

Supplementation of green coffee bean extract in healthy overweight subjects increases lean mass/fat mass ratio: A randomized, double-blind clinical study

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Abstract

Objective: In this study, we have demonstrated that supplementation of a complex of chlorogenic acid isomers (CGA-7™) could significantly mitigate the risk of obesity in healthy overweight subjects.

Method: In a double-blind, placebo-controlled clinical study, healthy overweight (body mass index ≥ 25 to <30 kg/m²) male and female subjects ($N = 71$) were randomly allocated to receive 500 mg CGA-7 or placebo daily for 12 weeks. Changes in body weight and body mass index were recorded alongside vital signs and anthropometric measurements at week 4, 8 and 12. Body composition was assessed at baseline and the end of treatment using dual-energy X-ray absorptiometry. Safety analysis included serum biochemical and haematological assessments and measurement of vital signs. In addition, any adverse or serious adverse events were recorded during the study.

Results: Sixty subjects completed the study. Mean body weight and body mass index were significantly reduced in CGA-7 group as compared to placebo ($p < 0.001$). CGA-7 group showed significant changes in body fat (%), fat mass and lean mass in comparison with placebo group ($1.38\% \pm 1.4\%$ vs $-0.22\% \pm 0.86\%$, 1.97 ± 1.44 kg vs -0.39 ± 1.31 kg; 0.81 ± 1.20 kg vs -0.13 ± 0.97 kg, $p < 0.001$). Consumption of CGA-7 significantly improved the serum lipid profile. Importantly, CGA-7 consumption in humans had no adverse effects and was well tolerated during the study. The blood biochemical and haematological parameters marginally varied in the treatment groups throughout the study.

Conclusion: To conclude, this study provides scientific validation of the functionality of green coffee bean extract and recommends the safety of the supplementation in healthy individuals.

Keywords

Overweight, green coffee bean, chlorogenic acids, dual-energy X-ray absorptiometry, safety

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Introduction

Overweight and obesity are increasingly common conditions affecting a large population worldwide.¹ Obesity being a serious medical condition is characterized by an excessive accumulation of adipose tissue that can cause complications such as metabolic syndrome, high blood pressure, atherosclerosis, heart disease, diabetes, high blood cholesterol, cancers and sleep disorders.² Obesity management include lifestyle changes, such as heart-healthy eating and increased physical activity, and Food and Drug Administration (FDA)-approved weight-loss medicines.^{3,4} In addition, natural medicine of plant origin has been welcomed by the public at large for weight loss.⁵ A raft in research on obesity management is evident following the recent interest on consumption

of natural supplements.^{6,7} A variety of natural products, including crude extracts and isolated pure natural compounds can induce body weight reduction and prevent diet-induced obesity.⁸ Phytochemicals exhibit anti-obesity effects by multiple mechanisms, which includes pancreatic lipase inhibition,^{9,10} appetite suppression,¹¹ energy expenditure stimulation,¹² adipocyte differentiation inhibition^{13,14} and regulation of lipid metabolism.¹⁵

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Green coffee bean extract is reported to have several health benefits including weight management.^{16,17} The physiological functions of the extract are mainly attributed to the chlorogenic acids (CGAs) present as a major phytoconstituent.¹⁸ Other bioactive constituents include caffeic, vanillic, p-coumaric and feruloyl acids, trigonelline, tannins and anthraquinones.^{19,20} CGA-7 is a standardized extract from *C. arabica* green coffee beans (NLT 50% CGAs) containing seven isomers of CGAs, 5-caffeoylquinic acid being the major constituent. We have studied previously the effect of CGA-7 on factors involved in beta oxidation in high-fat-diet (HFD)-fed rats.²¹ Interestingly, we have observed through the findings that CGA-7 mediated fatty acid catabolism in rats through the activation of AMP-activated protein kinase (AMPK) and regulation of downstream proteins such as Acetyl CoA carboxylase (ACC), carnitine palmitoyl transferase CPT-1. These data from preclinical studies prompted us to evaluate the potency of CGA-7 further through clinical trial.

The available human clinical trials suggest that green coffee bean extract supplement may be effective in promoting weight loss in overweight/obese subjects. Studies performed on animals have suggested the possible mechanism of action with which CGA exerts its lipid-lowering effect and improving insulin sensitivity. The previous studies, however, considered the CGA-rich green coffee bean extract. Here, we have used the green coffee bean extract standardized to contain seven isomers of CGA (CGA-7). The validation of weight loss benefits of CGA-7 in overweight subjects was based on the subjective assessments using dual-energy X-ray absorptiometry (DEXA) analysis. Another important aspect of this trial was to assess the safety of the extract in human volunteers.

