

Effects of a Glucagon-like Peptide-1 (GLP-1) Booster™ on Blood Glucose, HbA_{1c}, Insulin, and GLP-1 Levels, Body Weight and Body Fat in Overweight Adults

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ABSTRACT

Background: Glucagon-Like Peptide-1 (GLP-1, a human hormone) drugs have unwanted side effects and limitations. One alternative is to utilize medicinal plants to boost endogenous secretion of GLP-1. **Materials and Methods:** GLP-1 Booster (GB) contains green tea leaf extract, Gardenia fruit extract, Turmeric root extract, Black pepper extract, Fenugreek seed extract, Ginseng root extract, and White kidney bean extract. A total of ten overweight (BMI 25.0 - 29.9 kg/m²) adults completed a 12-week study. **Results:** In 12 weeks participants saw significant reductions in fasting blood glucose (from 89.8 to 82.0 mg/dL, $p<0.001$), insulin (from 43.2 to 36.1 pmol/L, $p<0.001$), HbA_{1c} (from 5.33% to 5.13%, $p<0.01$), total cholesterol (166.4 vs 141.0 mg/dL, $p<0.001$), Systolic Pressure ($p<0.001$), Diastolic Pressure ($p<0.05$), Body Weight (171.29 vs 163.39 lbs, $p<0.001$), Body Fat Mass (42.26 vs 34.11 lbs, $p<0.001$), Body Fat Percentage (25.24% vs 21.24%, $p<0.001$), Body Fat Index (BFI) (6.81 vs 5.53 kg/m², $p<0.001$), Body Mass Index (BMI) (26.95 vs 25.69 kg/m², $p<0.001$), Waist Hip Ratio (WHR) (0.875 vs 0.857, $p<0.05$). Fasting GLP-1 level improved from 6.49 pmol/L to 7.27 pmol/L ($p<0.001$). Participants reported 42.2% decrease in Feeling of Hunger ($p<0.001$), 80.5% increase in Feeling of Fullness ($p<0.001$), 48.6% decrease in Desire to Eat ($p<0.001$), and 43.1% decrease in Eat How Much Food ($p<0.001$). **Conclusion:** GB can be effective in improving endogenous GLP-1 levels, reducing blood glucose, suppressing cravings, and losing body fat for overweight adults.

Keywords: Glucagon-like Peptide-1 (GLP-1), Glucose, Insulin, Hemoglobin A1c (HbA_{1c}), Fat Loss, Weight Loss.

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INTRODUCTION

Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA), a class of medications used in the treatment of type 2 diabetes and obesity, have gained widespread attention on social media in the past 3 years. They mimic the action of the endogenous hormone GLP-1, which is an incretin hormone secreted predominantly by intestinal enteroendocrine L cells in response to nutrient ingestion. By enhancing insulin secretion, delaying gastric emptying and promoting satiety, GLP-1 plays a crucial role in maintaining glucose homeostasis and energy balance. GLP-1 further contributes to glucose and weight management via glucose-dependent inhibition of glucagon secretion. Sustained GLP-1 receptor activation is associated with weight loss. GLP-1RA

drugs mimic GLP-1 to improve glucose control, reduce appetite, slow gastric emptying, and promote weight loss.

While GLP-1RA drugs have shown efficacy in the management of type 2 diabetes and obesity, they come with limitations. Most importantly, GLP-1RA drugs essentially alter the body's natural GLP-1 signaling, tricking the body to think there is sufficient GLP-1 secretion in the presence of GLP-1RA. This has caused strong undesirable dependence on GLP-1RA drugs. Studies have shown that patients regained most of their lost weight within 12 months after stopping GLP-1 RA drugs, and their glucose levels increased back as well (Wilding *et al.*, 2022). Additionally, patients lost muscle mass because of GLP-1RA drug use, which is counterproductive to long term weight management (Wilding *et al.*, 2021).

Instead of enhancing the body's own natural response to nutrients intake, GLP-1RA drugs likely interfere with the body's natural regulatory and feedback mechanisms. GLP-1RA drugs also have obvious unwanted side effects, including but not limited to, gastrointestinal distress, hypoglycemia, pancreatitis, renal impairments, immunogenicity, and even thyroid cancers.



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GLP-1RA drugs are expensive (up to \$1300/month without insurance). GLP-1RA drugs are only available to obese patients or patients with BMI>27 AND a related medical condition via prescription, and thus have limited accessibility.

