THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

EVIDENCE OF PEER REVIEW
HEALTH & DISABILITY ETHICS COMMITTEES (HDEC)

Applicant	Prof Sally D Poppitt	**Department**	Human Nutrition Unit, School of Biological Science
Co-applicants	Dr. John Ingram Hyun Sang Shin (PhD student)	**Department(s)**	
Title of Research	Activation of the ileal brake by carbohydrates and plant extracts – A pilot study in ileostomy patients to develop sample collection and analytical methods		

Brief **abstract** of research: describe the purpose, population, intervention, outcomes to be analysed and any unusual features (eg. detail any novel therapeutic procedure or agent).

Background: There is a rapidly growing epidemic of weight gain and obesity worldwide, as well as nationally within New Zealand. The gastrointestinal (GI) tract and specifically the most distal part of the small intestine, the ileum, has become a renewed focus of interest for mechanisms targeting appetite suppression. The 'ileal brake' is stimulated when energy-containing nutrients are delivered beyond the duodenum and jejunum and into the ileum, and is named for the feedback loop which slows or 'brakes' gastric emptying and duodenojejunal motility. More recently it has been hypothesised that the ileal brake also promotes secretion of satiety-enhancing GI peptides and suppresses hunger, and hence in turn places a 'brake' on food intake. Human trials have shown that the direct delivery of nutrients into the ileum via a tube may enhance satiety and reduce food intake. Our research group has recently shown that satiety and food intake can be altered acutely by NI infusion of glucose (NTY/11/03/034), demonstrating that the area with the greatest satiety effect is the ileum. There are no studies to date that have demonstrated suppression of food intake following oral delivery of available, mono /disaccharide carbohydrate (CHO) to the ileum. In order to ensure arrival of CHOs into the ileum it is necessary to block uptake from the proximal small intestine (duodenum and jejunum). In vitro tests by our research team have identified a number of plant source candidates that can both prevent polysaccharide starch breakdown and uptake of monosaccharide glucose. Efficacy of these blockers has not yet been assessed in a human study population.

Objective: This is a nutritional intervention study aimed to prevent obesity and designed to assess the efficacy of a starch breakdown inhibitor and a glucose uptake inhibitor present in the plant extracts, on the oral delivery of CHOs to the ileum, in a group of ileostomy patients in whom it is possible to sample the contents of the ileum directly.

Design: This is a pilot study in five ileostomy patients, aged 20-65 years with a wide range of BMI 18-40kg/m2 who have undergone prior large bowel resection but are otherwise healthy. A high starch breakfast will be given with a capsule containing either quercetin at a low dose (500 mg) and a high dose (2000 mg), grape seed extract at a low dose (500 mg) and a high dose (2000 mg), quercetin + grape seed extract combined (2000 mg each), a positive control containing acarbose (50 mg) or negative control, which is just a breakfast with no capsule. This design allows us to assess the dose-response relationship of the plant extracts on the appearance of glucose in the ileostomy pouch and plasma.

The study requires up to seven visits. Participants will arrive at the Human Nutrition Unit in the fasted state at 08.30am for each visit. A 2MJ high starch breakfast (185 g of white bread) will be consumed at 9am, immediately followed by one of the five different treatment capsules or either positive or negative control. Ileostomy bag contents and plasma will be collected at 0, 15, 30, 45, and 60 minutes and then at 5 minute intervals for the following 2 hours to sample appearance of glucose in the ileum or plasma.

Methods: Subjects are screened for eligibility on the screening day. The participant information sheet (PIS) will be provided, the study explanation will be given and written consent will be obtained. Then, demographics (age, ethnicity) and anthropometry (height, body weight, BMI) will be obtained and the participant completes medical history questionnaire on the screening day. For each study visit, participants will arrive at the Human Nutrition Unit in the fasted state at 08.30am. A 2MJ high starch breakfast (185 g of white bread) will be consumed at 9am immediately followed by one the five treatments or positive control or no treatment. Participants will be allowed 15 minutes to consume the breakfast, and all components of the meal must be consumed. Ileostomy bag contents, to sample the nutrients that are delivered into the ileum, will be collected at 0, 15, 30, 45, and 60 minutes, and then at 5 minute intervals for the following 2 hours. At the bottom of pouch, there is an opening and contents from the pouch are drained through this opening. Contents will be emptied into a container and collected using a 50 mL syringe. If gut contents arrive at the ileum prior to 60 minutes then the 5 minute sampling regime will be brought forwards. Changes in glucose level will be monitored using a finger prick glucometer at 0, 15, 30, 45, and 60 minutes, and then at 5 minute intervals for the following 2 hours.

This is a pilot study with no statistical analysis.The different treatment interventions tested are solely to assess the effect of plant extracts on gluco se appearance in plasma and the ileum.

Findings:

The results of the study may help to raise awareness that the plant extracts that our research team identified can both prevent polysaccharide starch breakdown and uptake of monosaccharide glucose in humans.This study will help provide the basis of a larger study testing plant extracts for the activation of the ileal brake to prevent obesity.

SOURCE OF FUNDING

- Has this protocol been peer reviewed? yes/no
- If so, by whom? ...Dr. Russell Wamlseley, consultant gastroenterologist at Waitemata District Health Board (WDHB), North Shore and Waitakere Hospitals
- Has this protocol been reviewed by SCOTT yes/no/irrelevant
- If yes, has it been approved yes/no
- Is this a phase 1 or phase 2 trial yes/no
- Has this protocol been referred to GTAC yes/no/irrelevant
- If so, has it been approved yes/no

Signature APPLICANT: ..... **Date:** .....

Name:.....

I approve of this research being conducted from my Department/School:

Signature of HOD: ..... **Date:** 24/10/13

Name: Gillian Lewis
Head, School of Biological Sciences

Locality Assessment by Locality Organisation

Refer to pages 13–15 of Guidelines for Completion of the National Application Form for Ethical Approval of a Research Project (NAFG-2009-v1).

Locality organisation sign off

Ethics committees review whether investigators have ensured their studies would meet established ethical standards if conducted at appropriate localities. Each locality organisation is asked to use the locality assessment form to check that the investigator has also made the appropriate local study arrangements.

Ethics approval for study conduct at each site is conditional on favourable locality assessment at that locality.

Please note that the locality organisation may have additional requirements to be met before a study may commence at that locality.

Part One: General

To be completed by the principal investigator for this locality.

Full project title:	Activation of the ileal brake by carbohydrates and plant extracts – A pilot study in ileostomy patients to develop sample collection and analytical methods
Short project title:	Ileal brake activation – a pilot study in ileostomy patients
Locality to be assessed:	Human Nutrition Unit, University of Auckland 18 Carrick Place, Mount Eden. Auckland 1024.

Brief outline of study:

Background: There is a rapidly growing epidemic of weight gain and obesity worldwide, as well as nationally within New Zealand. The gastrointestinal (GI) tract and specifically the most distal part of the small intestine, the ileum, has become a renewed focus of interest for mechanisms targeting appetite suppression. The 'ileal brake' is stimulated when energy-containing nutrients are delivered beyond the duodenum and jejunum and into the ileum, and is named for the feedback loop which slows or 'brakes' gastric emptying and duodenojejunal motility. More recently it has been hypothesised that the ileal brake also promotes secretion of satiety-enhancing GI peptides and suppresses hunger, and hence in turn places a 'brake' on food intake.
Human trials have shown that the direct delivery of nutrients into the ileum via a tube may enhance satiety and reduce food intake. Our research group has recently shown that satiety and food intake can be altered acutely by NI infusion of glucose (NTY/11/03/034), demonstrating that the area with the greatest satiety effect is the ileum. There are no studies to date that have demonstrated suppression of food intake following oral delivery of available, mono /disaccharide carbohydrate (CHO) to the ileum. In order to ensure arrival of CHOs into the ileum it is necessary to block uptake from the proximal small intestine (duodenum and jejunum). In vitro tests by our research team have identified a number of plant source candidates that can both prevent polysaccharide starch breakdown and uptake of monosaccharide glucose. Efficacy of these blockers has not yet been assessed in a human study population.
Objective: This is a nutritional intervention study aimed to prevent obesity and designed to assess the efficacy of a starch breakdown inhibitor and a glucose uptake inhibitor present in the plant extracts, on the oral delivery of CHOs to the ileum, in a group of ileostomy patients in whom it is possible to sample the contents of the ileum directly.
Design: This is a pilot study in five ileostomy patients, aged 20-65 years with a wide range of BMI 18-40kg/m2 who have undergone prior large bowel resection but are otherwise healthy. A high starch breakfast will be given with a capsule containing either quercetin at a low dose (500 mg) and a high dose (2000 mg), grape seed extract at a low dose (500 mg) and a high dose (2000 mg), quercetin + grape seed extract combined (2000 mg each), a positive control containing acarbose (50 mg) or negative control, which is just a breakfast with no capsule. This design allows us to assess the dose-response relationship of the plant extracts on the appearance of glucose in the ileostomy pouch and plasma.
The study requires up to seven visits. Participants will arrive at the Human Nutrition Unit in the fasted state at 08.30am for each visit. A 2MJ high starch breakfast (185 g of white bread) will be consumed at 9am, immediately followed by one of the five different treatment capsules or either positive or negative control. Ileostomy bag contents and plasma will be collected at 0, 15, 30, 45, and 60 minutes and then at 5 minute intervals for the following 2 hours to sample appearance of glucose in the ileum or plasma.
Methods: Subjects are screened for eligibility on the screening day. The participant information sheet (PIS) will be provided, the study explanation will be given and written consent will be obtained. Then, demographics (age, ethnicity) and anthropometry (height, body weight, BMI) will be obtained and the participant completes medical history questionnaire on the screening day. For each study visit, participants will arrive at the Human Nutrition Unit in the fasted state at 08.30am. A 2MJ high starch breakfast (185 g of white bread) will be consumed at 9am immediately followed by one the five treatments or positive control or no treatment. Participants will be allowed 15 minutes to consume the breakfast, and all components of the meal must be consumed. Ileostomy bag contents, to sample the nutrients that are delivered into the ileum, will be collected at 0, 15, 30, 45, and 60 minutes, and then at 5 minute intervals for the following 2 hours. At the bottom of pouch, there is an opening and contents from the pouch are drained through this opening. Contents will be emptied into a container and collected using a 50 mL syringe. If gut contents arrive at the ileum prior to 60 minutes then the 5 minute sampling regime will be brought forwards. Changes in glucose level will be monitored using a finger prick glucometer at 0, 15, 30, 45, and 60 minutes, and then at 5 minute intervals for the following 2 hours. This is a pilot study with no statistical analysis. The different treatment interventions tested are solely to assess the effect of plant extracts on glucose appearance in plasma and the ileum.
Findings: The results of the study may help to raise awareness that the plant extract that our research team identified can both prevent polysaccharide starch breakdown and uptake of monosaccharide glucose in humans. This study will help provide the basis of a larger study testing plant extracts for the activation of the ileal brake to prevent obesity.

Principal investigator (for this locality):

Prof Sally Poppitt, Director of Human Nutrition Unit, School of Biological Sciences and University of Auckland

Contact details:

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Fax: (09) 630 5764
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Other local investigators (list all at this site):

Hyun Sang Shin, PhD student, Human Nutrition Unit, School of Biological Sciences at University of Auckland

Contact details:	1. Work phone no. (09) 630 1162 Fax: (09) 630 5764 Email: h.shin@auckland.ac.nz

Part Two: Locality Issues

To be completed by the principal investigator for this locality and signed by the authorised locality representative. (See the Guidelines (NAFG-2009-v1) (pages 13–15) for more information and examples.) Identify any local issues and specify how these issues will be addressed.

1. **Suitability of local researcher**

   For example, are all roles for the investigator(s) at the local site appropriate (for example, has any conflict the investigator might have between her or his local roles in research and in patient care been adequately resolved)?

   [√] Yes [ ] No

2. **Suitability of the local research environment**

   a) Are all the resources (other than funding that is conditional on ethical approval) and/or facilities that the study requires appropriate and available (for example, is staffing adequate? Is this site accessible for mobility-impaired people where necessary)?

   [√] Yes [ ] No

   b) Have all potentially affected managers of resources such as patient records or laboratory managers been notified?

   [n/a] Yes [n/a] No

3. **Have issues such as cultural issues specific to this locality or to people being recruited at this locality been addressed?**

   [√] Yes [ ] No

4. **Have the local investigator contact details and other important contact details been provided to the locality organisation for checking?**

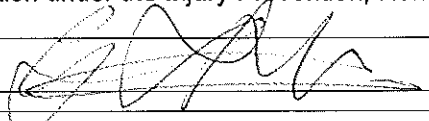
   [√] Yes [ ] No

Part Three: Declaration by locality organisation

I am authorised to complete locality approval on behalf of this locality organisation. I understand that I may withdraw locality approval if any significant local concerns arise. I agree to advise the principal investigator and then the relevant ethics committee should this occur.

(Questions 1–4 at Part Two above must be completed prior to signing.)

I confirm the organisation has sufficient indemnity insurance to compensate participants for harm that does not qualify for compensation under the Injury Prevention, Rehabilitation and Compensation Act 2001.

Signature:		Date:	24/10/13
Name:	Prof Gillian Lewis	Position:	Head of School (Biological Sciences)
Contact details:	THOMAS BUILDING, University of Auckland, 3A Symonds St, Auckland 1010, New Zealand Ph. (09)9237396. Email: g.lewis@auckland.ac.nz		