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ORIGINAL RESEARCH

Randomized, double-blind, placebo-controlled, linear dose, crossover study to evaluate the efficacy and safety of a green coffee bean extract in overweight subjects

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Background: Adult weight gain and obesity have become worldwide problems. Issues of cost and potential side effects of prescription weight loss drugs have led overweight and obese adults to try nutraceuticals that may aid weight loss. One promising nutraceutical is green coffee extract, which contains high concentrations of chlorogenic acids that are known to have health benefits and to influence glucose and fat metabolism. A 22-week crossover study was conducted to examine the efficacy and safety of a commercial green coffee extract product GCA™ at reducing weight and body mass in 16 overweight adults.

Methods: Subjects received high-dose GCA (1050 mg), low-dose GCA (700 mg), or placebo in separate six-week treatment periods followed by two-week washout periods to reduce any influence of preceding treatment. Treatments were counterbalanced between subjects. Primary measurements were body weight, body mass index, and percent body fat. Heart rate and blood pressure were also measured.

Results: Significant reductions were observed in body weight (-8.04 ± 2.31 kg), body mass index (-2.92 ± 0.85 kg/m^2), and percent body fat ($-4.44\% \pm 2.00\%$), as well as a small decrease in heart rate (-2.56 ± 2.85 beats per minute), but with no significant changes to diet over the course of the study. Importantly, the decreases occurred when subjects were taking GCA. Body mass index for six subjects shifted from preobesity to the normal weight range (<25.00 kg/m^2).

Conclusion: The results are consistent with human and animal studies and a meta-analysis of the efficacy of green coffee extract in weight loss. The results suggest that GCA may be an effective nutraceutical in reducing weight in preobese adults, and may be an inexpensive means of preventing obesity in overweight adults.

Keywords: green coffee bean extract, chlorogenic acid, body mass index, weight loss, body fat mass, blood pressure, heart rate

Introduction

The World Health Organization predicts there will be 2.3 billion overweight adults in the world by 2015, and more than 700 million of them will be obese. Worldwide obesity has more than doubled since 1980. In 2008, 1.5 billion adults, 20 years of age and older, were overweight. Of these, over 200 million men and nearly 300 million women were obese. Over 65% of the world population lives in countries where overweight and obesity kills more people than underweight.[1] With the high cost of prescription weight loss drugs and the fear of side effects, the general public is turning to nutraceuticals. The estimated global market for 2014 is over 350 billion US dollars, as published by Market Research News.[2]

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At the present time, there is only one nonprescription nutraceutical product that is currently under investigation (Pharmachem Laboratory, Phase II) and is approved by the US Food and Drug Administration, with a qualified health claim for assistance in weight control and a structure-function claim for its mechanism, which is that it blocks starch absorption by means of an α-amylase inhibitor.[3,4] Coffee is of interest as a possible nutraceutical for weight loss because caffeine is a well known stimulant, and an epidemiology study found that coffee consumption resulted in less weight gain in obese men over an 18-month period.[5] A polysaccharide ingredient in coffee caused weight reduction when added to the diet of obese men but was not effective for women.[6] Freeze-dried coffee was found to cause weight loss when given to rats. It also increased antioxidant enzymes.[7] Caffeine, the major stimulant in coffee, has been linked to weight loss and to reduction in the risk of metabolic syndrome.[8] Existing but limited evidence suggests that substituting coffee for energy-containing soft drinks may facilitate weight management.[9] Several epidemiological investigations have found that coffee consumption reduces the risk of type 2 diabetes, and one of the mechanisms proposed for this benefit is that coffee consumption is inversely associated with weight gain.[10] The purpose of this study was to investigate the efficacy of a high chlorogenic acid green coffee bean extract in reducing weight, body mass, and body fat percentage, in preobese, euthyroid (normal thyroid functioning), otherwise healthy human subjects.