Considering the unwanted side effects and limitations of GLP-1RA drugs, safer and cheaper alternative solutions are urgently needed to help people control glucose and lose weight. Many medicinal plants, their extracts and compounds have the potential to modulate the endogenous secretion and activity of GLP-1 and thus help glucose and weight management in humans. These plants, extracts and compounds may boost the endogenous secretion of GLP-1, acting as a booster to GLP-1, or increase the activity of GLP-1, acting as a potentiator to GLP-1, or increase the body's sensitivity to GLP-1, acting as an enhancer to GLP-1, or a combination of any above-mentioned mechanisms. These plants, extracts and compounds may work independently, additively, or synergistically to modulate the endogenous secretion and activity of Glucagon-Like Peptide 1 (GLP-1), and thus help with glucose and weight management in animals (including humans). Unlike GLP-1RA drugs, these plant-based extracts and compounds work within the body's natural regulatory and feedback mechanisms, and thus may offer advantages compared to GLP-1RA drugs in the treatment of type 2 diabetes and obesity.

Green tea extract and its active ingredient (Epigallocatechin Gallate, EGCG) have been used for glucose control and weight loss for a long history. Clinical studies (Chen *et al.*, 2016; Liu *et al.*, 2016) further showed that supplementation with green tea extract resulted in significant weight loss, reduced waist circumference, and a consistent decrease in total cholesterol and LDL plasma levels without any side effects or adverse effects in women with central obesity, and suggested that the antiobesity mechanism of green tea extract might be associated with inhibiting ghrelin secretion and increasing adiponectin levels, improving insulin sensitivity and increasing GLP-1 production.

Inhibiting related digestive enzymes (such as amylase) is an alternative way to decrease carbohydrate digestion to support glucose control. Gardenia fruit extract was shown to robustly inhibit pancreatic α -amylase activity (Luo *et al.*, 2020). It was also shown to significantly increase GLP-1 production, even higher than that of green tea extract (Luo *et al.*, 2020).

Turmeric (*Curcuma longa*) root extract and its major active curcumin, have versatile application in Traditional Chinese medicine and Ayurvedic medicine. Numerous studies (Kasprzak-Drozd *et al.*, 2022) have shown that Turmeric (*Curcuma longa*) root extract can help protect against diet-induced obesity via multiple pathways, including anti-inflammatory properties, regulation of fat metabolism, modulation of gut microbiota. The potent anti-inflammatory and antioxidant effect of curcumin may play a big role in its antiobesity effect, considering that extra fat often causes harmful systemic chronic inflammation and

oxidative stress. Curcumin has low bioavailability, primarily due to poor absorption, rapid metabolism, and rapid elimination. Black pepper (*Piper nigrum*) extract or its major active piperine can significantly improve curcumin bioavailability up to 20-fold (Hewlings *et al.*, 2017).

Fenugreek (*Trigonella foenum-graecum*) seed extract, a traditional medicine, has been extensively studied (Visuvanathan *et al.*, 2022) for its glucose control, fat loss and weight loss benefits. Specifically, preclinical study showed that an active compound N55 isolated from fenugreek seed, lowers plasma glucose according to prandial status by enhancing the response of physiological levels of GLP-1 and is much less likely to disrupt tight regulation of GLP-1R signaling as compared to GLP-1 RA drugs (Chou *et al.*, 2017).

Ginseng (*Panax ginseng*) root extract and its active ginsenosides have a long history for antiobesity and antidiabetic effect in Traditional Chinese medicine (Kim *et al.*, 2014). Recent studies have shown that such antiobesity and antidiabetic effects might be partially attributed to its ability to increase the production of GLP-1 (Kim *et al.*, 2014; Liu *et al.*, 2013; Xiong *et al.*, 2010), which reduces blood glucose level, suppresses appetite and promotes weight loss.

White kidney bean (*Phaseolus vulgaris*) extract has been shown to inhibit the enzyme α -amylase, limiting carbohydrate digestion and absorption with beneficial effects on body weight and metabolic health (Udani *et al.*, 2007; Nolan *et al.*, 2020).

GLP-1 Booster (GB) is designed to increase the endogenous production of GLP-1, improve the activity of GLP-1, enhance the body's response to GLP-1, and thus eventually help people reduce blood glucose, suppress food intake, and lose body fat. GB contains green tea (*Camellia sinensis*) leaf extract, Gardeniae (*Gardenia jasminoides* Ellis) fruit extract, Turmeric (*Curcuma longa*) root extract, Black pepper (*Piper nigrum*) extract, Fenugreek (*Trigonella foenum-graecum*) seed extract, Ginseng (*Panax ginseng*) root extract, and White kidney bean (*Phaseolus vulgaris*) extract. Each of these ingredients has been commonly consumed by humans as food sources or supplements and thus has a good safety profile.