Materials and methods

Investigational product

The investigational product was a standardized decaffeinated green coffee bean extract containing not less than 50% of CGAs (CGA-7TM). Details of high-performance liquid chromatography (HPLC) analysis are provided in Supplementary file 1. CGA-7 is the proprietary extract from Vidya Herbs Pvt Ltd. CGA-7 was administered to the subjects in capsular form. The placebo was a capsule with the same appearance and taste (odourless) as the test supplement. The investigational product was stored in a secure location with limited access under room temperature, in a cool dry area.

Ethics, consent and permission

The Institutional Ethics Committee (IEC) of Sri Kalabyraveshwara Swamy Ayurvedic Medical College, Hospital and Research Center, Karnataka, India approved the study protocol and informed consent form (SKAMC/189/2016-17). This clinical study was retrospectively registered in Clinical Trials Registry – India (CTRI/2017/04/008295 dated 05/04/2017).

Subjects

The study population included male and non-pregnant female subjects of age between 18 and 60 years without any significant medical history that may interfere with the conduct of the study as per the discretion of the principal investigator. Overweight subjects with a body mass index (BMI) of 25–30 kg/m² and willing to give written informed consent were included for the study. Criteria for exclusion from the study included patients with heart, liver, kidney disease, hypertension, type 1 diabetes. Pregnant or lactating women, or having smoking habit or undertaking weight loss medication were also excluded from the study. Before enrolment, the subjects were detailed about the clinical study protocol approved by the IEC. The informed consent and the consent to publish were obtained before beginning the study.

Study design

This study was conducted in compliance with ICH-GCP (International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use – Good Clinical Practice) guidelines and Helsinki Declaration Standards. This clinical study adheres to the CONSORT guidelines. The study was conducted in the year 2017 (date of first subject enrolment: 4 January 2017; date of last subject completed: 24 November 2017).

This was a single-centred, randomized, double-blind, placebo-controlled, parallel group study including a total of 71 male and female subjects randomized in a 1:1 ratio (CGA-7 vs placebo). As subjects signed a consent form, each subject was sequentially issued a subject ID, and upon qualifying, randomized to the investigational product based on the randomization scheme. Block randomization was used wherein the block size was 4 assigning the participants according to the specified sequence. The interventions were double blinded. Study medications were dispensed through an unblinded pharmacist as per the randomization schedule, along with instructions for the proper storage and administration of the same.

The study was conducted at Sri Kalabyraveshwara Swamy Ayurvedic Medical College, Hospital and Research Center, Karnataka, India. The total duration of the study was 14 weeks including a 12-week treatment and 2 weeks follow-up period. The subjects consumed oral doses of 250 mg capsules twice daily (before breakfast and dinner) for 12 weeks. Based on our previous studies in preclinical model, we have ascertained the dosage for therapeutic intervention.²¹ No diet restrictions were advised in the study and throughout the treatment period, the subjects were instructed to follow normal diet (2000–2500 cal). However, all the subjects were provided with the caloric information of diet for reference. The diet chart is provided as Supplementary file 2.

Following the baseline visit, there were three visits during the treatment period every 4 weeks. Two weeks after the 12-week treatment period, there was a follow-up visit scheduled. The details of study procedures are provided in Supplementary file 3.

