STUDY PROTOCOL: DICHROSTACHYS GLOMERATA AND CISSUS QUADRANGULARIS EXTRACTS INCREASE GLP-1 LEVELS IN PATIENTS WITH OVERWEIGHT AND OBESITY: A RANDOMISED CONTROLLED TRIAL

General information

NCT Number: NCT06827002
Protocol title: Effect of Standardised Cissus Quadrangularis and Dichrostachys Glomerata Extracts on GLP-1 Concentration and DPP-4 Activity in Healthy Adults who are Overweight and or Obese
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Project summary

Obesity is a growing global health crisis, currently affecting over 2.3 billion individuals worldwide. This study aims to evaluate the comparative effects of standardised Cissus quadrangularis extract (CQE) and Dichrostachys glomerata extract (DGE) on obesity-related metabolic parameters, with a specific focus on glucagon-like peptide-1 (GLP-1) levels and dipeptidyl peptidase-4 (DPP-4) enzyme activity in adults who are overweight/obese. In this 12-week clinical trial, participants will receive either standardised Cissus quadrangularis extract (CQE), Dichrostachys glomerata extract (DGE), or placebo. Key outcomes assessed include GLP-1 levels, DPP-4 activity, food intake, body weight, blood lipid profiles, fasting blood glucose, and visceral fat mass, measured at baseline and at designated intervals. This clinical study is informed by prior preclinical research involving 18 adult male Wistar rats (150–200 g), randomly divided into three groups: a control group on a normal diet, and two treatment groups receiving either DGE (400 mg/kg) or CQE (300 mg/kg) alongside a normal diet. Results showed that both extracts significantly increased GLP-1 levels and inhibited DPP-4 activity compared to the control group. These effects were associated with reductions in food intake, body weight, and fasting glucose levels, as well as favourable changes in lipid profiles, including HDL, LDL, and triglycerides. The findings suggest that Cissus quadrangularis extract (CQE) and Dichrostachys glomerata extract (DGE) may exert anti-obesity effects through mechanisms involving GLP-1 enhancement and DPP-4 inhibition. This clinical study is designed to provide human evidence supporting the potential

of these plant extracts as alternative therapies for weight management and metabolic health improvement.

Investigators and Roles

- **Janvier Youovop**[1,3]- write the original draft, develop and execute the methodology, formally analyse the data, review and edit the manuscript
- **Guy Takuissu**[2,3]- write the original draft, develop and execute the methodology, review and edit the manuscript
- **Régine Minoue**[3]- develop and execute the methodology, review and edit the manuscript
- **Felix Nwang**[3]- develop and execute the methodology, review and edit the manuscript
- **Maryam Adeboyega**[3]- write the original draft, formally analyse the data, review and edit the manuscript
- **Crista Arrey**[4]- develop and execute the methodology, review and edit the manuscript
- **Inelle Makamwe**[1]- formally analyse the data, review and edit the manuscript
- **Julius Oben**[1,3*]- conceptualised and will supervise the study, review and edit the manuscript

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Rationale & background information

Obesity is a health burden affecting over 2.3 billion people of all ages globally [1]. The development and progression of obesity involve a complex pathogenesis, and several drugs have been developed to target these pathways. In recent years, dipeptidyl peptidase-4

(DPP-4) inhibitors or gliptins, such as sitagliptin, saxagliptin, and vildagliptin, have been considered viable obesity management options. Gliptins inhibit DPP-4, an enzyme known to deactivate the glucagon-like peptide-1 (GLP-1) hormone, contributing to the development and progression of obesity and other metabolic diseases. GLP-1 is an important incretin hormone secreted in the L-cells of the gut for the maintenance of blood sugar homeostasis. It has other pleiotropic effects through its receptors in the liver, brain, and stomach to delay gastric emptying, reduce appetite, and induce significant weight loss [2]. In healthy individuals, GLP-1 has a half-life of >2 minutes due to the activities of DPP-4 [3]. Some studies have reported increased DPP-4 levels in people with obesity [4], further reducing the incretin effects of GLP-1. Gliptins are primarily invented to manage type 2 diabetes. However, their weight loss effects are quite significant, suggesting their potential as a weight loss management option.