Materials and methods
Subjects
The study included 16 subjects (eight males and eight females) aged 22–46 (mean 33.19 ± 6.75) years. Average body mass index (BMI) at the start of the study was 28.22 ± 0.91 kg/m². The mean values for additional measures taken at baseline are listed in Table 1. Subjects exhibited overweight (preobesity) levels, as indexed by BMI 25–30, with the average

duration of prevalent BMI being 10.9 ± 3.9 months prior to the onset of the study. Duration of prevalent BMI was determined by examining health records of each subject prior to the beginning of the study. All subjects were euthyroid, nondiabetic (mean blood glucose 107 ± 9 mg/dL), and nonhypertensive (mean systolic/diastolic blood pressure 125.38/81.88 ± 5.10/2.68 mmHg), and were not on or been receiving steroids in the recent past. No subject was on or had been recently on medications known to influence weight for the past 6 months. All subjects had similar diet and exercise profiles and diet was recorded before and at the end of the study (see Table 3 for average diet information). All subjects gave their written informed consent before beginning the study. Informed consent was of a standard format, as per Indian regulatory requirements governing research human subject research, which are consistent with the ethical principles put forth in the Declaration of Helsinki.

Materials
The green coffee extract utilized for this study was provided by Applied Food Sciences Inc (Austin, TX) under the trade name GCA®. GCA contains a standard green coffee extract of total chlorogenic acids assayed at 45.9%, with other hydroxycinnamic acids that are known to have antioxidant health benefits. The total chlorogenic acid and other hydroxycinnamic acid content was 56.66%. Caffeine content was 2%–4% and assayed at 2.60% ± 0.18% for two lots. The relevant polyphenols and caffeine assay was done by ChromaDex Analytical (Irvine, CA) using high-performance liquid chromatography and appropriate standards. This study utilized two dosage levels of GCA, as well as a placebo. The high-dose condition was 350 mg of GCA taken orally three times daily. The low-dose condition was 350 mg of GCA taken orally twice daily. The placebo condition consisted of a 350 mg inert capsule of an inactive substance taken orally three times daily. The two dosages of GCA used here were based on previous

Table 1 Characteristics of 16 preobese subjects at baseline and end of study

Characteristic	Baseline (week 0) M ± SD	End of study (week 22) M ± SD	Difference (week 22 – week 0) M ± SD	Change
Weight (kg)	76.69 ± 7.91	68.65 ± 7.78	−8.04 ± 2.31**	−10.5%
BMI (kg/m²)	28.22 ± 0.91	25.25 ± 1.19	−2.92 ± 0.85**	−10.3%
Percent body fat	28.13 ± 4.95	23.69 ± 4.95	−4.44 ± 2.00**	−15.8%
HR (bpm)	77.44 ± 4.15	74.88 ± 3.42	−2.56 ± 2.85*	−3.3%
SBP (mmHg)	125.38 ± 5.10	130.25 ± 9.60	4.88 ± 11.24	3.9%
DBP (mmHg)	81.88 ± 2.68	83.38 ± 3.70	1.50 ± 4.41	1.8%

Notes: *$P < 0.005$; **$P < 0.0001$.
Abbreviations: BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; M, median; SD, standard deviation.

experience using chlorogenic acids in a human study of the decrease in postprandial glucose.

Study design

This was a randomized, double-blind, 22-week study that implemented a crossover design to compare a low-dose green coffee extract, a high-dose green coffee extract, and a placebo. Subjects were randomly assigned to a high-dose/low-dose/placebo sequence (n = 6), low-dose/placebo/high-dose sequence (n = 4), or placebo/high-dose/low-dose sequence (n = 6). Subjects stayed on a treatment for a period of 6 weeks, followed by a 2-week washout period, before the next treatment period began.

