University of Guadalajara
Health Sciences University Center
Institute for Translational Nutrigenetics and Nutrigenomics

Effect of coffee and agave inulin-based beverage on appetite sensations, food intake, and ghrelin, GLP-1, and PYY concentrations in adults with obesity

June 2024 – July 2025

ABSTRACT

Obesity is a disease that currently represents a great challenge from different areas, such as health, economy, society, and politics since it represents a problem with different negative consequences in each of these areas, not to mention that its prevalence worldwide is increasing. The main treatment for this problem is a lifestyle change, including diet and physical activity modifications. Specifically, nutritional treatment is usually based on balanced meal plans with caloric restriction to generate a negative energy balance. However, when a nutritional treatment is carried out, adherence to the treatment can be compromised by experiencing low satiety, or the patient's remaining hungry with the meal plan.

In this sense, some studies show evidence of increased satiety and reduced energy intake when coffee is consumed in certain doses. In the case of inulin, a decrease in appetite, an increase in GLP-1 and PYY concentrations, and even a decrease in energy intake have been reported. These effects have been attributed to certain bioactive compounds present in coffee, such as caffeine and chlorogenic acids, and in the case of inulin, to its effect on the microbiota that produces certain short-chain fatty acids, which in turn stimulate the secretion of peptides related to satiety and, being a fiber, slows gastric emptying. However, with coffee and inulin, there is contradictory evidence; in many cases, no significant changes are observed. In other words, there are still many questions to be answered.

Therefore, more scientific evidence is needed to contribute to nutritional recommendations for hunger control and satiety. Therefore, this study aims to evaluate the chemical and sensory characteristics of a coffee and agave inulin-based beverage and its effect on appetite, dietary intake, and biochemical profile in subjects with obesity. For this purpose, a randomized crossover clinical trial with an estimated n of 30 participants has been proposed to evaluate the effect of daily and two-week consumption of a coffee beverage with agave inulin in comparison with the daily and two-week consumption of a placebo beverage for two weeks (Sedes: Instituto de Nutrigenética y Nutrigenómica Traslacional (INNUGET) of the CUCS and the Bariatric and Metabolic Surgery Unit of the Civil Hospital "Juan I. Menchaca"). The measurement of appetite hormones (acetylated ghrelin, GLP-1, and PYY) will be measured by ELISA assays. Visual analog scales measure appetite sensations, and the biochemical profile is determined by dry chemistry. The study will be conducted from April 2024 to March 2025. The results of this research will be disseminated at international

congresses in a high-impact international journal, and its completion will allow several students to complete doctoral and bachelor's theses.

BACKGROUND

Globally, obesity has almost tripled since 1975, as more than 650 million adults had obesity in 2016, representing about 13% of the world's population (1). In Mexico, obesity is a health problem that continues to increase, having in 2018, 75.2% of adults aged 20 years and older with overweight and obesity (2). In Jalisco, in the same year, it was reported a prevalence of obesity of 39.2% in women and 29.5% in men (3).

Obesity results from a combination of genetic, biological, sociocultural, and lifestyle factors (4). In that sense, two lifestyle habits that are very important in its development are high consumption of sugary beverages and low fiber intake. According to the National Health and Nutrition Survey (ENSANUT) 2018, 85.8% of the Mexican population over 20 years of age consumes sweetened beverages, and a large part of the Mexican population has a deficient fiber intake (2). On the other hand, appetite regulation also plays an important role in body weight control (5). Under normal conditions, hunger and satiety are well connected to allow a balance between energy consumed and energy expended; however, this does not occur in obesity (6). When there is a dysregulation in the hunger signals given by peptides such as ghrelin and in the satiety signals given by peptides such as PYY, GLP-1, and CCK, among others, or when there are alterations in the cognitive and hedonic regulation of hunger, excessive consumption of kilocalories is produced, which are stored in the form of fat, that is obesity is predisposed (7).

