PARTICIPANT INFORMATION SHEET

Study title: A double blinded, randomised controlled trial to determine the efficacy of FBCx (a formula based on α-cyclodextrin) on cholesterol, and the efficacy of Ginst15 (a ginseng extract formula based on Compound K) on glycaemic control

Investigators: Associate Professor Emily Hibbert & Dr Kathryn Williams
Department of Academic Medicine, Sydney Medical School Nepean

Introduction

You are invited to take part in a research study looking at the effectiveness of a fibre supplement called FBCx (a formula based on α-cyclodextrin) on cholesterol control and Ginst15 (a ginseng extract formula based on Compound K) on blood glucose control. The objective is to investigate whether these investigational products have potential use in the prevention of Type 2 Diabetes.

α-cyclodextrin, marketed under the trade name FBCx, is a polysaccharide (a complex sugar) derived from corn. It has been demonstrated to prevent the absorption of 9 times its own weight in dietary fat in an animal study. Previous research has shown that FBCx is effective in reducing and/or maintaining body weight in obese patients with type 2 diabetes. Studies also suggest that FBCx may increase insulin sensitivity and improve cholesterol and triglyceride levels in people with high levels of triglycerides.

The root of ginseng has long been used in traditional Chinese medicine, most recently for improving glycaemic control. Compound K (CK), marketed under the trade name Ginst15, has been shown to be the active ingredient in ginseng for this anti-diabetic action. Significant improvements have been shown in both plasma glucose and insulin levels in diabetic mice when they are given combination therapy with CK and metformin compared with therapy with metformin alone.

It is proposed that these products may over-lap in their function and therefore are being compared in the same study in the prevention of type 2 diabetes.
At six months (visit 8) three behavioural approaches to maintaining weight loss are being investigated. There are many studies that help people to lose weight, however we need to identify behavioural strategies to keep the weight off. Currently we don't know what the most effective methods are, and therefore examining what helps is important.

The study is being conducted within this institution by:

- Dr Kathryn Williams (Endocrinologist), University os Sydney, Nepean Hospital
- Associate Professor Emily Hibbert (Endocrinologist), University of Sydney, Nepean Hospital

The study is being sponsored by The University of Sydney with funding and investigational products being provided by SOHO Flordis International, an international provider of clinically proven natural medicines.

Study Procedures

If you agree to participate in this study, you will be asked to sign the Participant Consent Form at a "screening" visit. You will then be asked to undergo the following procedures:

- Measurement of height, body weight, and waist circumference;
- Recording of your medical history (including any forthcoming procedures);
- Recording of any medications you are currently taking;
- Measurement of blood pressure and heart rate;
- Electrocardiogram (ECG);
- Collection of a 50 mL blood sample;
- Handgrip strength test;
- DXA scan;
- Urine collection (for women of child bearing potential only);
- Completion of questionnaires. These will seek information on quality of life, perception of pain, and the extent to which you can control events affecting you in relation to weight loss. They will also collect information on your personality, the personality of others, and your attitudes about risk and the future. You have the chance to win up to $70 in these questionnaires. To make the payments to you we will ask you for your bank account details (Name, BSB, and account number). They will take in total 75 minutes to complete.

If the results of the above procedures show that the study is suitable for you, you will be asked to come in for at least 9 clinic visits over the next 12 months. The first visit will occur approximately one week after the "screening", and will be referred to as the "baseline" visit. The study will last 12 months. There will be 6 months of active treatment during that period.

You will be "randomised" to one of four treatment groups. "Randomised" means that, if you decide to participate, your treatment will be assigned to you by chance (like throwing a dice). You will not be able to choose which treatment you receive. We will not be able to choose or change the treatment group to which you are allocated. You will be asked to take two tablets before each meal and two tablets after each meal per day for six months.

The four treatment groups are:

- FBCx;
- Ginst15;
- combined FBCx and Ginst15; and
- placebo (ie tablet and capsule that looks like the study drugs but contains no active ingredients).

You will be asked to meet with the study dietitian at each visit. Advice will also be given on other aspects of a healthy lifestyle, including the moderation of your alcohol intake. If you are a current smoker, you will be given advice about a "Quit" smoking program before the commencement of the study treatment.