Subjects were examined at weeks 0, 6, 8, 14, 16, and 22 of the study. Subjects were examined individually at Trinity Hospital, Bangalore, India. During each visit, the following measurements were taken: body weight to nearest 0.01 kg, height to nearest 0.01 cm, and a body fat percentage analysis using a SFB7 Bioimpedance device. BMI was determined using the formula of BMI = weight in kg divided by the square of the height in meters. All subjects were counseled for diet and exercise compliance at every visit, with the initial interview to establish diet details at the start of the study done by the site nutritionist. Data gathered included daily calorie intake, nutrient composition, micronutrient intake, and incidence of binge eating (see Table 3 for average diet intake information). The same procedure was repeated at the beginning of each cycle to reflect the diet during the previous cycle and subjects underwent pre- and post-assessment systolic and diastolic blood pressure and heart rate measurements, at every visit. Blood pressure was measured in the right forearm of the subject in a sitting position after a 10-minute rest using a standard mercury sphygmomanometer.

Statistical analysis

The primary measures in this study were weight, BMI, and body fat percentage; however, heart rate and blood pressure taken at each visit were also analyzed. Statistical analyses were carried out with a repeated-measures analysis of variance and post hoc t-tests. Factors for the analysis of variance were sequence (high-dose/low-dose/placebo versus low-dose/placebo/high-dose versus placebo/high-dose/low-dose), treatment arm (first versus second versus third treatment), and time (two evaluations per treatment arm). For the time factor, the first evaluation within each treatment arm (weeks 0, 8, 16) was considered a pretreatment evaluation, and the second evaluation within each treatment arm (weeks 6, 14, 22) was a post-treatment evaluation.

A statistically significant time × arm interaction indicates drug effects, ie, individually for the high-dose, low-dose, or placebo conditions. A significant sequence × arm × time interaction would indicate significant differences between the drug effects. Finding these interactions significant in the omnibus analysis of variance would validate the comparisons made between the beginning and end data.

Results

The statistical analyses report the test statistic P value. From the mean data reported in Table 1 there were statistically significant reductions in weight, BMI, percent body fat, and heart rate after consuming GCA for two-thirds of the 22-week crossover study, but there was no overall significant change in systolic or diastolic blood pressure. The mean values on all measures at the beginning and end of each treatment arm (high-dose, low-dose, placebo) assessed for all 16 subjects, are displayed in Table 2. The data show a reduction in weight, BMI, and percent body fat in the high-dose and low-dose arms, but not the placebo arm, and a reduction in heart rate in the high-dose arm, but not the low-dose and placebo arms. Figure 1 shows the mean weight change across the 22-week study for each of the three groups, and Figure 2 shows the mean change in BMI. A three-way repeated-measures analysis of variance (factor 1: sequence [high-dose/low-dose/placebo versus low-dose/placebo/high-dose versus placebo/high-dose/low-dose]; arm [first versus second versus third treatment]; and time [two evaluations]) on the data from all 16 subjects who were randomized into the crossover design was conducted on each of the primary outcome measures (weight, BMI, and percent body fat), as well as diastolic blood pressure, systolic blood pressure, and heart rate.

Primary outcome measures

There was a significant treatment arm effect for weight ($P < 0.001$), BMI ($P < 0.001$), and percent body fat ($P < 0.001$), showing an improvement in each measure over the course of the study. There was a significant time effect for weight ($P < 0.001$), BMI ($P < 0.001$), and percent body fat ($P < 0.001$), showing an improvement between the beginning and end for each arm. There was no significant difference between the three sequences ($P > 0.373$).

The sequence × arm interaction was significant for weight ($P < 0.004$), BMI ($P < 0.004$), and percent body fat ($P < 0.002$), indicating an overall difference in the arms across the three sequences, ie, a differential influence of each arm on each sequence. The arm × time interaction was

Table 2 Characteristics at start and end of each treatment arm for 16 preobese subjects

Characteristic	HD arm		P	LD arm		P	PL arm		P
	Start M ± SD (95% CI)	End M ± SD (95% CI)		Start M ± SD (95% CI)	End M ± SD (95% CI)		Start M ± SD (95% CI)	End M ± SD (95% CI)	
Weight (kg)	72.86 ± 8.91 (68.11–77.61)	70.82 ± 8.40 (66.34–75.30)	0.002	71.25 ± 7.30 (67.36–75.14)	69.71 ± 7.30 (65.82–73.60)	0.003	72.15 ± 8.64 (67.55–76.75)	72.47 ± 8.47 (67.96–76.98)	0.353
BMI (kg/m²)	26.78 ± 1.55 (25.95–27.61)	26.03 ± 1.36 (25.31–26.75)	0.002	26.25 ± 1.37 (25.52–26.98)	25.66 ± 1.20 (25.02–26.30)	0.003	26.55 ± 1.96 (25.51–27.59)	26.67 ± 1.72 (25.75–27.59)	0.384
Percent body fat	25.94 ± 5.35 (23.09–28.79)	24.75 ± 5.20 (21.98–27.52)	0.001	25.94 ± 4.99 (23.28–28.60)	24.88 ± 4.99 (22.22–27.54)	0.002	25.88 ± 5.40 (23.00–28.76)	25.00 ± 5.52 (22.20–27.82)	0.014
HR (bpm)	76.94 ± 2.64 (75.53–78.35)	75.12 ± 3.63 (73.19–77.05)	0.031	74.62 ± 4.56 (72.19–77.05)	74.87 ± 4.50 (72.47–77.27)	0.752	76.19 ± 5.13 (73.46–78.92)	75.81 ± 4.10 (73.63–77.99)	0.549
SBP (mmHg)	129.12 ± 8.10 (124.80–133.44)	129.62 ± 6.74 (126.03–133.21)	0.843	131.00 ± 6.93 (127.31–134.69)	128.25 ± 6.40 (124.84–131.66)	0.221	125.62 ± 6.90 (121.94–129.30)	131.62 ± 9.33 (126.65–136.59)	0.031
DBP (mmHg)	81.75 ± 3.00 (80.15–83.35)	81.62 ± 3.28 (79.87–83.37)	0.926	81.62 ± 9.24 (76.70–86.54)	83.00 ± 3.58 (81.09–84.91)	0.239	82.62 ± 2.39 (82.35–84.89)	83.50 ± 4.23 (81.25–85.75)	0.379

Abbreviations: CI, confidence interval; HD, high dose green coffee extract; LD, low dose green coffee extract; PL, placebo; BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; M, mean; SD, standard deviation.

significant for weight ($P < 0.001$), BMI ($P < 0.001$), and percent body fat ($P < 0.03$), indicating overall drug effects. This can be seen in Table 2, where there were improvements in weight, BMI, and percent body fat in the high-dose and low-dose arms, but not the placebo arm. For weight, the 2.04 ± 2.20 kg decrease in the high-dose arm was significant ($P < 0.003$), as was the 1.54 ± 1.74 kg decrease in the low-dose arm ($P < 0.005$); but the -0.34 ± 1.41 kg change in the placebo arm was not significant ($P = 0.355$). For BMI, the 0.74 ± 0.80 kg/m² decrease in the high-dose arm was significant ($P < 0.003$), as was the 0.58 ± 0.66 kg/m² decrease in the low-dose arm ($P < 0.004$); but the -0.12 ± 0.51 kg/m² change in the placebo arm was not significant ($P = 0.384$). For percent body fat, the $1.19\% \pm 1.22\%$ decrease in the high-dose arm was significant ($P < 0.002$), as was the $1.06\% \pm 1.12\%$ decrease in the low-dose arm ($P < 0.003$); surprisingly, the decrease was also significant in the placebo arm $0.88\% \pm 1.26\%$ ($P = 0.015$). The sequence × time interaction was marginally nonsignificant for weight, ($P = 0.08$), was marginally significant for BMI ($P = 0.049$), and was significant for percent body fat ($P < 0.001$).

Most importantly, the triple interaction was significant for weight ($P < 0.001$) and BMI ($P < 0.001$), but not for percent body fat ($P = 0.239$). For weight, the 2.04 ± 2.20 kg decrease in the high-dose arm was greater than the 0.34 ± 1.41 kg increase in the placebo arm ($P < 0.013$), and the 1.54 ± 1.74 kg decrease in the low-dose arm was greater than the 0.34 ± 1.41 kg increase in the placebo arm ($P < 0.001$). The change in weight in the high-dose arm was not different from the change in weight in the low-dose arm ($P = 0.544$). For BMI, the 0.74 ± 0.80 kg/m² decrease in the high-dose arm was greater than the -0.12 ± 0.51 kg/m² change in the placebo arm ($P < 0.013$), and the 0.58 ± 0.66 kg/m² decrease in the low-dose arm was greater than the change in the placebo arm ($P < 0.002$). The change in BMI for the high-dose arm and low-dose arm did not differ ($P = 0.589$). A telephone interview was done 4 months post-trial, and 14 of the 16 subjects maintained their weight loss at the end of the study, while two subjects gained 1 kg and 0.75 kg.

Vital measures

Similar repeated-measures analysis of variance were performed on vital measures (heart rate, systolic blood

Table 3 Diet profile for 16 preobese subjects at beginning and during each arm of the study

Measurement time	Daily calorie intake (%) M ± SD	Daily carbohydrate intake (%) M ± SD	Daily fat intake (%) M ± SD	Daily protein intake (%) M ± SD	Binge eating incidence (n)
Beginning of study	2443.75 ± 260.69	58.75 ± 8.06	25.00 ± 9.66	16.25 ± 6.19	0
Arm 1	2406.25 ± 161.12	60.00 ± 6.32	24.38 ± 8.14	15.62 ± 6.29	0
Arm 2	2393.75 ± 161.12	61.25 ± 7.19	23.12 ± 10.14	15.62 ± 6.29	0
Arm 3 (end of study)	2418.75 ± 137.69	59.38 ± 6.80	25.00 ± 8.94	15.62 ± 6.29	0

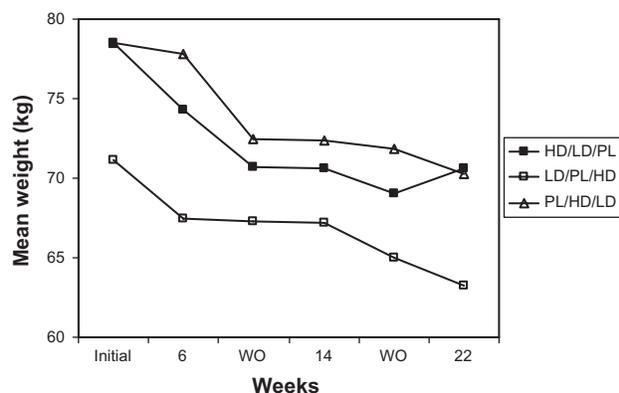**Abbreviations:** M, mean; SD, standard deviation.

Figure 1 Mean weight changes over time for 16 subobese subjects.
Abbreviations: WO, washout; LD, low-dose; HD, high-dose; PL, placebo.

pressure, diastolic blood pressure). For heart rate, there was a marginally nonsignificant sequence effect ($P = 0.065$), and arm × time interaction ($P = 0.083$). The only significant result was a time effect ($P < 0.007$), reflecting an improvement between the beginning and end for each arm. No other effect was significant ($P > 0.165$). There were no significant results in the analysis of diastolic blood pressure ($P > 0.202$). For systolic blood pressure, there was a significant arm effect ($P < 0.005$), reflecting a surprising increase in systolic blood pressure across the three arms. There was also a marginally nonsignificant triple interaction ($P = 0.055$) versus 14 weeks.

All subjects completed the study and there were no side effects of using GCA. Regarding nutrient intake, there were no significant changes in calories, percentage carbohydrates, percentage fat, or percentage proteins at any time during the study. In looking at the individual effects of the GCA; 16 of 16 lost weight, 16/16 had decreased percent body fat 16/16 had a reduction in BMI, 3/13 experienced a decrease in systolic blood pressure, and 5/16 a reduction
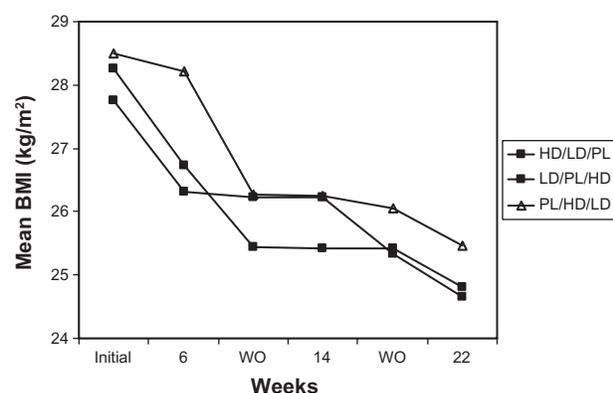

Figure 2 Mean BMI changes over time for 16 preobese subjects.
Abbreviations: WO, washout; LD, low-dose; HD, high-dose; PL, placebo.

in diastolic blood pressure. Twelve of 16 had a decrease in heart rate. The decrease in heart rate of 2 beats per minute was significant but was of a lower magnitude than produced by a thermogenic combination of polyphenols, hesperidin, naringenin, and p-synephrine.[11] The lowest heart rate at the end of the study was 68 beats per minute. According to one of the cited study authors a decrease of 2 beats per minute is not clinically significant (H Preuss, personal communication) but is of benefit for heart health.

Discussion

The mechanism(s) of the significant effects of GCA on weight loss, BMI, percent body fat, and heart rate are unknown. There have been some recent articles indicating that chlorogenic acid and its metabolite, caffeic acid, inhibit amylase at mM concentrations in vitro which, if it occurred in the gastrointestinal tract in vivo, would inhibit sugar absorption from starch consumption and thus decrease caloric input.[12] That chlorogenic acid has a significant influence on glucose metabolism was well demonstrated by Rodrigues de Sotillo et al when they were able to demonstrate a significant improvement in glucose tolerance in Zucker rats.[13] This relative deprivation of glucose could possibly explain the reduction in BMI as well as fat content seen in their other rat study[14] and in our human study. Another group has clearly demonstrated that chlorogenic acid may in fact have an antagonistic effect on human glucose transport.[15] Based on the dietary data in our study, the product was not an appetite suppressant. Extracts of green coffee beans inhibited pancreatic lipase in vitro with a 50% inhibitory concentration of 43 µM polyphenols.[16] In support of this result, caffeinated but not decaffeinated coffee supplementation in humans produced a decrease in lipoprotein lipase.[17]

Animal experiments have additionally demonstrated the effect of green coffee extract on fat metabolism, with chlorogenic acid alone having a moderate effect.[18] They were able to obtain significant data suggesting that chlorogenic acid not only retards the absorption of fats from the intestine but also activates fat metabolism in the liver. This was demonstrated by significantly lower levels of liver triglycerides after chlorogenic acid ingestion. A recent study in Japan found that coffee polyphenols enhance energy metabolism and reduce lipogenesis by downregulating sterol regulatory element-binding protein and similar molecules, which leads to the suppression of body fat accumulation.[19] Recently, intraperitoneal injection of chlorogenic acid to hamsters fed a high-fat diet caused an improvement in lipid profile, reduction in hepatic lipase, reduction in glucose and insulin and increased expression of peroxisome proliferator-

activated receptor. This is one of the key regulators of lipids and glucose.[20]