The increase in body fat, mainly at the visceral level, leads to metabolic alterations such as insulin resistance and dyslipidemia, increasing the risk of type 2 diabetes mellitus and cardiovascular disease (8). Therefore, to combat obesity and its consequences, the first thing recommended is a lifestyle change, such as an adequate diet, regular exercise, and psychotherapeutic interventions (7, 8). However, at present, it is a challenge to have strategies that allow successful nutritional interventions in patients with obesity. In this context, it has been observed that coffee consumption in overweight and people with obesity has been positively associated with satiety (9), reduction of body weight and hunger, and

even with a lower energy intake, partly due to mechanisms that directly or indirectly regulate the appetite mentioned above hormones (10,11).

In addition, caffeine can amplify the appetite-suppressing effect if combined with other compounds, such as fibers (12) like inulin. It has been observed that in overweight and subjects with obesity who had consumed a beverage with 24 g of inulin diluted in 300 ml of water with glucose, there was a decrease in ghrelin levels 6 hours after consumption compared to the ingestion of water with glucose (13). Inulin has also been associated with reduced hunger and energy intake (14) and increases in GLP-1 and PYY concentrations (15). However, the joint effect of coffee and inulin has not been studied, and many separate studies are inconclusive.

STATEMENT OF THE PROBLEM

The accelerated increase in the prevalence of overweight and obesity in our country has generated concern and the need to generate strategies that provide solutions for its prevention and treatment (16-18). The cost of various medical complications for a person with obesity and prediabetes, if he/she does not change his/her lifestyle habits, can reach up to 1.9 million pesos in 30 years. However, if he or she modifies his or her lifestyle, in 30 years, the total expense would decrease to only 92,860 pesos (19).

In that sense, a lifestyle habit that favors the development of obesity is the consumption of sugar-sweetened beverages. According to the National Health and Nutrition Survey (ENSANUT) 2018, 85.8% of the Mexican population over 20 years of age consumes sweetened beverages, and 16.8% consume sweetened dairy beverages (17). Likewise, the obesogenic environment in which we live favors easy access to this type of beverage, and there are very few healthy beverage options within the food industry (20). On the other hand, the average fiber consumption in Mexico is 27 g per day in men and 22 g per day in women, while the daily fiber recommendation for adults is 30 g per day.

High consumption of sugar-sweetened beverages combined with low fiber intake are risk factors for developing obesity and other chronic noncommunicable diseases (21). Obesity may arise from inappropriate food choices stemming from a strong urge to eat or weak hunger inhibition (22). In addition, there are hormones and molecules involved in appetite control, and when their functionality is altered (as occurs in obesity), they lead to overeating

and the progression of obesity. Among these hormones are peptide YY (PYY), glucagon-like peptide 1 (GLP-1), and ghrelin (23,24).

Currently, it is a challenge to have strategies that allow successful nutritional interventions in patients with obesity. In this context, coffee consumption in overweight and obese people has been positively associated with satiety (25), reduction of body weight and hunger, and even with a lower energy intake, partly due to mechanisms that directly or indirectly regulate the appetite mentioned above hormones (26, 27). For its part, caffeine can amplify the appetite-suppressing effect if combined with other compounds, as is the case with fibers (28) such as inulin, which has been associated with a reduction in hunger and energy intake (29), as well as with increases in GLP-1 and PYY concentrations (30). However, the joint effect of coffee and inulin has not been studied, and many separate studies are inconclusive.

Coffee is a popular beverage. Worldwide consumption is estimated at 168 million bags of 60 kilograms (31). At the national level, Mexicans consume an average of two and a half cups daily. However, inulin is not a food consumed significantly by the Mexican population; fiber consumption generally is below the nutritional recommendations. That is why, if its effects are proven, a beverage as widely consumed as coffee in combination with agave inulin could help people with obesity regulate their appetite.

JUSTIFICATION

The prevalence of obesity in 1988 in Mexico was only 9.5%, compared to 36.1% in 2018 (17), so it is necessary to start acting to improve the welfare of the Mexican population. In the search for evidence to complement a nutritional plan, the combined consumption of coffee and inulin has been proposed. Coffee consumption in our country increases by 2% each year and according to data from PROFECO (Procuraduría Federal del Consumidor), 85% of Mexicans beverage one to three cups a day (32). Agave tequilana Weber, the blue variety, is the most widely cultivated of the 117 species of agaves native to Mexico. This variety is an important source of inulin (33).