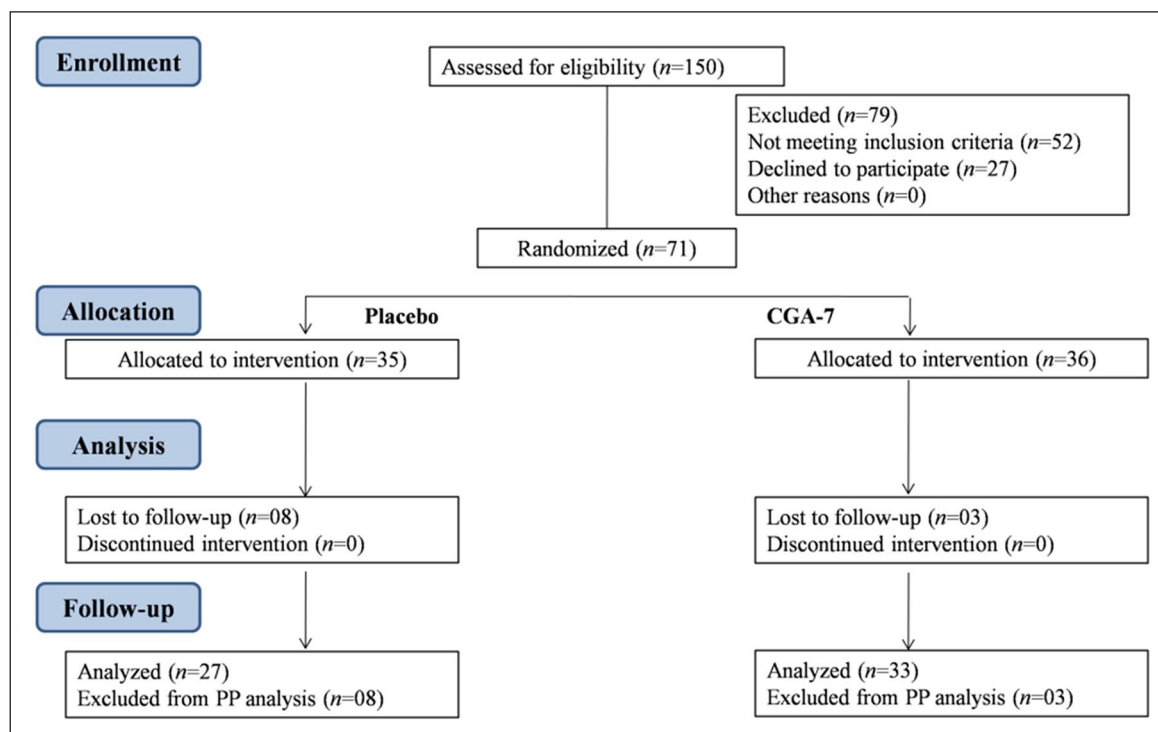


Figure 1. Study participant flow chart.

Sample size

The sample size calculation based on difference between the treatments are medically relevant. Assuming a common standard deviation (SD) of 1.5 at the end of treatment, 31 per group would be sufficient to detect a difference of 1.1 in mean difference between the two treatments with power of 80% and a 0.05 two-sided level of significance; considering a dropout of 10%, final sample size is calculated. Assumptions were based on the preclinical data. Details of sample size calculation are provided in Supplementary file 4.

Study parameters

The efficacy analysis included assessment of parameters such as body weight and BMI recorded during all the visits. DEXA analysis was employed to determine the body composition of the subjects, measured at baseline (visit 1) and the end of treatment (visit 4). DEXA scan was performed using a total body scanner (GE Healthcare, Lunar DPX NT, Madison, WI); at the end of the scan, the total and regional analyses were done through the software. The body fat (%), lean and fat mass were considered in this study. The blood lipid analysis included total cholesterol (TC), triglycerides (TG), low-density lipoprotein-cholesterol (LDL-c) and high-density lipoprotein-cholesterol (HDL-c) measured using commercial kits in an automated clinical chemistry analyzer (TurboChem 240, CPC Diagnostics Pvt Ltd., India). Anthropometric parameters such as waist and hip circumference of subjects

were measured using a tape at all the scheduled visits and the waist/hip ratio was determined.

The safety of CGA-7 was assessed by measuring the vital signs, haematological parameters, urinalysis and clinical chemistry parameters such as fasting blood glucose, glycosylated haemoglobin HbA1c, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), total bilirubin and direct bilirubin at baseline and the end of treatment.

Statistical analysis

The statistical analysis was performed using SPSS software (16.0). The data were expressed as mean \pm SD. Student's *t*-test was used to assess the differences between means. Difference between categorical variables was analysed by chi-square and, the analysis of variance (ANOVA) for continuous variables. All significance tests were two-sided using 0.05 significance level; $p < 0.05$ was considered as statistically significant.

Results

A total of 150 subjects were screened of which 71 subjects meeting the inclusion criteria were enrolled in the study. Of the 71 subjects randomized to two treatment groups, 60 subjects completed the study. There were 11 dropouts in the study (reason: lost to follow-up). The per protocol (PP) analysis was used to assess the outcome of the study. The participant flowchart is presented in Figure 1. The demographic characteristics of subjects between the groups were not

Table 1. Demographic characteristics of subjects.

Variable	Intervention (CGA-7) (n = 36)	Placebo (n = 35)	All (71)	p-value*
Age (years)	34.18 ± 9.37	31.71 ± 6.59	32.96 ± 8.16	0.204
Weight (kg)	165.67 ± 9.02	163.03 ± 9.31	164.37 ± 9.2	0.229
Height (cm)	75.23 ± 6.75	72.84 ± 7.89	74.05 ± 7.38	0.175
BMI (kg/m ²)	27.41 ± 1.19	27.37 ± 1.38	27.39 ± 1.28	0.908

n: number of subjects; BMI: body mass index.