There have been a few human studies with green coffee extract. Thom investigated the efficacy and tolerability of a green coffee extract (Svetol®) added to instant coffee and compared within a randomized, placebo-controlled, double-blind study.[21] The product reduces the absorption of different types of sugar from the gastrointestinal tract. Forty obese volunteers were included in the 12-week study. Body weight, body composition, and blood pressure were recorded at baseline and every month during the study. The results show a significant difference in weight reduction in favor of the active group (5.4 kg versus 1.7 kg, a 4% decrease versus the placebo). BMI decreased 2.9% or 10%. There was a significant inhibitory effect of the product compared to glucose, and instant coffee, on glucose absorption in a glucose tolerance test. This same commercial product was investigated by another group.[22] The weight loss after 12 weeks was almost 5 kg in the treated groups and 2.5 kg in the placebo. A roasted and blended Arabica coffee rich in both green and roast bean constituents was tested in humans.[23] The coffee product caused a significant weight loss averaging 0.7 kg and a significant 5% loss of body fat along with a significant decrease in lymphocyte DNA damage. A meta-analysis of the three published and unpublished studies on these products concluded that the average weight loss of 2.5 kg was moderate and the results were promising.[26]

The results of our study are much more dramatic for weight loss and BMI than previous green coffee extract investigations. The subjects averaged slightly over an 8 kg weight loss which was more than 10% of the body weight. For our study 10 of 16 subjects showed at least a 10% weight loss; five of the remaining six showed at least 5% weight loss; and the last individual showed a 4% weight loss. The most remarkable result was the fact that all 16 of the subjects were classified as overweight at the beginning of the study and at the end six of the subjects were now in the normal BMI category, ie, a normal weight for their height. It must be said that the daily dose of GCA in this study ranged from 700 to 1050 mg and previous studies ranged from 180 to 200 mg/day.[24] There were no adverse effects in our study with the higher doses nor in the previous human studies according to the authors of the meta-analysis paper. It should not be overlooked that there was a slight (4.88 ± 11.24 mmHg) though nonsignificant increase in systolic blood pressure over the course of the study, which appears to be isolated to the placebo arm (see Table 2).

Other limitations were the small sample size of the study and the short washout periods between arms. Also, taking GCA three times per day in the high-dose arm and twice per day in the low-dose arm may have alerted subjects to dosage amount, at least in the low-dose arm. We do not believe sample size to have been a problem, given the linear crossover design of the study. This eliminates any possibility of the results reflecting a difference between groups, instead of between dosages. Also, all variables were objective measures, and follow-up showed that a majority of subjects (14 of 16) were able to maintain their lowered weight after the completion of the study.

Five drugs had been approved by the Food and Drug Administration, all of which exhibit weight loss. There are two currently approved for weight loss with sibutramine having been withdrawn from approval in 2011 due to tachycardia.[25] A recent review performed a meta-analysis of 30 trials of weight loss drugs of 1–4 years' duration, ie, 16 orlistat (n = 10,631 participants), 10 sibutramine (n = 2623), and four rimonabant (n = 6365). Attrition rates averaged 30%–40%. Compared with placebo, orlistat reduced weight by 2.9 kg (2.9%) sibutramine by 4.2 kg (4.3%), and rimonabant by 4.7 kg (4.1%). BMI reductions were 1.0 with orlistat and 1.5 with sibutramine. Lack of adherence to treatment seems to be a major factor limiting the efficacy and effectiveness of antiobesity drugs.[26] Thus the GCA with a weight loss of 8 kg (10.5%) and a BMI reduction of almost 3 makes the product superior to the prescription drugs. Weight loss of 5%–10% of initial body weight reduces cardiovascular and metabolic health risks associated with obesity.[27]

In a recent Israeli postmarketing study of over one million individuals, fewer than 2% completed 12 months of weight loss medication.[28] Those who continued for at least 4 months experienced a decrease in BMI of only 1 with a cost of $50–100 per month. GCA should provide an all natural, lower cost source as an effective therapy for overweight individuals. The efficacy for type 2 diabetics who have more coronary heart disease risk remains to be investigated.

Disclosure
The authors report no conflicts of interest in this work.

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