Based on previous research, these two products of the Mexican countryside have been shown, each in their own right, to provide health benefits. In the case of coffee, it has been shown to improve endurance and exercise capacity, it has antioxidant capacity, it has been associated with a lower risk of Parkinson's and Alzheimer's disease, and several studies

report a hepatoprotective effect (34); regarding appetite control and weight loss, there is still great controversy within the scientific community about its effects, especially due to the lack of randomized clinical trials. On the other hand, inulin has been shown to improve intestinal transit, lower LDL cholesterol, and be an important prebiotic for the intestinal microbiota, although its relationship with appetite control is not clear (35). These effects on regulating appetite processes such as hunger and satiety have been studied in other countries, but not in Mexico, and much less so using inulin from agave tequilana Weber.

OBJECTIVE

To evaluate the chemical and sensory characteristics of coffee and agave inulin-based beverages and their effects on appetite, dietary intake, and biochemical profiles in subjects with obesity.

b. Specific

1. To compare the concentrations of appetite hormones when consuming a coffee and agave inulin-based beverage vs a control beverage.
2. To compare the subjective sensations of appetite when consuming a coffee and agave inulin-based beverage vs a control beverage.
3. To compare the dietary intake when consuming a coffee and agave inulin-based beverage vs a control beverage.
4. To compare the biochemical profile when consuming a coffee and agave inulin-based beverage vs a control beverage.

HYPOTHESIS

A beverage based on coffee and agave inulin modifies appetite, dietary intake, and biochemical profile in subjects with obesity.

METHODOLOGICAL DESIGN

a. Type of study

Double-blind randomized crossover clinical trial.

b. Research location

Instituto de Nutrigenética y Nutrigenómica Traslacional (INNUGET), Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara.

Unidad de Cirugía Bariátrica y Metabólica del Nuevo Hospital Civil de Guadalajara “Dr. Juan I. Menchaca”.

c. Study period

From June 2024 to July 2025

d. Inclusion and non-inclusion criteria

Inclusion criteria

Men and women

25 to 55 years of age

BMI ≥ 30 and <35 kg/m2

Habitual coffee consumption (1 - 3 cups of 240 ml daily).

Willingness to stop consuming food and/or supplements with coffee, caffeine, and/or inulin during the study except for the intervention.

Availability of time in the mornings

Residents of the Guadalajara Metropolitan Area

Signed informed consent form

Non-inclusion criteria

Hypersensitivity or intolerance to coffee or inulin

Allergy or intolerance to any of the test foods

Current or within the last 6 months use of weight-loss or appetite-altering medications appetite altering medications

Diagnosis of diabetes, hypertension or any heart disease, thyroid disease, infectious disease (COVID-19, flu, etc.), digestive or inflammatory bowel disease or dysgeusia

Smoking

Women who are pregnant, want to become pregnant or are breast-feeding

Peri-menopausal or menopausal women

Who is on any dietary regimen for weight loss

Currently or within the last 12 months, participated in another study

Consumption of prebiotics or probiotics in the last three months

e. Exclusion criteria

Incomplete data and/or measurements

Lack of expected compliance (drink at least 5 of the 7 days of each week is considered compliance).

Individuals who decide to leave the study

f. Sample size calculation

The information reported in the article by Rahat et al., which had a double-blind randomized crossover design, was used to calculate the sample size (13). In this study, a significant

increase in the active PYY response was found when consuming 24 g of inulin mixed with 75 g of glucose dissolved in water (increase in the area under the curve from 0 to 4 h (iAUC04) = 5.69 pmol×h/L ± 9.8 pmol×h/L), compared with consumption of only 75 g of glucose dissolved in water ((iAUC04) = 1.06 pmol×h/L ± 10 pmol×h/L) with a p=0.003.
The program G*Power v.3.1.9.7 (36) was used for the sample size calculation, and an n=24 was obtained using the formula for dependent mean difference and considering a loss of 25% (which is common in this type of study); 30 subjects would be required for this project.

g. Dependent and independent variables

Independent variable
Consumption of coffee and agave inulin-based beverage

Dependent variables
Appetite hormones
Subjective appetite sensations
Dietary intake
Biochemical profile

Confounding variables
Sex
Age
Habitual coffee consumption
Self-perceived stress
Score in the "Food restriction" section of the three-factor eating questionnaire (TFEQ)

h. Ethical considerations
This protocol adheres to the ethical principles of the General Health Law on Health Research regulations. According to Article 17 of this law, it is classified as "with higher than minimal risk" since it uses a method of assignment to therapeutic schemes. Likewise, each participant will be given an informed consent form based on the requirements of Article 22 (37).

On the other hand, the Good Clinical Practice (GCP) standards, issued by the International Conference on Harmonization (ICH), will be considered, which detail guidelines for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials, to ensure that the data and results obtained are accurate and credible and that the rights, integrity, and confidentiality of the study subjects are protected (38).

In addition to the above, the international ethical guidelines for health-related research on human subjects elaborated by the Council for International Organizations of Medical Sciences (39) will be considered, in particular, guideline 5 (choice of control mechanism in clinical trials), guidelines 9 and 10 (on informed consent), guideline 11 (collection, storage and use of biological materials and related data), guideline 12 (collection, storage and use of data), guideline 20 (in disease outbreak situations (for the context of COVID-19)) and guideline 22 (use of online data and digital tools).

i. Biosafety Considerations

Instituto de Nutrigenética y Nutrigenómica Traslacional

This institute has a laboratory safety regulation that requires the use of protective clothing such as lab coats, mouth masks, gloves according to the technique to be performed, appropriate footwear, and safety glasses. In addition, all students working on this project will receive a laboratory safety course in which the previously mentioned information is presented, training in good laboratory practices, and their practice will be constantly supervised and advised by trained personnel from the institute. INNUGET has a specific area for storing biohazardous and infectious waste, a specific area for storing reagents, a shower, separate areas for different types of techniques, emergency telephones, evacuation route signs, and a route for transporting biohazardous and infectious waste.

Laboratory techniques to be performed at INNUGET include handling blood, serum, plasma, and genomic DNA extraction (the latter for future use). Blood is collected in vacutainer tubes, and serum, plasma, and genomic DNA are packaged in 1.5 ml Eppendorf tubes at 80% of their capacity and stored at -80°C. Vacutainer tubes containing traces of liquid blood, as well as Eppendorf tubes containing serum, plasma, or genomic DNA that will not be stored, are disposed of in hermetically sealed red containers that comply with the characteristics specified in NOM 087-SEMARNAT-SSA1-2002 (40), temporarily in the area designated for this purpose within INNUGET.

Sharps will be deposited in a rigid red polypropylene container with a lid. Disposable materials used to transfer, contain, inoculate, and mix biological waste will be deposited in red plastic bags. Finally, disposable gloves will be disposed of in the regular trash if not soaked with blood. All this is done according to the specifications of the aforementioned official standard (40). Once the red containers and bags are filled to 80% of their capacity, they are taken to the appropriate containers at the CUCS where a company collects them for incineration.

Likewise, the handling and disposal of chemical reagents with CRETI characteristics will follow the stipulations of NOM-052-SEMARNAT-2005 (41) and their corresponding safety data sheets. It is worth mentioning that before each investigator and student uses the chemical reagents, he/she should carefully read the manufacturers' instructions and make a flow chart of the entire procedure for their use, recorded in the laboratory logs.

Personal protective equipment should be worn in any contingency, and precautionary signs should be followed. The institution's civil protection personnel will be called and asked for help if a spill occurs. They are trained to apply the cleaning and evacuation protocol (if required) based on the nature of the residue or spill. The contact information for this unit is as follows: Unidad Interna de Protección Civil CUCS, Edificio E, Tel. 3310585200. Ext. 33964, e-mail proteccioncivil@cucs.udg.mx.

