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Study of Oral Anthocyanins on Insulin Resistance

Research Protocol
11/NS/0024

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The aim of this study is to determine the effects of anthocyanin supplementation on insulin resistance and inflammation following a three week supplementation period.

Volunteers: Male or postmenopausal female subjects who are overweight, obese or type 2 diabetic controlling their diabetes by diet alone (n=28). Volunteers will be given either a total daily dose of 1.4 grams of mirtocyan a day in capsules (0.47 gram per capsule) or control capsules administered thrice a day for 21 days provided by Indena S.p.A. (http://www.mirtoselect.info/) followed by a three week wash out period. Following the wash out period volunteers will be given the opposite capsule to which they took the first time either a total daily dose of 1.4 grams of mirtocyan or control capsules thrice a day for 21 days in a blinded randomised cross over study. This will involve a total of five visits to the Human Nutrition Unit.

Volunteers will be recruited through adverts, posters, University plasma screens and staff email lists.
Information will be sent to the volunteer who will respond if they want to continue further.

Suitable volunteers will be asked to come into the Human Nutrition Unit for their first of five visits. This protocol is summarised in the enclosed summary protocol.

Visit 1
The volunteer will meet the research team and discuss with them any issues or concerns they may have about the study after reading the volunteer information sheet. They will then be asked to sign a consent form if they wish to take part in the study by the Principle Investigator (P.I.) Nigel Hoggard or one of the study team Morven Cruickshank or Kim Moar. We will then obtain the volunteers consent to inform their GP of their participation in the study and to confirm their recent medical and medication status. All volunteers will have the opportunity to discuss the study with the P.I.

• Medical: Weight, age, etc (medical pack)

Visit 2 (After we receive the GP consent form from the GP):
• Volunteer will be asked to fast overnight from 11.00 pm.
• Collect faecal and urine sample – We will ask volunteers to provide a faecal and urine sample at home the day in a suitable container provided by the study team and to bring it into the Rowett.

• Oral Glucose Tolerance Test: This will involve taking small blood samples at -15,-10, -5 minutes (8ml) and then drinking a sugary drink (lucozade or equivalent) and then collecting small amounts of blood (5mls) at 15, 30, 45, 60, 90, 120, 150, 180 and 240 minutes.
• The volunteer will be given either Blaeberry concentrated extract in capsules or control capsules enough for 3 weeks and asked to take these capsules 3 x a day once when they wake up, just prior to lunch and finally just before going to sleep. One capsule at each time point. They will be asked to take a note of the time the capsule was taken in the sheet provided.
• Measure the volunteers weight/body fat using bioelectrical impedance scales
• A contact telephone number will be provided in case of any problems arising during the next three weeks.

In addition female volunteers as a precautionary measure will be asked to take a simple urine pregnancy test to rule out pregnancy if the HNU GP determines at the medical that there is any possibility of the volunteer getting pregnant.
• Breakfast provided.

Volunteers will be contact either by phone or email each week to ensure that they have not had any problems with capsules.

Visit 3 (Three weeks later):
• Volunteer will be asked to fast overnight from 11.00 pm.
• Collect faecal and urine sample – We will ask volunteers to provide a faecal and urine sample at home in a suitable container provided by the study team and to bring it into the Rowett.
• Oral Glucose Tolerance Test: This will involve taking small blood samples at -15,-10, -5 minutes (8ml) and then drinking a sugary drink (lucozade or equivalent) and then collecting small amounts of blood (5mls) at 15, 30, 45, 60, 90, 120, 150, 180 and 240 minutes.
• Breakfast provided.

There will then be a three week break from the study where nothing is asked from the volunteer (washout period in the study) before the volunteers is asked to return and repeat visits 2 and 3 taking the opposite capsule.

The volunteer will be asked to fill in a questionnaire at home on four separate occasions just before and just after taking the both the blaeberry and the control capsules about what they ate over a four day period.

Once all the measurements are complete, we will send the volunteer a booklet of their body composition measures containing details of the measurement results taken during the study. In addition relevant information will also be sent to the volunteers GP.

Adverse events

We do not anticipate any but any adverse events but any incident will be treated seriously and followed through as described below.
In the event of any adverse effects the volunteers GP will be advised and they will be withdrawn from the study. The incident will be recorded and discussed with the Rowett medic. If appropriate the study will be reviewed by the Rowett Human Studies Management Committee and the study terminated.

There have been no reported adverse effects of the mirtocyan, a standardized extracted from bilberries, which is widely marketed as a nutraceutical in health shops and is known to be tolerated well. In addition no adverse effects, due to the mirtocyan, were reported for the pilot study where eleven volunteers took the same dose for the same period as intended for this study. However this will be monitored with weekly contact with the volunteers and the availability of a 24hr contact number should problems arise.
The clinical and non clinical interventions in this study are regularly performed in the Rowett Human Nutrition unit under strict Standard operating procedures with appropriate medical supervision.

Statistical analysis

The area under the curve (AUC) was calculated using the trapezoid approximation. For the incremental version (AUCi), only the extent of interpolated values above baseline contributed.

Treatment effects were assessed by Analyses of variance of the endpoint of each intervention period, with terms for volunteer (random effect), period (1st or 2nd) and treatment (placebo or extract) and baseline values as a covariate.