Synthetic drugs used for obesity management are often associated with side effects and contraindications. For conditions such as obesity, patients with obesity often require individualised management options owing to sensitivity and the high likelihood of comorbidities. For example, patients with obesity are more vulnerable to pancreatitis and pancreatic cancer [5], whereas gliptins are associated with a high incidence of acute pancreatitis.[6] In terms of cost, gliptins are considerably expensive [7]. The current FDA-approved gliptins are intended for the management of diabetes. The off-label use of gliptins for obesity management may lead to increased demand, higher prices, and potential shortages. Therefore, there is a need to explore safe, cost-effective, and potent alternatives for obesity management.

Owing to their potency and low toxicity, natural products continue to emerge as potential drug leads for several metabolic disease conditions. *Dichrostachys glomerata* is a popular Cameroonian spice, and *Cissus quadrangularis* is an ornamental and medicinal plant that grows in Africa and Asia and has shown tremendous effects on weight loss. Youovop *et al*. [8] reported that *Dichrostachys glomerata* extract (DGE) induced 22.85% weight loss in 60 subjects at 12 weeks. In a double-blind, placebo-controlled study involving 35 subjects, *Cissus quadrangularis* extract (CQE) reduced body fat by 12.8% in 8 weeks [9]. The mechanisms by which these two extracts exert their weight loss effects are not fully understood. It has been suggested that DGE and CQE may exert weight loss effects through anorectic mechanisms. Studies by Kim *et al*. [10] and Lee *et al*. [11] proposed that DGE and

CQE may reduce food intake through increased adiponectin secretion and the AMPK pathway. To date, no study has investigated the effects of DGE or CQE on GLP-1 levels or DPP-4 activity. Hence, this study aims to evaluate the effects of DGE and CQE on blood GLP-1 levels and the enzyme dipeptidyl peptidase-4 (DPP-4) in healthy patients who are overweight and/or obese as potent alternatives in the management of obesity.

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Study Goal

The primary goal of this study is to evaluate the efficacy of the standardised extract from two Cameroonian spices, Dichrostachys glomerata (DGE) and Cissus quadrangularis (CQE), as potential safe, cost-effective, and potent alternatives for enhancing GLP-1 production for the management of obesity.

Specific Objectives

1. To evaluate the effect of DGE and CQE on circulating GLP-1 levels in overweight or obese individuals.
2. To assess the impact of DGE and CQE on DPP-4 activity.
3. To determine the effect of DGE and CQE on cardiometabolic parameters and the extent of weight loss achieved through supplementation over the study period.

Study design

This is a double-blind, placebo-controlled clinical trial.

Inclusion Criteria: Healthy males and non-pregnant, non-lactating females aged 18–65 years with a BMI between 25–34 kg/m².

Exclusion Criteria: Age <18 or >65 years, morbid obesity (BMI >34.9 kg/m²), insulin-dependent diabetes, pregnancy or breastfeeding, active infections, systemic diseases (e.g., HIV/AIDS, hepatitis, malignancy within 5 years), or use of medications/natural products that may interfere with study parameters.

Randomisation and Blinding

Participants will be randomised using a random number generator. Treatments (DGE, CQE, or placebo) will be packaged in identical opaque containers, sequentially numbered according to the randomisation sequence. Allocation concealment is maintained, with investigators and participants blinded to treatment assignments.

Methodology

Test Material

Standardised Cissus quadrangularis extract (CQE) and Dichrostachys glomerata extract (DGE) are procured from Gateway Health Alliances, Fairfield, California, USA, as 400 mg and 300 mg capsules, respectively. Identical placebo capsules containing 400 mg of dextrin are also procured. Oral semaglutide (Rybelsus®) was purchased and then repackaged into capsules identical to CQE, DGE and placebo capsules.