You will be asked to undergo the following procedures at each visit during the 12 months of the study (see Table 1 at the end of this document for a summary of which procedures will be done at each visit):

- Measurement of body weight and waist circumference;

- Measurement of body fat and muscle mass by Dual-energy X-ray absorptiometry (DXA) scan. This involves laying still on an examination table for approximately 10 minutes whilst an X-ray is taken;

- Measurement of blood pressure and heart rate;

- Handgrip strength test to monitor muscle strength changes throughout the study;

- Completion of a food and activity diary before each visit. You will be asked to record the food you eat for three days (including one weekend day) and your activity for five days. The diary will be provided to you at the proceeding visit.

- Collection of blood samples (approximately 50 mL). Samples will be stored at minus 80 degrees Celsius and, pending the receipt of funding, will be used to measure lipids, glucose, inflammatory markers, adipokines and gut hormones at a later stage.

- Return stool samples that have been collected at home. Stool collection materials will be provided along with detailed instructions. A small group of participants will be invited to return additional stool samples. If you are interested in this additional aspect of the study, please inform your research investigator. You will be given a separate information sheet and consent form about it.

- Dispensing of study drug. You will be asked return any unused drug to the site so that the study team can check that you have been taking the study drug correctly.

- Completion of questionnaires. These will seek information about your quality of life, pain, weight control, your perception of the treatment's effectiveness, your goal weight, expected weight loss, your commitment, your perception of your effort in weight loss, your belief in your own capacity to achieve a goal,

personality assessment, your risk and time preferences, your estimate that a certain behaviour will produce a resulting outcome, dissatisfaction, and improvements in employment and wages/salary following weight loss. They will take about 60 minutes to complete.

- Randomisation to one of three behavioural programmes. One group will be given standard care, the second group will be asked to self-monitor themselves and the third group will be asked to self-monitor themselves and be provided with feedback. The self-monitoring groups will be asked to make a record in diaries provided.
- We would also like to ask at least ten people in the third group to verbally record what they do on a smart phone application. Not everyone will be asked to do this.

In addition, we will review current and new medications and any changes in your health at each visit and we would like to have access to your medical records to obtain information relevant to this study.

Risks

All medical procedures, whether for diagnosis or treatment, routine or experimental, involve some risk of injury. In addition, there may be risks associated with this study that are presently unknown and unforeseeable. In spite of all precautions, you might develop medical complications from participating in this study.

The risks of participating in this study are:

Study drugs

Some of the supplements may cause you some constipation, bloating, flatulence or interact with blood clotting at times. It is possible that unknown or other side effects may occur. Please let the study staff know about any symptoms or illnesses you experience during the study.

It is important that women participating in this study are not pregnant and do not become pregnant during the course of the study. If you are a woman of child-bearing potential and there is any possibility that you are pregnant, the researchers will perform a pregnancy (urine) test before you start in the study. If necessary, you should use reliable contraception (such as oral or implanted contraception, an IUD or have had a tubal ligation prior to enrolling in the study) during the course of the study. If at any time you think you may have become pregnant, it is important to let the researchers know immediately.

Exposure to radiation

This research study involves exposure to a very small amount of radiation during the DXA scan. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 to 3 millisieverts (mSv) each year. Therefore if you have recently undergone radiological examinations, it is important that you inform your study doctor so that they can evaluate the corresponding impact. The effective dose from most machines is of the order of 1 microsievert (1uSv), which is less than everyone receives from natural ‘background’ radiation each day. At this dose level, no harmful effects of radiation have been demonstrated and the risk is very low.

Please inform us if you have participated in any other research studies using

radiation in the last five years. Please keep this participant information statement in a safe place for the next five years in case you volunteer for any more studies using radiation, you should show it to the Investigator.

Blood collection

Blood collection involves some discomfort at the site from which the blood is taken. There is also a risk of some minor bruising at the site, which may last one to two days. Fainting and local infection can also occur when blood is taken, although these are rare.

Physical activity

You may be encouraged to engage in regular physical activity. You may experience mild physical discomfort associated with the commencement of an exercise program.

Inconvenience

You will be required to store your stool samples for a short time in your home freezer. You will be supplied with all the appropriate double sealed containers to do this. There is no risk storing stool samples in your home freezer although you may feel a little hesitant at first.

You may find being in the study a little inconvenient, e.g. giving up time to participate in study visits and activities.

Benefits

While we intend that this research study furthers medical knowledge and may improve the treatment of overweight and obesity and the prevention of type 2 diabetes, it may not be of direct benefit to you. However, by taking part in this study you will receive diet and lifestyle advice for weight loss and management of your pre-type 2 diabetes at no cost to you. You will also have regular blood tests and provide stool samples for laboratory analysis.

Compensation for injuries or complications

In the event of loss or injury, the parties involved in this study agree to be bound by the Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in an Industry-Sponsored Clinical Trial. A copy of these guidelines is available from the Executive Officer of the Ethics Review Committee.

Costs

You will not be paid for taking part in this study; however you will receive a grocery voucher of $20 for each visit to help with dietary compliance. The study drug will be provided to you at no cost, but there is no provision to supply it to you after the end of the study. In addition, you have the chance to win up to $70 when completing the questionnaires at baseline, month 6, and month 12 follow up.

Voluntary Participation

Participation in this study is entirely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason.

Whatever your decision, please be assured that it will not affect your medical treatment or your relationship with the staff who are caring for you.

If you wish to withdraw, we ask you to contact one of the study team to arrange a final appointment and, if possible, to consider attending the visits scheduled for Month 6 and Month 12 of the study. This would significantly help us with our data collection.

Sometimes during the course of a study, new information becomes available about the treatment that is being studied. While you are participating in this study, you will be kept informed of any significant new findings which may affect your willingness to continue in the study.

Confidentiality

All the information collected from you for the study will be treated confidentially, and only the researchers named above will have access to it. The study results may be presented at a conference or in a scientific publication, but individual participants will not be identifiable in such a presentation.

Further Information

If you would like to know more at any stage, please feel free to contact the Nepean study team by Email: clinicaltrials.boden@sydney.edu.au

This information sheet is for you to keep.

Ethics Approval and Complaints

This study has been approved by the Human Research Ethics Committee of the University of Sydney. Any person with concerns or complaints about the conduct of this study should contact the Manager of Ethics Administration on 02 8627 8176 or human.ethics@sydney.edu.au and quote protocol number X14-0328 Study FBCx and Ginst 15 (SFI 121). The identification of potential participants has been approved by Nepean Blue Mountains Local Health District (NBMLHD), although NBMLHD is not conducting this study.

Table 1. Schedule of procedures for all treatment arms

Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Month	-1 wk	Day 0	1	2	3	4	5	6	7	8	9	12
Days	Screen	Baseline	28 +/-7	56 +/-7	84 +/-7	112 +/-7	140 +/-7	168 +/-7	196 +/-7	224 +/-7	273 +/-7	357 +/-7
Consent, Height, Medical History	✓											
Urine collection*	✓				✓			✓				✓
Body Weight	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓
Waist Circumference	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓
Electrocardiogram	✓											
Blood Pressure and Heart Rate	✓				✓			✓			✓	✓
Blood collection	✓				✓			✓				✓
Handgrip strength test	✓				✓			✓				✓
Dispense stool collection kit (main study)	✓						✓				✓	
Stool collection (Main Study)		✓						✓				✓
Dispense stool collection kit (Microbiota Dynamics Cohort)		✓	✓					✓	✓			
Weekly stool collection (Microbiota Dynamics Cohort)			✓	✓					✓	✓		
DXA Scan		✓						✓				✓
Dispense study compound		✓	✓	✓	✓	✓	✓					
Reconcile study compound			✓	✓	✓	✓	✓	✓				
Dietician review		✓	✓	✓	✓	✓	✓	✓			✓	✓
Completion of questionnaires		✓						✓				✓
Record current/new medications	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓
Adverse event monitoring		✓	✓	✓	✓	✓	✓	✓			✓	✓
Randomisation to the weight maintenance intervention								✓				
ESTIMATED TIME (minutes)	60	165	40	40	120	40	40	165	5	5	30	165