPANTS

BDM RESC Protocol Number **BDM/16/17-3782**

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Dose response effect of an apple extract on postprandial glycaemia: a randomised controlled trial. THE GLU-POMME STUDY.

We would like to invite you to participate in this original research project undertaken as part of a PhD programme. You should only participate if you want to; choosing not to take part will not disadvantage you in any way. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of this study?
This research project is a dietary intervention study to investigate effects of natural plants constituents found in high amounts in fruit, called polyphenols, on the rise in blood sugar (glucose) that occurs following a meal. The purpose of this study is to test whether different doses of an apple extract can reduce the levels of blood glucose during a 4-hour period after a carbohydrate-containing meal, and to test if the different apple extract doses improve the functioning of your blood vessels for up to 5 hours.

Why have I been chosen?
You have been contacted as you have expressed an interest in our research. In order to participate in this study you need to be able to say 'Yes' to the following:

- I am male and aged between 18 and 70 years old
  - **OR** I am female and aged between 18 and 70 years old, and I am not pregnant nor intending to become pregnant, nor breastfeeding
- I do not smoke and have not recently given up smoking (within the last 6 months)
- I have never had a heart attack, stroke, angina, thrombosis, liver or kidney diseases, diabetes, chronic gastrointestinal disorder or cancer
- I do not have phenylketonuria (PKU) - *this is a rare genetic metabolic disorder which prevents the breakdown of an amino acid, phenylalanine and is apparent from early infancy.*
- I do not take medication to lower blood fats (e.g. statins, fibrates) or to stabilise blood glucose (e.g. acarbose, metformin or sulfonylureas)
- I do not have a history of excess alcohol intake or substance abuse
- I do not have food or paracetamol intolerances, allergies or hypersensitivity
- I am not already participating in a clinical trial
- I am prepared to follow dietary instructions before and during the study
- I have not recently donated blood (within the last 3 months)
- I have not recently changed weight (lost or gained) by more than 3 kg/7 lb (in the last 2 months)

What will happen to me if I take part?
If you would like to participate you would first need to complete a screening questionnaire with us over the telephone, in person or via email (approx. 15 mins), after which potentially eligible volunteers will be invited to attend a clinic screening appointment (approx. 45 mins) in the Metabolic Research Unit on the 4th Floor, Corridor A, Franklin-Wilkins Building, 150 Stamford Street, SE1 9NH.

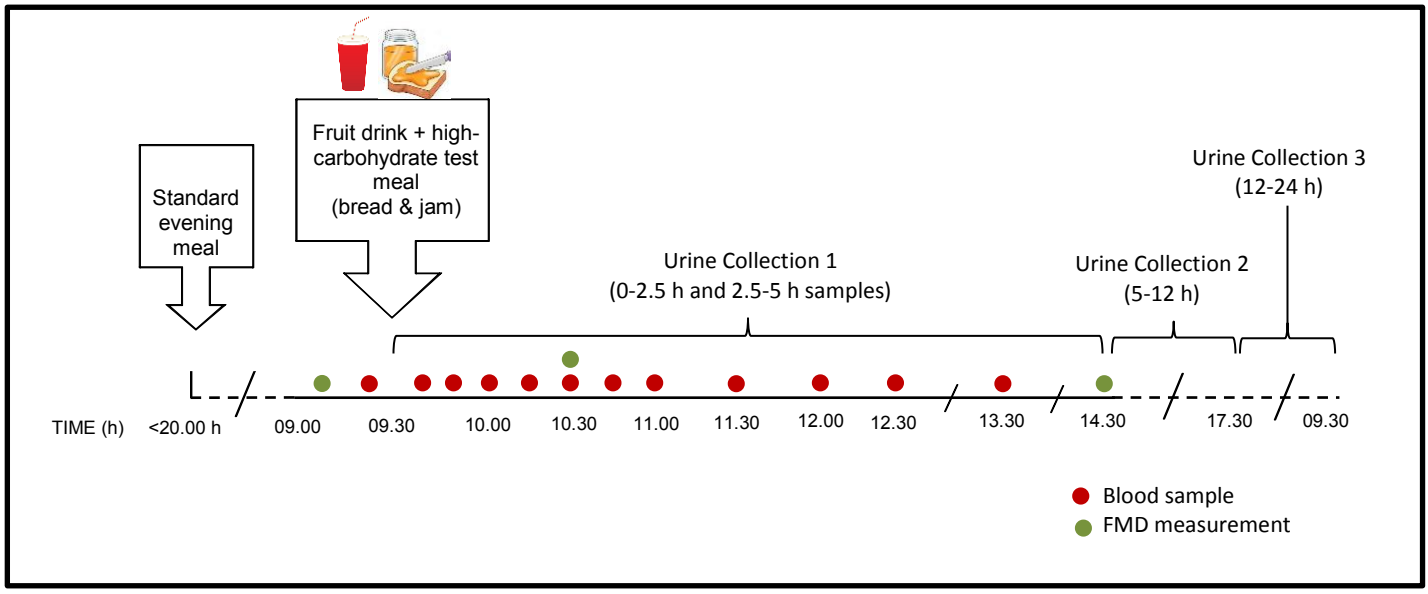
Summary of screening visit:

1) **You should avoid eating or drinking anything, except water, from after 20.00 h the previous night.**
2) **The visit will last approximately 45 min.**
3) **We will give you a copy of this information sheet, explain to you all the details of the study and answer any questions you have. If you are still happy to take part in the study, you will be asked to sign a consent form.**
4) **We shall ask you questions about your medical history, your food habits and measure your weight, height, % body fat, blood pressure and waist and hip circumference. Female participants will complete a women's health questionnaire.**
5) **We will need to take a small venous blood sample to extract capillary blood (16.5 ml, about 3¼ teaspoons) to check that your blood biochemistry is normal.**
6) **Then you will be provided with breakfast.**

The results of the screening blood test will be provided within 2 weeks. If any abnormal results are found we will offer to provide you with a letter for your GP. If, after screening, you are discovered to be unsuitable for the study your data will be destroyed.

If you are eligible for the study you will attend the Metabolic Research Unit at the Franklin-Wilkins Building for four study visits. Prior to the first visit you will be given a "Food and Drink Diary" in which we would like you to record everything that you eat and drink for 7 days. During each study day, frequent blood samples will be taken, in addition to flow-mediated dilation (FMD) measurements (i.e. functioning of the inner lining of your blood vessels). You will consume a fruit drink followed by a high carbohydrate meal (white bread with jam) after the first blood samples and FMD measurement have been taken. On each of these study visits the fruit drink will contain either a higher, medium or lower dose of apple extract or will be a placebo drink (containing no apple extract). On each study visit, you will be provided with a container to collect your urine throughout the visit (0-5 h). You will be provided with two containers to collect your urine throughout the rest of the day, between 5-12 h and 12-24 h; we kindly ask that these urine containers are returned to us once your 24 h collection period has ended. Each study visit takes approximately 5.5-6 h, including time to consume lunch afterwards. The total time you will be participating in this dietary intervention study will be at least 5 weeks, and a maximum of 11 weeks, depending on when the study visits are scheduled.

The overall study day visit is shown in a diagram below:



Summary of study day visit:

1) **Following screening, if your results comply with the study inclusion criteria you will be invited to attend the Metabolic Research Unit in the Franklin-Wilkins Building on 4 further occasions at least 7 days apart; each of these visits will take approximately 5.5-6 h each.**
2) **We will ask you to avoid high-polyphenol foods (list to be supplied) two days prior to each visit.**
3) **We will ask you to avoid fatty foods, oily fish, drinking alcohol, and any strenuous exercise the day prior to each visit.**
4) **We shall also ask you not to consume caffeine from midday the day before each visit and to avoid eating or drinking anything, except water, from after 20.00 h.**
5) **You will be asked to report to the Metabolic Research Unit in the Diabetes & Nutritional Sciences Division between 08:00 h and 10:00 h, in the fasted state (i.e. without having consumed breakfast and without having consumed any food or drink from after 20.00 h the previous night, apart from water). Make sure you drink some water on the morning of the study to avoid dehydration. Your weight and blood pressure will be taken upon arrival.**
6) **At each of the 4 visits, a small flexible tube called a cannula will be inserted in a vein in your arm and a sample of blood will be taken (at baseline 17 ml, or 3¼ tsp). Just before this, we will measure the function of your blood vessels by using a device called an ultrasound FMD assessment; 3 small electrodes will be placed on your upper front body and a cuff will be placed around your forearm (opposite side to cannula). The cuff is inflated for 5 min; this causes a tingling sensation in your arm, but does not cause pain. The entire FMD assessment takes approximately 20 min.**
7) **You will be given the test meal to consume within 7 min. The test meal on all study days will consist of a fruit drink, consumed immediately before a high carbohydrate meal (white bread with jam).**
8) **Following the test meal we would ask you to stay in the Metabolic Research Unit but you are free to work/read/use your laptop for the remainder of the study day in between measurements.**
9) **10 minutes following commencing eating the test meal you will have a second blood sample taken (11.5 ml/ 2¼ tsp) and further blood samples will be taken at 20 min, 30 min, 45 min, 1 h, 75 min, 90 min, and 2 h, 2.5 h, 3 h, 4 h after the meal. In total you will have 142 ml/ 29 tsp blood taken on each study day, and up to 584.5 ml/ 120 tsp blood taken over the course of the study, including the screening visit. The cannula will be removed after the final blood sample has been drawn and you wait for the last FMD measurement (taken at 5 h).**
10) **Throughout the study visit (0-5 hours) you will collect your urine into containers. You will be provided with two empty containers to continue to collect your urine for the remainder of the day (first container used between 5-12 hours and the second container to collect your urine between 12-24 hours). You will be provided with a cool bag to store these containers throughout the collection period. After the 24 h collection, you will need to return the containers to KCL (i.e. the day after your study visit). All travel expenses will be reimbursed.**

How will this benefit me?
You will have a free health check, including liver function tests, full blood count, blood lipid profile and glucose levels, blood pressure measurements and body composition measurements. Should you wish to find out the results of this study you are welcome to contact Dr Wendy Hall (details below) for a copy of the final report once the study is finished.

