

# Modified citrus pectin as therapy in heart failure

<b>Submission date</b> 28/05/2012	<b>Recruitment status</b> Stopped	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 09/07/2012	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 18/04/2019	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Chronic heart failure (HF) is a leading cause of death and disability, despite great advances in medical, interventional and device therapies. Patients suffering from heart failure often have raised levels of a substance in their blood known as Galectin-3. Studies have shown that Galectin-3 controls the production of a protein in the body called collagen. Collagen is known to accumulate within tissues, causing cirrhosis and fibrosis (the collection of fibrous deposits), which if severe enough can cause scarring and damage to some of the bodys organs, including the heart. This damage could, if severe enough, lead to the heart not functioning properly. Reducing the levels of Galectin-3 in the body could therefore have an important role in improving the health of patients suffering from heart failure. The harmful effects of Galectin-3 can be blocked by Modified Citrus Pectin (MCP). MCP is available to buy from a variety of retailers (health shops and supermarkets) and is made from the peel and pulp of citrus fruits, such as oranges. The aim of our study is to test if MCP could be helpful as an additional treatment for patients with chronic HF. In order to prove this we need to carry out a study to compare MCP with a placebo (dummy) tablet.

### Who can participate?

You should be at least 18 years old, have a clinical diagnosis of heart failure, be attending the Hull and East Yorkshire Hospitals NHS Trusts heart failure service, and have high levels of galectin-3 in your blood (we will do a blood test to find this out).

### What does the study involve?

If you are suitable to enter the study following a screening visit, you will be given a prescription to take either MCP or a matched placebo for 18 weeks. Which capsule you take will be decided randomly like tossing a coin. After that period you will take the other capsule for another 18 weeks. It means you will take both the active and placebo in turn during your time in the study. This way, we directly compare the effect of the active capsule and the placebo on your health. During the study, we will use echocardiography to take ultrasound pictures of your heart to look for any physical changes such as structural changes and how efficiently the heart pumps. We will also take some blood samples to look at certain biomarkers (natural substances in your blood associated with the severity of heart failure) and to see if Galectin-3 levels are reduced by the capsules. Some of the blood samples will be analysed by our research partners in Scotland. These samples will be coded so that they cannot be traced to you. We will give you some dietary sheets to fill out each day.

What are the possible benefits and risks of participating?

It is not known whether taking MCP has any direct benefits to your health. This is the purpose of the study, and as such you should assume that there are no direct benefits to you in participating in this study. We hope that the results of this study will help others in the future. MCP contains fibre which may cause transient minor stomach upset, including wind, but has no lasting side-effects. MCP may raise levels of a substance in the body called potassium. We will provide advice about how best to prepare your meals to help with this and we will regularly measure levels of potassium in your blood so that this does not become a problem for you. Providing a blood sample can cause bruising and soreness.

Where is the study run from?

The study is run from the Castle Hill Hospital in Cottingham, East Yorkshire.

When is the study starting and how long is it expected to run for?

The study will start in 2015 and will run for 2 years.

Who is funding the study?

We are applying for funding from the British Heart Foundation (UK).

Who is the main contact?

Kenneth Wong  
Kenneth.Wong@hey.nhs.uk

## Contact information

### Type(s)

Scientific

### Contact name

Dr Kenneth Wong

### Contact details

Department of Cardiology  
Daisy Building  
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## Additional identifiers

## Study information

### Scientific Title

Modified citrus pectin as Anti-Galectin-3 therapy In heart Failure Trial (MAGnIFicent): a pilot randomised study of the effects of modified citrus pectin on biomarkers of collagen turnover and left ventricular function in optimally medicated patients with heart failure

### Acronym

MAGnIFicent

## **Study objectives**

Current hypothesis as of 27/10/2014:

The present study is intended as a pilot and feasibility study of using Modified Citrus Pectin (MCP) as an adjunctive nutritional therapy in heart failure. We aim to investigate the following hypotheses:

1. MCP inhibits galectin-3 mediated adverse remodelling resulting in a reduction of , or smaller increase in, N-terminal prohormone of brain natriuretic peptide (NT-proBNP).
2. MCP reduces collagen turn-over in patients with elevated baseline galectin-3 levels.
3. MCP improves left ventricular systolic and/or diastolic function and reduces left ventricular size and hypertrophy.
4. The effects of MCP on serial measurements of Galectin-3, NT-proBNP, fibrosis biomarkers, and anti-galectin assay are seen early (6 weeks compared with 18 weeks).

Previous hypothesis:

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2. MCP reduces collagen turn-over in patients with elevated baseline galectin-3 levels.
3. MCP improves left ventricular systolic and/or diastolic function and reduces left ventricular size and hypertrophy.
4. MCP improves exercise capacity and left ventricular function during exercise.
5. The effects of MCP on serial measurements of Galectin-3, NT-proBNP, fibrosis biomarkers, and anti-galectin assay are seen early (6 weeks compared with 18 weeks).

