Activation of Key Metabolism Hormones, including GLP-1, in a Placebo-Controlled, Double-Blind, and Randomized Human Clinical Study Using a Combination of Two Unique Ingredient Blends

Objective: To evaluate the effects of two unique ingredient blends, used in combination, on GLP-1 concentration and other metabolism-related hormones in the blood, and on associated weight loss and other biometric data in a 12-week clinical study.

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Introduction

Emerging research shows the GLP-1 hormone has wide-ranging beneficial effects across multiple organ systems, such as the central nervous system, cardiovascular system, kidney, liver, pancreas, and brain. And approaching weight loss by significantly increasing the GLP-1 hormone or attaching to its receptors has become a popular means to lose weight quickly.

However, several other metabolism hormones are also implicated, such as insulin, GIP (Glucose-dependent Insulinotropic Polypeptide), leptin, and PP (Pancreatic Polypeptide). These key hormones all contribute to energy metabolism as they help control appetite, satiety, digestion, and blood sugar.

Levels of these hormones can become imbalanced due to age, poor diet, lack of gut diversity, or other lifestyle factors. Imbalances in these hormones, especially GLP-1, can impact many aspects of your health, including healthy glucose regulation, bone health, cardiovascular and gastrointestinal function, and more. Low GLP-1 levels can also lead to constant thoughts about eating or "food noise," intense cravings, more hunger, and, ultimately, weight gain.

This study set out to investigate if two unique ingredient blends could holistically and sustainably increase GLP-1 and other relevant hormone concentrations in overweight adults, without unwanted side effects. Blend 1 contained peptides from yeast hydrolysate, acacia gum, citrus bioflavonoids, and cinnamon bark. Blend 2 contained primarily resistant starches from potato and tapioca, kombucha, grape seed extract, and blueberry and cranberry juices powders.

In a previous *in-vitro* study, these two unique ingredient blends were shown to increase GLP-1 hormone production by 122% in L-cells—specialized cells that produce GLP-1. These encouraging results warranted further investigation into the capabilities of the two blends to increase GLP-1 concentration in overweight subjects.

METHODS

A total of 80 participants were recruited to participate in a 12-week randomized, placebo-controlled, double-blind study. Potential participants were screened by phone for inclusion/exclusion criteria by a Clinical Research Organization (CRO). The screening consisted of a brief description of the study and its importance and risk factors. This was followed by a screening questionnaire, where eligibility criteria were reviewed and current medication, supplement, and allergy inventory were taken.

After participants were deemed eligible, they were asked to complete an enrollment form and sign a consent form. They were then randomized into placebo or treatment group and asked to continue their normal lifestyle:

1. Placebo (P)
2. Treatment with the two-herbal blend combination

At each study timepoint (Baseline, Week 4, Week 8, and Week 12), each group had to arrive at the CRO's facility in the morning at a predetermined time between 7–9 AM. All subjects arrived at the testing facility in an overnight fasted state. Blood samples were taken for C-peptide, active Glucose-dependent Insulinotropic Polypeptide (GIP), active Glucagon-like Peptide 1 (GLP-1), glucagon, insulin, leptin and Pancreatic Polypeptide (PP) and fasting A1C analysis; anthropometric/biometric measurements using a Renpho scale were taken, and subjective questionnaires of food behaviors and cravings were filled in. Before and after pictures were taken at each timepoint. All subjects were compensated for their participation in the trial.

Anthropometric/biometric measurements

At each timepoint, each group was asked to step onto a Renpho scale (ES-30M or ES-CS20M model) that was connected to the Renpho Health app via Bluetooth. The scale uses impedance (resistance of electrical flow through the body) to measure biometric parameters. Muscles contain more water than fat and conducts electricity better, which allows the scale to estimate body fat percentage based on resistance.

The following parameters were measured: weight (lbs. or kg), BMI (kg/m2), body fat (%), fat-free-mass (lbs.), subcutaneous fat (%), visceral fat score, body water (%), skeletal muscle (%), muscle mass (lbs., %), bone mass (lbs., %), protein (%), basal metabolic rate (BMR, kcal), metabolic age (yrs.).

A Renpho tape measure (ES Tape) was also connected via Bluetooth to the Renpho Health app and waist circumference was measured at each timepoint.

Before/after pictures

At each timepoint, subjects in each product group had a picture taken from each side, back and from the front, in the same location and under the same conditions. Subjects were asked to wear same or similar clothing.

Questionnaires

A questionnaire was given to each participant at each timepoint. This questionnaire asked about food behavior and cravings between the study timepoints.

Blood samples for metabolic hormones and fasting A1C levels

Fasting blood samples were obtained by a licensed phlebotomist at each timepoint for each subject. Specialized tubes were used to collect at least 2 mL of venous blood and transported to a certified lab to analyze for all the metabolic hormones. These BD800 blood collection tubes (Becton Dickenson BD800 tubes contain spray-dried K2EDTA—an anticoagulant that contains DPP-4 and other protease inhibitor cocktails) provide the means to analyze plasma metabolic markers such as GLP-1, glucagon, ghrelin, and GIP.

Blood sample preparation: Samples were centrifuged at 1,000–1,300 rpm using a swing-out rotor centrifuge for 10–20 minutes and separated into plasma and red blood cells. Aliquots of plasma were then frozen and stored at ≤70° Celsius until further analyzed. At the end of the study, all samples were thawed and prepared according to manufacturer recommendations. A metabolic quantification kit (V-Plex Metabolic Panel 1 Human Kit K15235D; www.mesoscale.com) was used to analyze for C-peptide, active GIP, active GLP-1, glucagon, insulin, leptin, and PP concentrations.

Fasting A1C was measured by a licensed phlebotomist using a commercially available portable A1C test kit.

RESULTS

A total of 80 participants were recruited (50% males and 50% females) in this 12-week study. At baseline, ages ranged from 30–78 years (average of 47.6 ± 12.0 years), weight ranged from 135–327 lbs. (61.2-148.3 kg), waist circumferences ranged from 33.2–62 inches (84.3–157.5 cm), body fat (%) ranged between 21.6–70.0%, and subcutaneous (%) and visceral fat-score ranged from 13.7–59.1% and 8-30, respectively. Skeletal muscle (%) and muscle mass (lbs.) ranged from 17.5–53.8% and 84.2–170 lbs. (38.2-77.1 kg), respectively. There were no statistical differences between the groups at baseline. Biometric measurements are summarized in Table 1 below.

Table 1. Baseline measurements

Biometrics (Baseline)	Treatment group	Placebo	P-value
Weight	220.4 ± 49.3 lbs. (99.9 ± 22.4 kg)	216.8 ± 35.6 lbs. (98.3 ± 16.1 kg)	n.s.
Weight (range)	136–316 lbs. (61.7–143.3 kg)	135–327 lbs. (61.2 –148.3 kg)	n.s.
Waist circumference (in.)	33.2–62.0 in (84.3–157.5 cm)	33.7–57.5 in (85.6–146 cm)	n.s.
Body fat %	21.6–70.0%	21.6–64.8%	n.s.

Biometrics (Baseline)	Treatment group	Placebo	P-value
Subcutaneous fat (%)	13.7–59.1%	18.7–55.4%	n.s.
Visceral fat score	8–30	8–30	n.s.
Skeletal muscle (%)	17.5–53.8%	19.2–50.6%	n.s.
Muscle mass (%)	28.2–79.2%	31.2–74.5%	n.s.

n.s. no significant difference between the treatment groups

Objective Biometrics

By the end of the study, 5 people dropped out for scheduling reasons: 3 in the treatment group and 2 in the placebo group. There were significant changes ($p<0.05$) in weight loss of up to 6.4 kg (14 lbs.), body fat %, subcutaneous fat %, visceral fat score, and skeletal muscle % at 12-weeks. Table 2 summarizes the results. No significant changes were seen in the placebo group over the 12-week study.

Table 2. Biometric results at the end of week-12.

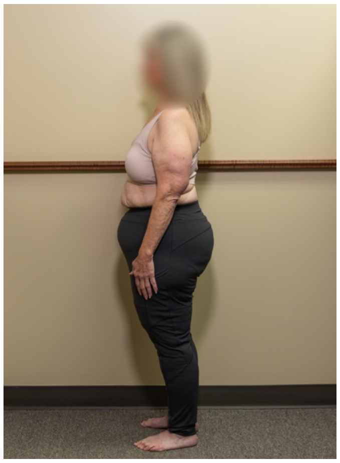
Biometrics	Week-12 (% change) **
Weight (lbs./kg)	Up to 13.8 lbs./6.4 kg lost (average of 5.3 lbs./2.4 kg lost)
Body fat %	Up to 8.6% lost (average 3.5%)
Subcutaneous fat (%)	Up to 8.1% lost (average 3.3%)
Visceral fat score	Up to 18.8% lost (average 5.9%)
Skeletal muscle (%)	Up to 7.2% increase (average 2.2%)

** $p<0.05$; all measurements were significantly changed to placebo

Before and After Pictures

Pictures taken at baseline and at week 12 show significant changes in body profiles (Figures 1– 4). All participants pictured showed an improvement in waist, hip, and buttock circumferences, weight, and visceral fat change percentages.

A. Baseline picture of a 73-year-old woman.



B. Week 12 pictures of a 73-year-old woman.

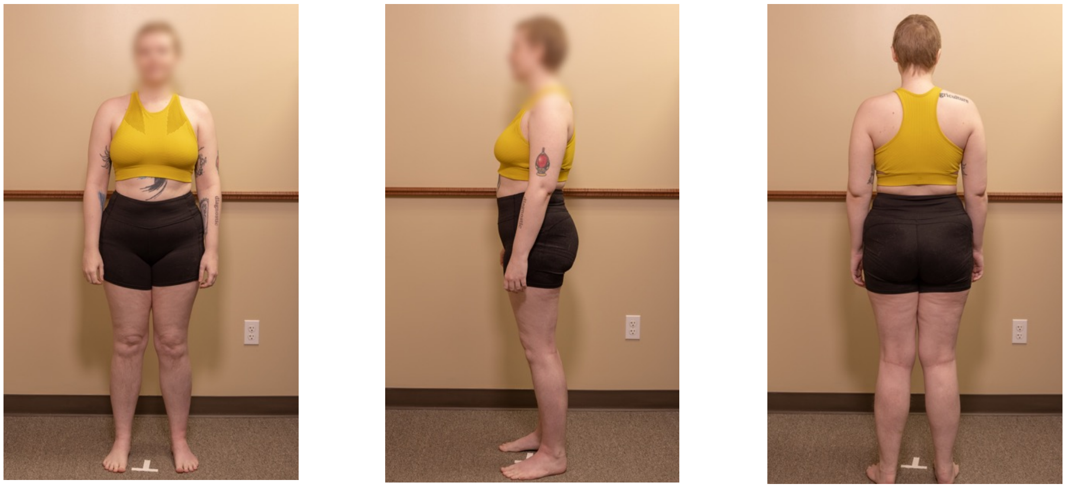
Figure 1. Biometric results: Age: 73 years; starting weight 83.1 kg; weight loss 6.4 kg; body fat % loss 8.6%; skeletal muscle % gain 7.2 %; subcutaneous fat % loss 8.1%; and visceral fat change 18.8%. Her waist circumference decreased by 6.7 cm and her buttock measurement decreased by 12.3 cm.

A. Baseline pictures of 48-year-old female.

B. Week 12 pictures of 48-year-old female.

Figure 2. Biometric results: Age: 48 years; starting weight 63.4 kg; weight loss 2.9 kg; body fat % loss 5.9%; skeletal muscle % gain 2.7%; subcutaneous fat % loss 5.5%; and visceral fat change 12.5%. This participant lost 10.8 cm around her waist, 16 cm around her hips, and 13.23 cm around her buttocks.

A. Baseline pictures of 30-year-old female



B. Week-12 pictures of 30-year-old female

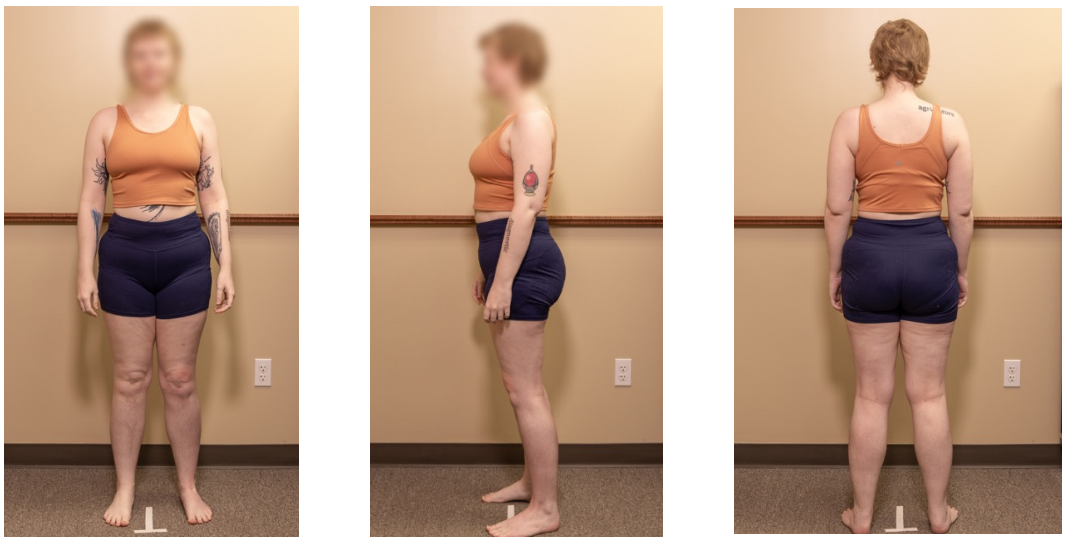


Figure 3. Biometric results: Age: 30 years; starting weight 84.5 kg; weight loss 2.5 kg; body fat % loss 3.9%; skeletal muscle % gain 2.1%; subcutaneous fat % loss 3.8%; and visceral fat change 9.1%. This female participant lost around 2 cm around her waist and about 3.2 cm around her buttocks.

A. Baseline picture of 72-year-old male

A. Week-12 picture of 72-year-old male.

Figure 4. Biometric results: Age: 72 years; starting weight 94.5 kg; weight loss 3.8 kg; body fat % loss 6.1%; skeletal muscle % gain 2.9%; subcutaneous fat % loss 5.9%; and visceral fat change 7.7%. This male participant lost 4.6 cm around his waist and about 2.1 cm around his hips and buttocks, respectively.

Subjective Questionnaire

The results were normalized to reflect percentage changes in responses as compared to placebo. The results are summarized in Table 3 below.

Table 3. Summary of subjective questionnare at the end of 12 weeks.

Question	Results
% Agreed that their food cravings decreased	80%
% Agreed that their sugar cravings decreased	80%
% Agreed that their fast-food cravings decreased	89%
% Agreed that their soda cravings decreased	97%
% Agreed that their salty cravings decreased	77%
% Agreed that their alcohol cravings decreased	94%
% Agreed that their portion sizes decreased	91%
% Agreed that their urge to resist snacking throughout the day decreased	77%
% Agreed that their appetite decreased	86%
% Agreed that they eat for health instead of emotional eating	86%
% Agreed that their satisfaction between meals increased	80%

GLP-1 and other metabolic hormones

In the treatment group, fasting GLP-1 levels increased by 220% on average. Other parameters such as GIP also increased by an average of 122%, leptin increased by an average of 5%, PP increased by an average of 74%. Additionally, 88% of participants saw an improvement in their A1C levels by an average decrease of 0.5 units as compared to baseline. (Figure 5). The other metabolic blood parameters glucagon, insulin, and C-peptide did not significantly change throughout the 12-week study period, and no significant changes were seen in the placebo group in any of the metabolic blood parameters.

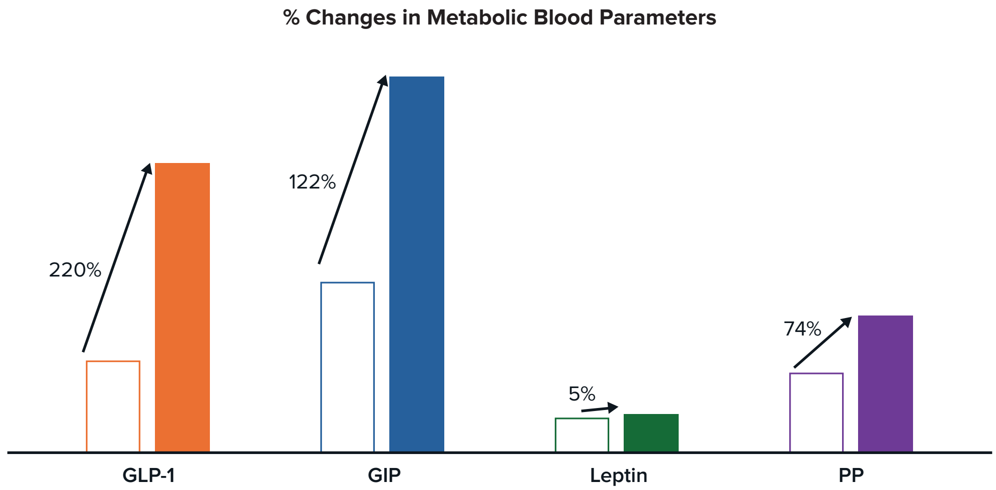


Figure 5. % Changes in average metabolic blood parameters.

Conclusion

The two unique ingredient blends were shown to increase GLP-1 concentrations in blood by an average of 220% when used together.

Subjects in the clinical trial experienced a significant decrease in food, fast-food, sugar, soda, and alcohol cravings. Their urge to snack also decreased, leading to measured weight loss. Subjects reported positive changes in the way they thought and felt about food, with more consuming food for their health instead of emotions.

The study further confirmed that the two unique ingredient blends are a natural, more holistic approach to weight loss. They work with the body by activating L-cells to produce GLP-1 and GIP and by acting through the microbiome to create the ideal environment for gut bacteria to make short-chain fatty acids, which fuel the L-cells to further produce GLP-1 and GIP. Complementary appetite hormones such as leptin and pancreatic polypeptides were also influenced. Positive changes to A1C levels were also observed.

The results show that, when used in combination, the two unique ingredient blends are a powerful tool to help people more easily make lifestyle changes needed to support their weight loss goals and general health. All of these benefits are achieved without requiring shots or prescriptions.

No side effects were seen, including gastrointestinal side effects.