Will my participation be kept confidential?
Any information collected about you during this research will be kept strictly confidential. Your GP will not be told that you are taking part in the study, nor will they receive any results from the study, unless you instruct us to provide a letter for you to pass on to them. Subject confidentiality and anonymity will be observed throughout the study by use of subject codes in place of names, and the storage of subject details in a secure place. Only the investigators have access to this data.

What will happen to my study results?
Your anonymised data will be shared with other researchers. We hope to publish the results of the whole study in a scientific journal. You will not be identified in any publication. We will be happy to discuss the overall results with you when the study is completed, and will let you know how you can get a copy of the published results if you wish.

Who is organising and funding the study?
The study is organised by the Diabetes and Nutritional Sciences Division, Kings College London and is funded by DIANA Food Ltd., a global supplier of functional solutions (e.g. extracts and powders) from natural ingredients. In recognition of your time commitment, you will be paid an honorarium of £25 per study day to be paid at the end of the study. Any travel expenses will also be refunded for the screening and study visits.

Do I have to take part?
It is up to you to decide whether to take part or not. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You can withdraw from the study at any time by informing one of the researchers and you are not obliged to give a reason. You can also withdraw your data from the study if you wish at any time until the final report is submitted to the funders, which will be 1st January 2018. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

If you decide to take part, please let us know if you have been involved in any other study in the last year.

Thank you for your interest.

For further information, please contact: Emily Prpa at glu-pommestudy@kcl.ac.uk or by telephone:
020 7848 4162 | 07542 012677.

Diabetes and Nutritional Sciences Division, King's College London, Franklin Wilkins Building, 150 Stamford Street, London SE1 9NH

If this study has harmed you in any way you can contact King's College London using the details below for further advice and information:

Chief Investigator: Dr Wendy Hall (tel: 020 7848 4197, wendy.hall@kcl.ac.uk)

Diabetes and Nutritional Sciences Division, King's College London, Franklin Wilkins Building, 150 Stamford Street, London SE1 9NH.

CONSENT FORM FOR PARTICIPANTS IN A NUTRITIONAL STUDY

KING'S College LONDON

Please complete this form after you have read the Information Sheet and you are satisfied that the research has been fully explained.

Title of Study: Dose response effect of an apple extract on postprandial glycaemia: a randomised controlled trial. THE GLU-POMME STUDY.

The GLU-POMME Study
King's College Research Ethics Committee Ref: BDM/16/17-3782

Thank you for considering taking part in this research. The person organizing the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to participate. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking/initialling each box I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes mean that I DO NOT consent to that part of the study. I understand that by not giving consent for any one element I may be deemed ineligible for the study.

1) **I confirm that I fit into the following criteria:**

A. I am 70 years or younger and I do not smoke	☐
B. I do not have a history of heart disease, stroke, high blood pressure, diabetes, thrombosis, liver disease, chronic gastrointestinal disorders or a cancer diagnosis (except basal cell carcinoma)	☐
C. I do not have a history of excess alcohol intake or substance abuse	☐

2) **I confirm that I have read and understood the information sheet dated 25th July 2017 for the above study. I have had the opportunity to consider the information and asked questions that have been answered satisfactorily.** ☐

3) **I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason. Furthermore, I understand that I will be able to withdraw my data up to 01/01/2018.** ☐

4) **I consent to the processing of my personal information for the purposes explained to me. I understand that such information will be handled in accordance with the terms of the UK Data Protection Act 1998.** ☐

5) **I understand that my information may be subject to review by responsible individuals from the College for monitoring and audit purposes.** ☐

6) **I agree that the research team may use my data for future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. Please note that in such cases, as with this project, confidentiality and anonymity will be maintained and it will not be possible to identify you from any publication.** ☐

7) **I understand that confidentiality and anonymity will be maintained and it will not be possible to identify me in any publications.** ☐

8) **I have informed the researcher of any other research in which I am currently involved or have been involved in during the past 12 months.** ☐

P.T.O

9) **I consent to being randomly assigned to a sub-group which involves the addition of paracetamol into my test drink at each study visit.** ☐

Participant's Statement:

I _____

agree that the research project named above has been explained to me to my satisfaction and I agree to take part in the study. I have read both the notes written above and the Information Sheet about the project, and understand what the research study involves.

Signed _____ Date _____

Investigator's Statement:

I _____

confirm that I have carefully explained the nature, demands and any foreseeable risks (where applicable) of the proposed research to the volunteer.

Signed _____ Date _____