On 28/10/2014 the following changes were made to the trial record:

1. The study design was changed from 'Controlled randomized single-centre cross-over study with blinded assessment of outcome' to 'Controlled randomized double-blind single-centre cross-over study'.
2. The target number of participants was changed from 50 to 100.
3. The sources of funding field was changed from 'BG Medicine Inc (USA) and University of Hull (UK)' to 'We are applying to the British Heart Foundation for funding'.
4. The anticipated start date was changed from 01/09/2012 to 01/01/2015.
5. The anticipated end date was changed from 01/08/2013 to 01/01/2017.

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Yorkshire and the Humber Bradford Leeds Research Ethics Committee, 04/09/2014, REC ref: 12 /YH/0105

## **Study design**

Controlled randomized double-blind single-centre cross-over study

## **Primary study design**

Interventional

## **Study type(s)**

## Treatment

### Health condition(s) or problem(s) studied

Heart failure

### Interventions

Current interventions as of 27/10/2014:

MCP (6) capsules three times a day (total daily intake 14.4 g) vs matched placebo. The placebo is a microcrystalline cellulose placebo in matching opaque capsule (vegetable capsule: natural vegetable cellulose, titanium dioxide, and water) with equivalent sodium (2-5%) and potassium (7-11%).

Previous interventions:

MCP (6) capsules three times a day (total daily intake 14.4g) vs placebo (Glucotabs) 1 x 4mg tablet three times per day (total daily intake 12g).

### Intervention Type

Drug

### Phase

Not Applicable

### Drug/device/biological/vaccine name(s)

Modified citrus pectin

### Primary outcome(s)

Current primary outcome measures as of 27/10/2014:

1. Effect of MCP supplementation on NT-proBNP (primary endpoint of the study). Natriuretic peptides such as NT-proBNP increase in response to myocardial stretch
2. Effect of MCP supplementation on collagen turnover and extracellular remodelling (PICP)

Previous primary outcome measures:

1. Effect of MCP supplementation on NT-proBNP (primary endpoint of the study). Natriuretic peptides such as NT-proBNP increase in response to myocardial stretch
2. Effect of MCP supplementation on collagen turnover and extracellular remodeling
3. Global longitudinal strain

### Key secondary outcome(s)

Current secondary outcome measures as of 27/10/2014:

1. Galectin-3, a mediator of heart failure development and progression secondary to myocardial fibrogenesis. Its levels are unaffected by myocardial stretch
2. Effect on microalbuminuria
3. Effect on vascular function and haemodynamics (ENVERDIS with GTN sublingually and NEXFIN)
4. Effect on clinical endpoints will include 6-minute walk distance
5. Effect on ventricular remodelling (with left ventricular end diastolic volume as the main secondary endpoint), and ventricular function with the main secondary endpoint as left ventricular global longitudinal strain, which is thought to be more reproducible (with less potential of measurement error) as well as more sensitive than ejection fraction (Pellicori et al. 2013)

6. Nutritional intake and weight change, this is part of safety monitoring to minimise the risk of undernutrition and cardiac cachexia which will be assessed and early nutrition support will be initiated as required

Previous secondary outcome measures:

1. Procollagen type I N-terminal propeptide (PINP) - main secondary endpoint of fibrosis
2. Procollagen type III N-terminal peptide (PIIINP) - marker of cardiac collagen synthesis
3. Type I collagen telopeptide (ICTP) - marker of cardiac collagen synthesis
4. Matrix metalloproteinase-1 (MMP-1) - marker of cardiac collagen degradation
5. Tissue inhibitor of metalloproteinase 1 (TIMP1) - marker of cardiac collagen degradation
6. Left ventricular end diastolic volume
7. Ejection fraction

### **Completion date**

01/01/2017

### **Reason abandoned (if study stopped)**

Lack of funding/sponsorship

## **Eligibility**

### **Key inclusion criteria**

1. Patients diagnosed with heart failure, who had been or are currently on diuretics, substantiated by a raised NT-pro BNP and /or evidence of left ventricular systolic or diastolic dysfunction
2. Plasma galectin-3 level > 17.8 ng/mL
3. Therapy with an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) and beta-blocker (BB) (unless documented intolerance) for at least 3 months duration.
4. Aged over 18
5. If female, not of childbearing age or, if of childbearing age and sexually active, willing to use birth control.

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

### **Key exclusion criteria**

1. Current decompensated heart failure
2. Inability to provide informed consent
3. Use of eplerenone or spironolactone within 30 days of randomization or for more than 7 days within the previous 6 months (because they suppress galectin-3 effects and have potassium sparing effects which could increase the risk of hyperkalemia)
4. Pregnant or breast-feeding women

**Date of first enrolment**

01/01/2015

**Date of final enrolment**

01/01/2017

## Locations

**Countries of recruitment**

United Kingdom

England

**Study participating centre****Department of Cardiology**

Cottingham

United Kingdom

HU16 5JQ

## Sponsor information

**Organisation**

Hull and East Yorkshire Hospitals NHS Trust (UK)

**ROR**

<https://ror.org/01b11x021>

## Funder(s)

**Funder type**

Charity

**Funder Name**

We are applying to the British Heart Foundation (UK) for funding

# Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration