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Can a dietary supplement providing natural cGP (cyclic Glycine-Proline) compliment the body's own internal levels of cGP and help improve the metabolic health of type 2 diabetes sufferers and aid in the recovery of complications associated with metabolic syndrome

Submission date
25/07/2024

Recruitment status
No longer recruiting

Registration date
29/07/2024

Overall study status
Completed

Last Edited
08/08/2025

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Metabolic syndrome is a cluster of clinical manifestations including type-2 diabetes mellitus (T2DM), hypertension and dyslipidemia. Elevated blood glucose and insulin levels damage capillary networks and cause diabetic peripheral neuropathy, hypertension and other complications due to loss of microcirculation. With no cure, the prognosis of peripheral neuropathy is poor and a major cause of limb amputation. The 5-year survival rate after limb amputation is about 2 years, shorter than colon, breast and prostate cancers. Cyclic glycine-proline (cGP) is a trophic molecule that keeps the function of insulin-like growth factor-1 (IGF-1) normal. The key function of IGF-1 is to maintain the network of small blood vessels and capillaries. Thus, we hypothesize that the administration of natural cGP, via an orally bioavailable dietary supplement, may improve foot sensation, blood pressure and glucose metabolism by supporting a healthy microcirculation.

Who can participate?
Male and females aged between 45 and 80 years with medical histories of T2DM, hypertension and foot peripheral neuropathy can volunteer to participate in the trial.

What does the study involve?
One group will take one capsule/day providing 20 - 25µg natural cGP (low dose) and the other group taking one capsule/day delivering 40 - 45µg natural cGP (high dose). The capsules are formulated using natural food ingredients sourced from New Zealand and encapsulated in a GMP facility. Three hospital visits are planned over a 6-month trial period. At each hospital visit foot sensation is to be assessed using Semmes-Weinstein monofilament, vibration and warm /cold perception threshold tests. These tests are the routine practice for assessing feet' sensory

function. Fasting blood samples (10ml) are to be collected, and blood pressure is measured during each hospital visit. Participants are instructed to remain on their medications for hypertension, hyperlipidemia, and diabetes and to maintain their current lifestyle throughout the trial.

What are the possible benefits and risks of participating?
Our body naturally produces cGP keeping the function of IGF-1 normal. When our own cGP production is insufficient we experience metabolic dysfunction. Oral supplementation with a physiological dose of natural cGP designed to top up the shortage of our own cGP would be beneficial and have minimal interaction with the medications that the participants are using.

Where is the study run from?
This study will be conducted at the Department of Endocrinology, Tianyou Hospital, Wuhan University of Science and Technology, China.

When is the study starting and how long is it expected to run for?
May 2020 to May 2023

Who is funding the study?
The study is co-funded by The Health Commission, Hubei, China, and The cGP Lab Ltd., New Zealand.

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Protocol serial number
MR-42-23-028752

Study information

Scientific Title
An observational study suggested a cause-effect relationship between plasma cGP and clinical manifestations of Type 2 diabetes mellitus (T2DM) and its associated vascular complications. To confirm such relationship, this open label trial is designed to examine the efficacy of natural cGP supplementation on manifestations of T2DM.

Study objectives
As a natural reaction, endogenous cGP (cyclic glycine-proline) increases, however, the response is insufficient to address metabolic disorders and vascular complications. This leads us to hypothesise that further increasing plasma cGP via oral administration of natural cGP may improve clinical outcomes of metabolic syndrome.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 01/05/2020, The Ethics Committee of Tianyou Hospital, Affiliated to Wuhan University of Science & Technology (Tianyou Hospital, 9 Tujialing, Wuchang, Wuhan, 430064, China; +8613554623321; yangyang1003@wust.edu.cn), ref: Approval number: 2021-02-28; Revised approval number LL2024-02-08-01

Primary study design
Interventional

Study design
Two-armed open-label study

Study type(s)
Prevention, Treatment, Efficacy

Health condition(s) or problem(s) studied
The efficacy of cGP in vascular complications in patients with diabetes

Interventions
To confirm the cause-effect relationship of cyclic glycine-proline (cGP) to manifestations of type 2 diabetes (T2DM), an open-label study is used to examine the efficacy of natural cGP supplementation on manifestations of T2DM.

The two-armed open-label trial is to be conducted at the Tianyou Hospital, Wuhan University of Science and Technology, China. Thirty-eight T2DM participants with foot sensory deficits will be allocated into 2 cohorts and receive either 20 - 25µg or 40 - 45µg natural cGP daily. There will be three hospital visits during a 6-month trial. Foot sensation is to be assessed using Semmes-Weinstein monofilament, vibration and warm/cold perception threshold tests. Blood pressure measured. Fasting blood samples will be collected.

Intervention Type
Supplement

Primary outcome(s)

Foot sensation measured using Semmes-Weinstein monofilament, vibration and warm/cold perception threshold tests at three hospital visits (Before supplementation, after 3 months of supplementation, and after 6 months of supplementation)

Key secondary outcome(s)
Measured before supplementation, after 3 months of supplementation, and after 6 months of supplementation:
1. Systolic and diastolic blood pressure measured using a sphygmomanometer at three hospital visits
2. Glucose intolerance measured using fasting blood glucose, HBA1c (%), and triglyceride /glucose index at three hospital visits

Completion date
01/05/2023

Eligibility

Key inclusion criteria
1. Male and female participants aged between 45 and 80 years old
2. More than 8 years of medical history of Type 2 Diabetes Mellitus (T2DM)
3. Current diagnosis of foot diabetic peripheral neuropathy (DPN)
4. Diagnosis of T2DM based on:
4.1. Fasting glucose ≥ 7 mmol/L and/or
4.2. HbA1c ≥ 6.5%
5. Diagnosis of foot DPN based on:
5.1. Self-reporting symptoms
5.2. Foot sensory testing scores
6. Inclusion criteria are independent of:
6.1. Body Mass Index (BMI)
6.2. Blood pressure
6.3. Plasma lipid profiles
6.4. Other complications of T2DM

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
45 Years

Upper age limit
80 Years

Sex

All

Total final enrolment
38

Key exclusion criteria
1. Type 1 diabetes
2. Diabetic foot ulcers
3. Any other cause of peripheral neuropathy (drug or injury or Covid-19 associated peripheral neuropathy)
4. Medical history of degenerative neurological conditions
5. History of cognitive impairment
6. Major mental health issues such as:
6.1. Schizophrenia
6.2. Severe depression
6.3. Anxiety

Date of first enrolment
01/05/2021

Date of final enrolment
01/05/2023

Locations

Countries of recruitment
China

Study participating centre
Tianyou Hospital, The Wuhan University of Sciences and Technology
9 Tujialing, Wuchang
Wuhan
China
430064

Sponsor information

Organisation
The cGP Lab

Organisation
Wuhan University of Science and Technology

ROR
https://ror.org/00e4hrk88

Funder(s)

Funder type
Industry

Funder Name
The cGP Lab Ltd

Funder Name
Health Commission of Hubei Province

Alternative Name(s)
Hubei Provincial Health Commission,

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
China

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Jian Guan, jian.guan@thecgplab.com
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

• The type of data that will be shared
Raw data that collected during the trial without any personal information of participants.

• Timing for availability
After the main data being published.

• Whether consent from participants was required and obtained
Yes

• Comments on data anonymization
The data will be shared without private information being divulged. The individual participant data were collected and recorded in Chinese.

IPD sharing plan summary
Available on request, Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		07/08/2025	08/08/2025	Yes	No