To evaluate GB's potential as a safe and effective solution for glucose control and weight loss, the present study was designed to explore its effects on glucose and weight management in relatively healthy yet overweight adult men and women over a period of 12 weeks.

MATERIALS AND METHODS

Study Materials

The study product GLP-1 Booster (GB hereafter) is a patent pending formula that was specifically designed to help people control blood glucose, lose fat, and lose weight (US Patent Application Number: 63/613,526). Participants were instructed

to take GB daily, right before their biggest meal of the day. GB contains green tea (*Camellia sinensis*) leaf extract, Gardeniae (*Gardenia jasminoides Ellis*) fructus extract, Turmeric (*Curcuma longa*) root extract, Black pepper (*Piper nigrum*) extract, Fenugreek (*Trigonella foenum-graecum*) seed extract, Ginseng (*Panax ginseng*) root extract, and White kidney bean (*Phaseolus vulgaris*) extract.

Study Procedure

The study was reviewed and approved by an ethics committee before its commencement. The participants were recruited in the Salt Lake City area, Utah, USA. This study was registered on ClinicalTrials.gov (NCT06333496) (16).

Inclusion Criteria

Individuals who were at least 18 years old, non-smokers, and with a BMI between 25 and 29.9 were eligible to participate, if not currently taking a dietary supplement or medications for glucose control or weight loss. Participants who exercised regularly were asked to maintain their regimen consistently throughout the course of the 12-week study and participants who regularly consumed caffeine were asked to maintain their caffeine intake consistently throughout the course of the 12-week study.

Exclusion Criteria

Participants were not allowed to participate if they were pregnant or planning to become pregnant in the following 12 weeks, or lactating. Individuals were not allowed to participate if they were taking any stimulant medications, or any other medications or supplements that might impact glucose control and weight loss.

Participants Characteristics

Twelve (12) adult subjects were screened, ten (10) of them were enrolled and completed the study. Study participants were asked to maintain a consistent diet and exercise regimen throughout the study. At the beginning of the study, study participants were asked to fill out and sign an Information Form and Informed Consent.

Participants were supplied with one bottle of GB for each visit, labeled with their participant number. They were required to take the product consisting of 4 capsules per day (500 mg GB), taken on an empty stomach right before their biggest meal of the day, every day. Product was taken at the beginning of each visit for a total of 12 weeks and empty bottles were returned at each visit. Any dosing days that were missed were skipped and noted in the Questionnaire. Visits occurred at Week 0, Week 4, Week 8, and Week 12. Prior to each visit, participants were asked to fast and refrain from exercise for at least 4 hr.

Measurements

Height was measured according to the US National Health and Nutrition Examination Survey III (NHANES III) protocol at Week 0 only. The following outcome measurements were measured at each visit.

Body weight, fat free mass, fat mass, Body Mass Index (BMI), and basal metabolic rate were measured by a pre-calibrated InBody570 Body Composition Analyzer following manufacturer instructions (Cerritos, California). Body Fat Index (BFI) was calculated using body fat mass and height.

Waist Hip Ratio (WHR) was measured according to NHANES III protocol.

Blood pressure and heart rate were measured using the Omron Intellisense digital blood pressure monitor, Model HEM-739 according to the equipment manual (Vernon Hills, IL).

Questionnaires for positive/negative effects, energy levels, feelings of hunger, and satiety parameters. The presence of positive and negative effects was measured by a participant survey. Energy, hunger, and satiety were measured by Visual Analog Scale (VAS) incremented from 1 to 10.

Cholesterol, glucose, insulin, HbA_{1c} and GLP1 levels in blood were measured by certified third party labs. Blood samples were taken by a certified phlebotomist.

DATA ANALYSIS

For the statistical analyses a series of linear mixed effects models were used. These are an extension of one-way analysis of variance that considers potential dependence within each subject. Week was used as the fixed effect, both as a numeric or linear term and as a categorical variable. Dunnett's post hoc test was used to compare weeks 4, 8, and 12 to week 0 while controlling for the multiple comparisons. The response variables included Energy, Hungry, Fullness, Desire to Eat, Appetite, RMR, Systolic blood pressure, Diastolic blood pressure, Heart Rate, Total Cholesterol, Glucose, Body weight, BMI, Body fat, Fat mass, Fat free mass, BFI, and WHR. All analyses were performed using R version 4.4.1 (R Core Team 2024). A *p* value of ≤ 0.05 was considered statistically significant.

RESULTS

Study Participants

Twelve (12) adult subjects were screened, and ten (10) participants (4 female and 6 male) completed the entire study, and thus were included for the data analysis. All participants were overweight (average BMI 26.95) at the beginning of the study. No adverse reaction was found or reported during the 1-month post-study follow-up period and 1 year after for self-reporting (Table 1).

Subjective Parameters

Though study participants reported decreased Frequency of Exercise (Week 12 vs Week 0), they reported moderately increased Energy Level at Week 4, 8, and 12 compared to baseline Week 0, with Week 12 seeing 10.2% increase on average ($p<0.05$). Participants reported a significant decrease in Feeling of Hunger at Week 4, 8, and 12 compared to Week 0, specifically a 42.2% decrease on average in Week 12 ($p<0.001$). Participants also reported a significant increase in Feeling of Fullness at Week 4, 8, and 12 compared to Week 0, specifically an 80.5% increase on average at Week 12 ($p<0.001$). When asked about their Desire to Eat and Eat How Much Food, participants further reported significant decreases in both: specifically, a 48.6% decrease on Desire to Eat at Week 12 ($p<0.001$) and a 43.1% decrease on Eat How Much Food ($p<0.001$) (Figure 1, Table 2).

Table 1: Demographic Information of Study Participants at Study Commencement.

Age (years) (Mean, SD)	35.80, 6.05
Body Height (inches) (Mean, SD)	66.68, 4.12
Body weight (pounds) (Mean, SD)	171.29, 24.27
BMI (kg/m ²) (Mean, SD)	26.95, 1.25
Race/Ethnicity	
White	4 (40%)
Asian	2 (20%)
Hispanic/Latino	2 (20%)
African	2 (20%)
Gender	
Female	4 (40%)
Male	6 (60%)

Demographic information of 10 participants who completed the study.

Basal Metabolic Rate, Blood Pressures, Heart Rate

There was no significant change in basal metabolic rate ($p>0.05$) among study participants during the study. Study participants saw a trending decrease in heart rate on average overtime during the study, but not statistically significant (Week 12 vs Week 0: 6.2% decrease; $p>0.05$). However, study participants saw significant decreases of blood pressure over time during the study, specifically, a 6.7% decrease in Systolic Pressure on average from Week 0 to Week 12 ($p<0.001$) and a 6.6% decrease of Diastolic Pressure on average from Week 0 to Week 12 ($p<0.05$) (Figure 2, Table 2).

Blood Biochemical Parameters: Fasting Glucose, Insulin, HbA_{1c}, GLP-1, Total Cholesterol

Study participants saw a significant decrease of fasting Total Cholesterol over time during the study, specifically an average 15.3% decrease from 166.4 mg/dL at Week 0 to 141.0 mg/dL at Week 12 ($p<0.01$).

Fasting blood glucose and insulin both saw significant reductions over time (from Week 0 to Week 4, 8 and 12) during the study. Specifically, from Week 0 to Week 12 on average, there was a 8.7% reduction of fasting blood glucose from 89.8 to 82 mg/dL ($p<0.001$) and a 16.4% reduction of fasting blood insulin from 43.2 to 36.1 pmol/L ($p<0.001$). Fasting HbA_{1c} levels did not see a significant reduction until Week 12: a 3.8% reduction of fasting HbA_{1c} from 5.33% to 5.13% ($p<0.001$). Study participants saw a significant improvement in fasting blood GLP-1 over time during the study, specifically a 12.0% improvement from 6.49 pmol/L at Week 0 to 7.27 pmol/L at Week 12 ($p<0.0001$) (Figure 2, Table 2).

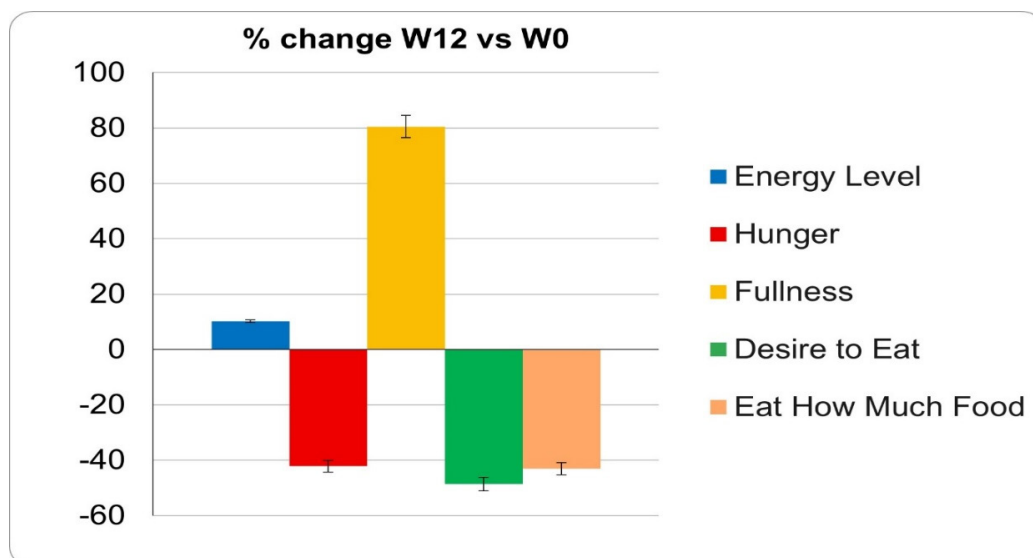


Figure 1: Averaged percentage change of measured subjective parameters from W0 to W12 among all study participants.

Table 2: Study Results of Participants at Week 0, 4, 8, and 12.

Measured Parameters	Week 0 (W0)	Week 4 (W4)	Week 8 (W8)	Week 12 (W12)
Exercise Frequency	3.3±1.3	3.3±0.5	2.7±0.8	2.4±1.2 *
Energy Level	5.9±1.5	6.5±1.3 *	6.5±1.6 *	6.5±1.6 *
Hunger Level	6.4±1.6	4.0±1.7 ***	4.2±1.1 ***	3.7±1.2 ***
Satiety Level	4.1±1.1	6.3±1.3 ***	6.1±1.2 ***	7.4±1.0 ***
Desire to Eat	7.2±1.4	4.6±1.1 ***	4.2±1.6 ***	3.7±2.1 ***
Eat How Much	5.8±1.0	4.2±0.8 ***	3.6±0.8 ***	3.3±1.4 ***
Basal Metabolic Rate (BMR) (kcal)	1633.7±278.2	1642.1±294.9	1634.2±287.9	1636.9±288.0
Systolic Pressure (mmHg)	122.8±10.7	119.7±11.8	119.3±11.5	114.6±8.9 ***
Diastolic Pressure (mmHg)	79.7±7.1	76.7±6.5	75.4±11.2 *	74.4±8.9 *
Heart Rate (bpm)	60.1±2.6	59.2±8.0	56.3±4.9	56.4±7.5
Total Cholesterol (mg/dL)	166.4±30.2	157.2±29.3	143.0±11.8 **	141.0 ±15.3 **
Fasting Glucose (mg/dL)	89.8±4.8	85.5±7.4 *	81.3±6.7 ***	82.0±6.3 ***
Insulin (pmol/L)	43.2±2.9	39.4 ±3.5 ***	38.3 ±2.9 ***	36.1±2.4 ***
HbA _{1c} (%)	5.3±0.2	5.3±0.1	5.3±0.1	5.1±0.1 ***
GLP-1 (pmol/L)	6.5±1.1	6.8±1.0 ***	6.9±1.0 ***	7.3±0.9 ***
Body Weight (lbs)	171.3±24.3	168.6±25.2 ***	166.1±25.0 ***	163.4±24.4 ***
Body Mass Index (BMI) (kg/m ²)	27.1±3	26.5±1.2 ***	26.1±1.3 ***	25.7±1.4 ***
Body Fat Percentage (%)	25.2±8.8	23.7±8.6 ***	23.1±8.7 ***	21.5±9.2 ***
Fat Mass (FM)(lbs)	42.3±13.5	38.9±12.4 ***	37.3±12.4 ***	34.1±13.5 ***
Fat Free Mass (FFM) (lbs)	129.0±28.6	129.8±30.0	128.8±29.6	129.3±29.5
Waist Hip Ratio (WHR)	0.875±0.034	0.862±0.027	0.860±0.016 *	0.857±0.018 *
Body Fat Index (BFI) (kg/m ²)	6.815±2.474	6.273±2.298 ***	6.031±2.304 ***	5.530±2.440 ***

Results were presented as Mean±SD. * indicates 0.01<*p*<0.05; *** indicates 0.001 <*p*<0.01; **** indicates *p*<0.001 in comparison to results at Week 0. Exercise Frequency is defined as follows: How frequently did you exercise this past month? [1- 0-5 days | 2- 6-10 days | 3- 11-15 days | 4-16-20 days | 5-20+ days]. Energy Level, Hunger Level, Satiety Level, Desire to Eat, and Eat How Much are on a scale from 1 to 10, with 1 being the lowest and 10 being the highest.

Anthropometric Parameters: Body Weight, Fat Mass (FM), Fat Free Mass (FFM), Body Fat Percentage, Waist Hip Ratio (WHR), Body Mass Index (BMI), Body Fat Index (BFI)

Study participants saw a significant reduction in Body Weight over the 12-week study duration, with an average 4.6% reduction at 7.9 lbs (171.29 vs 163.39 lbs, *p*<0.001). Interestingly, there was also a significant reduction in body Fat Mass (FM) among study participants, with an average 19.3% reduction at 8.2 lbs (42.26 vs 34.11 lbs, *p*<0.001). Fat Free Mass (FFM) did not show significant change over the 12-week study duration (*p*>0.05). Correspondingly, both Body Fat Percentage and Body Fat Index (BFI) of study participants saw significant decreases from Week 0 to Week 12; specifically, a 14.7% decrease of Fat Percentage from 25.24% to 21.24% (*p*<0.001) and an 18.8% decrease of BFI from 6.81 to 5.53 kg/m² (*p*<0.001). There was also a significant decrease in the Body Mass Index (BMI) for study participants over the 12-week duration: 4.7% decrease from 26.95 to 25.69

kg/m² (*p*<0.001). Waist Hip Ratio (WHR) also went down from 0.875 at Week 0 to 0.857 at Week 12 (*p*<0.05) (Figure 2, Table 2).

DISCUSSION

The comprehensive assessment of various parameters throughout the 12-week clinical study provided valuable insights into the efficacy and safety of GB in improving metabolic health and body composition. Each measured parameter reflects specific aspects of metabolic function, and the observed changes can be attributed to the individual and synergistic effects of the active ingredients contained in the study product.

Hunger, Satiety and Energy Levels

The subjective parameters assessed in this study provide valuable insights into the participants' perceived changes in energy levels, hunger, fullness, and eating behaviors during the 12-week study duration. The observed increase in energy levels, despite a reported decrease in exercise frequency, suggests a potential pro-metabolic effect of GB. This increase in energy could be

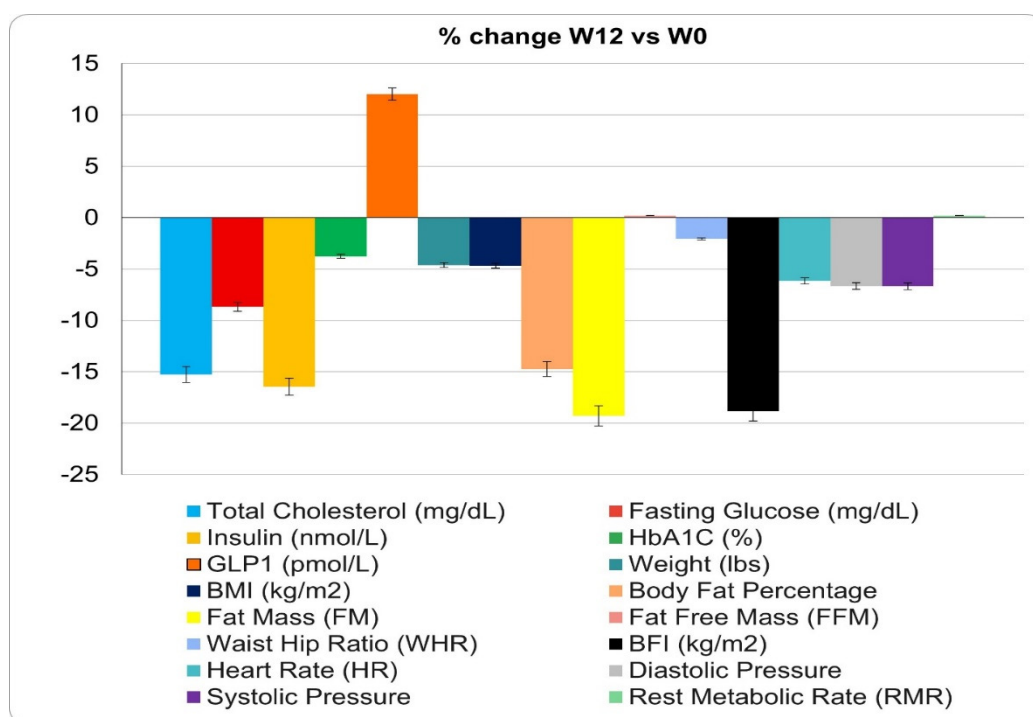


Figure 2: Averaged percentage change of measured objective parameters from W0 to W12 among all study participants.

attributed to the combination of botanical extracts and essential trace mineral chromium, such as green tea extract and ginseng root extract. Green tea extract has been associated with increased energy expenditure, fat oxidation, and thermogenesis due to its high catechin content (Hursel *et al.*, 2009), while ginseng extract has been shown to improve endurance, reduce fatigue, and enhance physical performance (Reay *et al.*, 2005).

The significant reductions in feelings of hunger, desire to eat and eat how much, coupled with increased feelings of fullness, indicate a strong appetite-suppressing effect of the study product. Components such as fenugreek seed extract and white kidney bean extract may play key roles in these effects. Fenugreek has been shown to delay gastric emptying and increase satiety due to its high soluble fiber content (Chevassus *et al.*, 2010), while white kidney bean extract inhibits starch digestion and reduces postprandial glucose spikes, potentially prolonging feelings of fullness.

Basal Metabolic Rate, Blood Pressures, Heart Rate

While basal metabolic rate remained unchanged throughout the study, significant decreases were observed in both systolic and diastolic blood pressures. This reduction in blood pressure aligns with previous research on the cardiovascular benefits of certain botanical extracts. For instance, turmeric root extract contains curcumin, which exhibits anti-inflammatory properties that may contribute to improved vascular health and reduced blood pressure (Cicero *et al.*, 2010).

The non-significant decrease in heart rate suggests a trend towards cardiovascular benefits, although further research may be needed to elucidate this effect. Components such as black pepper extract, containing piperine, have been associated with improved cardiovascular health through mechanisms such as enhanced vasodilation and reduced oxidative stress (Feng *et al.*, 2019).

Blood Biochemical Parameters: Fasting Glucose, Insulin, HbA_{1c}, GLP-1, Total Cholesterol

The significant reductions in fasting glucose, insulin, HbA_{1c}, and total cholesterol levels indicate improved glycemic control and lipid metabolism with GB. Several active ingredients may contribute to these effects. For instance, green tea extract has been shown to improve insulin sensitivity and reduce fasting glucose levels (Hursel *et al.*, 2009). Additionally, fenugreek seed extract has been shown to improve glycemic control and lipid profiles in individuals with type 2 diabetes (Neelakantan *et al.*, 2014).

The observed increase in fasting GLP-1 levels further supports the potential of GB to enhance glucose homeostasis and help glucose control. GLP-1 is an incretin hormone involved in glucose-dependent insulin secretion and appetite regulation (Drucker *et al.*, 2016). Components contained in GB have been shown to increase GLP-1 production via multiple pathways.

It is also interesting that GB significantly reduced fasting glucose, and increased GLP-1 level as early as Week 4 and through Week 12 yet did not significantly reduce HbA_{1c} level until Week 12. These outcomes are consistent with the fact that HbA_{1c}

level reflects average fasting glucose over the past 3 months (International Expert Committee, 2009). It is counterintuitive that GB also reduced insulin levels considering that GLP-1 level tends to increase the release of insulin. This might suggest that the effect of GB on insulin might not be primarily mediated by GLP-1 itself, rather also by the positive effect of GB on improving insulin sensitivity thus less of insulin was required and produced to exert the same effect. This counterintuitive observation calls for further investigation of such hypothesis, which is beyond the scope of the present study.

It should be noted that the significant reduction of total cholesterol along with blood pressure indicated a strong cardioprotective effect of the study product. High cholesterol and high blood pressures are the top risk factors for cardiovascular diseases in the USA and globally (Fryar *et al.*, 2012). By reducing the top 2 risk factors, the study product can be an effective approach to help reduce the risk of people getting cardiovascular diseases such as heart attacks and strokes.

Anthropometric Parameters: Fat Loss, Weight Loss and Body Composition

The significant reductions in body weight, fat mass, body fat percentage, BFI, and BMI highlight the potential of the study product for fat loss and weight management. Active ingredients such as gardenia fructus extract and turmeric root extract have been associated with anti-obesity effects through mechanisms such as inhibition of adipogenesis and modulation of lipid metabolism (Ejaz *et al.*, 2009). Similarly, white kidney bean extract may contribute to weight loss by inhibiting starch digestion and reducing caloric absorption (Udani *et al.*, 2007).

The observed improvements in waist-hip ratio suggest a favorable redistribution of body fat, potentially further reducing cardiovascular risk. Components such as black pepper extract and ginseng root extract have been associated with reductions in visceral fat and improvements in body composition (Reay *et al.*, 2005; Jwa *et al.*, 2012).

Brief Comparison of GB to Rybelsus (Semaglutide)

Different GLP-1 RA drugs showed variable outcomes in reducing blood glucose levels, HbA_{1c} levels, body weight and fat mass in different study settings (Rodbard *et al.*, 2019). For this brief comparison, the study of Rybelsus which is an oral format of GLP-1RA drug Semaglutide, is used.

The observed average weight loss among study participants in the present study is about 7.9 lbs over the 12-week study period. This amount does not seem a lot, however, is comparable to and even better than weight loss outcome among study participants who took Rybelsus (high dose 14 mg), who on average lost 8.4 lbs over the course of 6-months (Rosenstock *et al.*, 2019). Daily take of 14 mg of Rybelsus for 6-months among obese patients also significantly reduced blood HbA_{1c} level. The present study

showed daily take of GB for only 12 weeks already significantly reduced blood HbA_{1c} levels.

Of note, the present study did not show significant change in muscle mass among study participants. This can be a significant advantage compared to GLP-1 RA drugs, which are often associated with muscle loss (Wilding *et al.*, 2021). Maintaining or increasing muscle mass is especially important for healthy weight management, as an equal amount of muscle mass tends to burn more calories than the same amount of fat mass.

Another notable difference between GB and GLP-1 RA drugs such as Rybelsus, is that all these drugs come with a long list of side effects, ranging from common ones such as digestive blockage to severe ones including thyroid cancers, while no adverse effects were found or reported for GB during the 1-month post-study follow-up period and 1 year after. It is important to note that it is not a head-to-head comparison due to a variety of differences between GB and GLP-1RA drugs studies and thus should be interpreted with caution.

Potential Mechanism of Action

Though further and more specific investigations are needed to reveal the detailed mechanisms of action of GB, the observed outcomes from the present study suggested that all active components individually and synergistically increased the secretion of endogenous GLP-1 hormone and employed multiple pathways to metabolic modulation. Elevated GLP-1 levels stimulate insulin release, which helps reduce blood glucose levels. Improved endogenous secretion and regulation of GLP-1 positively impacted insulin sensitivity. Elevated GLP-1 levels also suppress appetite and slow gastric emptying and thus helps body weight loss and body fat loss. Elevated GLP-1 level itself and the resulting fat loss, healthier cholesterol and blood pressure levels further contribute to better overall metabolic health and cardiovascular health.

CONCLUSION

In this study, we formulated a GLP-1 Booster (GB) containing a combination of botanical extracts. Our data demonstrated that GB exerts beneficial effects on subjective parameters, blood pressures, biochemical parameters, and anthropometric parameters associated with metabolic health, glucose control and weight management. The results showed that GB significantly reduces the fasting blood glucose and insulin levels and specifically lowered body weight and fat mass among study participants. The effective outcomes were observed and are consistent with the known pharmacological properties of the active ingredients. Moreover, GB contributed to improvements in energy metabolism, appetite regulation, glycemic control, lipid metabolism, and body composition. Furthermore, a randomized placebo-controlled double-blind study with a bigger number of study participants should be carried out to confirm the efficacy

of GB. More research should be performed to elucidate the underlying mechanisms and clinically applied to the management of metabolic disorders.

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ABBREVIATIONS

GLP-1: glucagon-like peptide-1; **GB:** GLP-1 Booster™.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

This 12-week clinical study evaluated the efficacy of a novel multi-herbal GLP-1 Booster™ (GB) -containing green tea, gardenia, turmeric, black pepper, fenugreek, ginseng, and white kidney bean extracts-in overweight adults (BMI 25.0-29.9 kg/m²). Significant improvements were observed across metabolic, anthropometric, and subjective parameters. Fasting glucose decreased by 8.7% (89.8 to 82 mg/dL, $p < 0.001$), insulin by 16.4% (43.2 to 36.1 pmol/L, $p < 0.001$), HbA_{1c} by 3.8% (5.33% to 5.13%, $p < 0.001$), and total cholesterol by 15.3% (166.4 to 141.0 mg/dL, $p < 0.01$). Fasting GLP-1 levels increased by 12.0% (6.49 to 7.27 pmol/L, $p < 0.001$). Body weight reduced by 4.6% (171.29 to 163.39 lbs, $p < 0.001$), with a 19.3% decrease in fat mass ($p < 0.001$) and preserved muscle mass. Appetite control improved substantially: hunger (-42.2%), fullness (+80.5%), and desire to eat (-48.6%) ($p < 0.001$). Systolic/diastolic blood pressure also decreased significantly. No adverse effects were reported. GB demonstrates promise as a natural alternative for enhancing endogenous GLP-1 secretion, improving glucose homeostasis, and promoting fat loss in overweight individuals, warranting further large-scale trials.

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