Intervention

Participants will receive capsules of either DGE (400 mg), CQE (300 mg), semaglutide (4-week dose escalation from 3 to 7 to 14mg) or placebo (400 mg dextrin) daily for 12 weeks. The size and shape are made so that neither the researcher nor the participant would distinguish the capsules. Patients are instructed to maintain their usual lifestyle and dietary habits and to report any delays in taking the capsules. Patients are monitored for adverse effects throughout the study.

Dietary and exercise restrictions

No dietary or exercise restrictions are recommended for patients. Patients are encouraged to continue their normal lifestyle routine.

Primary efficacy endpoint evaluation

Anthropometric parameters: body weight, height, and body fat percentage

Height is measured at the screening visit (visit 1). Body weight and body mass index (BMI, kg/m^2) are measured at baseline, week 4, week 8, and week 12. The body fat percentage (%) is measured using an impedance meter at the same time points.

Metabolic parameters

Blood samples are collected after a 12-hour fast at baseline, week 4, week 8, and week 12 to assess fasting blood glucose levels, blood lipid levels, GLP-1 levels and DPP-4

activity. Glucose levels are measured using the glucose oxidase–peroxidase enzymatic method with a touch glucometer. Blood lipid levels (cholesterol, triglyceride, and HDL-c) are assessed using commercial kits. LDL-c is assessed using the Friedewald *et al.* formula [12]. GLP-1 levels are determined using the Ray Bio® GLP-1 ELISA kit. DPP-4 activity is assessed with Cayman's DPP-4 inhibitor screening kit according to the manufacturer's instructions, and activity is expressed as a percentage relative to the positive control using the following formula:

$$\% \text{ remaining activity} = (\text{slope of test sample}/\text{slope of positive control}) \times 100$$

Secondary efficacy endpoint evaluation: Energy intake

Food intake and calorie content are monitored via a self-reported 7-day food diary. The FAO Food Composition Table for Cameroon is used to estimate carbohydrate, lipid, and protein intake. Energy intake (EI) is calculated using the following formula:

EI (Kcal/day) = Ecarb + Elip + E prot

With:

Ecarb/prot (Kcal/day) = (Amount of carb/prot ingested (g) × 4 kcal)/7

Elip(Kcal/day) = (Amount of lip ingested (g) × 9 kcal)/7

Considering that: 1 g carbohydrate or protein = 4 kcal and 1 g lipid = 9 kcal

Statistical analysis

All variables were expressed as a means ± standard error of the mean. The normality of the data is confirmed by the Kolmogorov-Smirnov test and Q-Q plots. The statistical analysis is conducted using the Statistical Package for Social Sciences (SPSS v.24, Inc. Chicago, IL, USA). The ANOVA with post hoc Tukey test is used for descriptive and comparative analysis. The Pearson correlation is used to assess the association between GLP-1, DPP-4, body fat, and energy intake. The significance is set at $p \leq 0.05$.

Expected outcomes of the study

1. **Scientific and Clinical Impact**

This study will advance the understanding through which Dichrostachys glomerata (DGE) and Cissus quadrangularis (CQE) exert anti-obesity effects, especially their influence on the GLP-1/DPP-4 pathway. It will potentially expand safer and effective therapeutic options for obesity, particularly for patients with comorbidities and contraindications to synthetic drugs.

2. **Economic Impact**

Pharmacological discovery with natural products such as Dichrostachys glomerata and Cissus quadrangularis could encourage local economies through cultivation, processing, and commercialisation. It will also encourage investment in functional foods or supplements derived from African biodiversity, increasing global visibility of African plant-based health solutions.

Duration of the project: 12 weeks

Ethics

The project aligns with the International Conference on Harmonisation Guidelines for Good Clinical Practice (ICH GCP) and the Declaration of Helsinki and is registered on clinicaltrials.gov (NCT06827002)on 02/11/2025. This study protocol and the informed consent form are also approved by the University of Yaounde I Joint Institutional Review Board for Animal & Human Bioethics (JIRB) under number BTC-JIRB2023-084. Written informed consent from patients is also obtained by the principal investigator after the study's nature, scope, and expected results are explained.

Informed consent forms

The informed consent form is uploaded on figshare with DOI 10.6084/m9.figshare.29294219

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