Unidad de Cirugía Bariátrica y Metabólica (Hospital Civil de Guadalajara “Dr. Juan I. Menchaca”

No chemical reagents will be used at this site. Blood samples will be taken from participants in vacutainer tubes, which will be transferred to INNUGET in a cooler for biological samples for handling and disposal as mentioned in the section of the institute. The sharps used for sample collection will be deposited in a rigid red polypropylene container with a lid, in the area where the sample was collected, in accordance with the specifications of NOM-087-SEMARNAT-SSA1-2002 (40).

The protocol has also been submitted to the Ethics Committee of the Civil Hospital "Juan I. Menchaca" (0602-23 HCJIM-2023).

METHODOLOGY

Study group

All participants will be assigned to two interventions separately, according to the random assignment sequence corresponding to the crossover design.

The interventions consist of consuming a beverage (intervention or control) 30 minutes before breakfast daily for 2 weeks, with an intermediate washout period of 2 weeks between each treatment, as shown in Figure 1. Participants will be assigned randomly to the sequence AB (intervention beverage/control) or BA (control/intervention beverage) by generating a table of random numbers in the SPSS software.

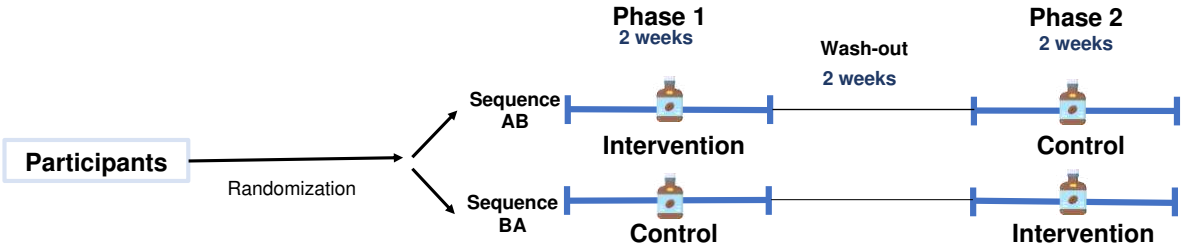

Figure 1.Scheme of the crossover study design

Intervention procedure

Subjects who attend the Bariatric and Metabolic Surgery Unit of the Nuevo Hospital Civil de Guadalajara “Dr. Juan I. Menchaca” and who meet the selection criteria. Subjects attend six sessions, one each week. The times and procedures can be seen in the following figure:

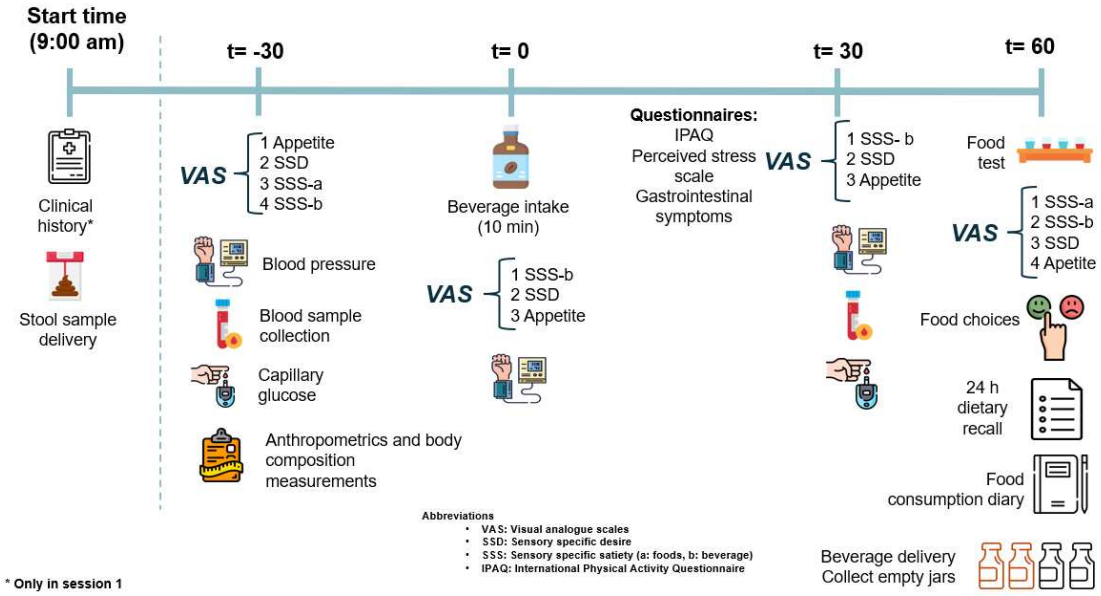

Figure 2. Intervention study procedure

Appetite assessment

Appetite hormones

The hormones and peptides ghrelin are measured in their acetylated form (Biovendor brand kit, catalog #: RA194062400R), GLP-1 (Biovendor brand kit, catalog #: YK160), and PYY (Biovendor brand kit, catalog #: YK080), by an ELISA assay and using a Thermo Scientific brand Multiskan Sky spectrophotometer.

Subjective sensations of appetite

The subjective sensations of appetite consist of 9 questions that are asked in the fasting state and after drinking the beverage. Specifically, 30 minutes before drinking the beverage, immediately after consuming it, 30 and 60 minutes after consumption. These scales assess hunger, fullness, satiety, desire to eat, prospective consumption, and the desire for sweet, salty, fatty, and savory foods. Visual analogue scales are made up of lines, usually 100 mm long, with the term “None” or “Not at all” at one end and “Yes, very much” at the other end. or "As much as I have never felt." The subject marks a point between these two extremes, and the quantification is done by measuring the distance from the left end of the line to the mark to which a score is given (49).

Sensory specific satiety (SSE)

SSE will be evaluated by visual analog scales of liking and wanting of 100 mm each. The subjective taste or liking of certain sensory characteristics of the food before and after consumption is asked; it is complemented by the evaluation of desire, which is a motivational aspect of appetite or the inclination to consume a specific food (15).

Specific sensory desire (SSD)

Fasting, post-beverage, and post-food test participants will be instructed to rate their desire to eat something sweet, salty, sour, bitter, fatty, and spicy using visual analog scales.

Food testing

It consists of serving 9 samples of foods with certain sensory properties:

1. Sweet: peach in syrup (13 g)
2. Sour: green apple (8 g) with lemon drops (4 drops)
3. Salty: salted biscuit (4 g)
4. Bitter: cocoa nibs (3 pieces)
5. Spicy: chilled peanuts (3 g)
6. Fatty: avocado (11 g)
7. Ultra-processed sweet: sandwich-type chocolate cookie with flavored filling vanilla (10g)
8. Ultra-processed salty: cheese-flavored corn chips (4 g)
9. Test beverage: it will be the intervention beverage or the control beverage, depending on the phase in which each participant is (20 ml)

Participants will evaluate these foods using scales for sensory-specific satiety and sensory-specific craving. Finally, they will be asked to choose the 3 test foods they would eat the most and the one they would eat the least at that time (15,16).

Dietary intake

Dietary record

In session 1, participants will receive instructions to complete the dietary record form to evaluate their diets. They are asked to record all food and beverages consumed 3 days: a weekday, a weekend day, and the day before the session. This is done in each of the six

sessions. The Nutritionist ProTM Diet Analysis software (Axxya Systems, Stafford, TX, USA) will be used for analysis.

Biochemical profile

Blood sample collection

Of the 6 sessions that the participants attend, two blood samples will be taken at the beginning and end of each phase, that is, in 4 sessions.

The first is in the morning, after 8 to 12 hours of fasting by venipuncture, and later 30 minutes after ingestion of the beverage. Two red and one purple vacutainer tubes are obtained, each with 5 ml of blood, centrifuged at 3500 rpm for 15 minutes at 4ºC to separate the serum and plasma.

The serum will be used for glucose and lipid profile determinations, the plasma will be used for determining appetite hormones,

Glucose and lipid profile determinations

The determinations are carried out on the VITROS® 350 automated dry chemistry analyzer equipment. 10 µl of biological sample (serum) is used, which is applied to a slide that contains the reagents that allow the detection of the analyte. These measurements are carried out while fasting and later 30 minutes after ingestion of the beverage.

In addition, capillary glucose measurements will be made with a glucometer (Accu-Check® Roche) while fasting and 30 minutes after ingestion of the beverage. The measurement is done through a puncture with a new, sterile lancet, which obtains a drop of blood that is applied to the reactive area of a strip (Accu-Check® Roche) to be read on the glucometer.

Body composition and blood pressure

Height measurement is done with a Seca stadiometer which has a precision of 0.1 cm. The subject remains standing with feet together (heels together and toes slightly apart). The heels, glutes, upper back, and occipital are in contact with the stadiometer. The head is placed in the Frankfort plane.

Waist and hip circumference

Waist circumference measurement is performed with a Lufkin brand anthropometric tape, which has an accuracy of 1 mm. The subject keeps his arms crossed on his chest, heels

together with the toes slightly apart, and eyes in the Frankfort plane. The measurement is made at the narrowest level, between the edge of the lower costal rib (tenth rib) and the iliac crest. The subject breathes normally, and the measurement is taken at the end of an exhalation. For waist measurement, the circumference is taken at the maximum posterior level of the gluteal bulge.

Electrical bioimpedance

Measurements of fat mass, fat percentage, fat-free mass, and bone mass are obtained through the InBody 370 equipment, under the same conditions described for measuring body weight.

Blood pressure

Blood pressure measurement is performed in the morning, after 10 minutes of rest, with a LifeSource digital sphygmomanometer. The patient must be relaxed, sitting, not stretched out, with the back well supported on the back of the chair. His legs should be touching the floor, not crossed, and his hand should be relaxed, without squeezing, and in a resting position. The measurement is carried out on the reference or dominant arm supported more or less at the height of the heart. The subject's clothing does not cover the arm or fit tightly to it.

Questionnaires

Medical history

A clinical history will be applied in the first session to obtain information on pathological history, clinical data, nutritional aspects, sociodemographic aspects, and lifestyle.

Physical Activity Questionnaire (IPAQ) short version

This instrument is a physical activity evaluation format; it examines different dimensions of the patient's physical activity. Weekly physical activity is measured by recording METs per minute per week. Subjects are classified into 3 categories of physical activity: high, moderate, and low (50). This questionnaire will be applied in the second and third sessions.

The Three-Factor Eating Questionnaire

This questionnaire consists of 51 items, is applied in the first session, and evaluates three dimensions of eating behavior: food restriction, disinhibition, and susceptibility to hunger (51). This questionnaire is included in the clinical history.

Obtaining a stool sample

At the beginning and the end of each intervention, participants will be asked to provide a stool sample (according to NOM-087-SEMARNAT-SSA1-2002, they are not considered an RBPI). They will be given a kit (sterile collection cup with buffer, collection strip, gloves, and stirrer) and written instructions for the collection procedure. Once subjects submit the sample, aliquots are made into Eppendorf tubes and stored at -80°C for later use.

Statistical analysis

Quantitative variables will be expressed as mean ± standard deviation or median and interquartile range for descriptive statistics, and qualitative variables as frequency or percentage. The normality of the variables is evaluated with the Shapiro-Wilk test. The general linear mixed model will be used to compare the two treatments. The data will be emptied into an Excel spreadsheet to be later imported into the SPSS v.21 program for analysis, considering a value of $p<0.05$ as statistically significant. The graphs will be made with Gradhpad software version 9.3.1.

VIABILITY

a. Financing

This project is funded by “Fondo para Proyectos de Impulso a la Investigación, 2022 III”.

b. Infrastructure

There is access to the 2 study sedes and collaboration with the researchers responsible for the laboratories and hospital. These spaces already have the necessary equipment to carry out this project.

c. Human resources training

This research project will train two PhD students in Translational Nutrition Sciences and two undergraduate students. Furthermore, given its scope, it will allow the acceptance of professional internships and social service students.

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