Date presented as mean ± standard deviation.

*p-values were derived from analysis of variance (ANOVA).

Table 2. Summary of mean bodyweight and BMI changes during the study.

Visit	CGA-7				Placebo				p-value between groups
	N	Mean ± SD	Median	Min, Max	N	Mean ± SD	Median	Min, Max	
Body weight (kg)									
Visit_1	33	75.34 ± 6.70	73.0	65, 86	27	72.40 ± 6.81	73.0	60.4, 85	0.099 ^a
Visit_4	33	72.71 ± 6.56	71.5	60, 84	27	73.07 ± 6.71	74.0	62, 85	0.834 ^a
Change	33	2.63 ± 1.46	2.0	-0.1, 5	27	-0.67 ± 1.54	-1.0	-4, 2.5	<0.001 ^{a***}
p-value (visit_1 vs visit_4)		<0.001 ^{b***}				0.031 ^{b*}			
BMI (kg/m²)									
Visit_1	33	27.52 ± 1.20	27.5	25.1, 29.7	27	27.33 ± 1.38	27.5	25, 29.4	0.570 ^a
Visit_4	33	26.58 ± 1.12	26.6	24.4, 28.6	27	27.58 ± 1.49	27.8	24.9, 30.1	0.005 ^{a*}
Change	33	0.93 ± 0.57	0.8	-0.1, 2.3	27	-0.25 ± 0.60	-0.3	-1.7, 0.9	<0.001 ^{a***}
p-value (visit_1 vs visit_4)		<0.001 ^{b***}				0.040 ^{b*}			

CGA: chlorogenic acid; BMI: body mass index.

Change = Visit_1 – Visit_4.

^aIndependent t-test.

^bPaired t-test (visit_1 vs visit_4).

*p < 0.05.

**p < 0.001.

significantly different (Table 1). The efficacy and safety analysis were performed using PP population.

Effect of CGA-7 treatment on body weight and BMI

Table 2 shows the mean change in body weight and BMI during the study. The mean body weight of subjects in the CGA-7 group decreased from baseline 75.09 ± 6.6 to 72.71 ± 6.56 at visit 4 (12 weeks; $p < 0.001$). The reduction in mean body weight from baseline to visit 4 in CGA-7 group (2.63 ± 1.46) was highly significant ($p < 0.001$) as compared to placebo (-0.67 ± 1.54). Similar trend was observed in the mean BMI changes from baseline to visit 4 in CGA-7 group as compared to placebo ($p < 0.001$).

Effect of CGA-7 on body composition and anthropometric measures

The body composition of subjects was measured at baseline visit and after 12-week treatment by DEXA analysis (Table 3). There was a significant decrease ($p < 0.001$) in body fat

percentage in the CGA-7-treated subjects from baseline (42.88 ± 8.19) to visit 4 (41.00 ± 9.19). The subjects in the CGA-7 group showed a significant body fat reduction (1.38% ± 1.40%) from baseline to the end of treatment compared to placebo (-0.22% ± 0.86%; $p < 0.001$).

DEXA analysis revealed that CGA-7 administration significantly reduced the fat mass and the lean mass among the subjects, from baseline to the end of treatment ($p < 0.001$). However, in the placebo group, there was no significant change observed in the fat and lean mass. Furthermore, there was significant increase in the lean mass/fat mass ratio after the treatment with CGA-7 ($p < 0.001$). The changes in fat mass, lean mass and lean mass to fat mass ratio were significant in the CGA-7 group as compared to placebo at the end of study ($p < 0.001$).

In this study, anthropometric measurements of the study participants were recorded (Table 4). A 12-week treatment with CGA-7 significantly reduced the waist ($p < 0.001$) and hip circumference ($p < 0.05$) of the subjects as compared to baseline. The waist circumference changed significantly compared to placebo, while there was an insignificant change in hip circumference observed in CGA-7 treatment group.

Table 3. Summary of mean body fat (%), fat mass and lean mass changes during the study.

Visit	CGA-7				Placebo				p-value between groups
	N	Mean ± SD	Median	Min, Max	N	Mean ± SD	Median	Min, Max	
Body fat (%)									
Visit_1	33	42.38 ± 8.38	45.3	30, 51.9	27	43.94 ± 7.72	47.0	25.5, 53.4	0.460 ^a
Visit_4	33	41.00 ± 9.19	45.1	24.3, 51	27	44.16 ± 7.63	47.2	26.1, 53.8	0.151 ^a
Change	33	1.38 ± 1.40	1.10	0.1, 6.9	27	-0.22 ± 0.86	-0.30	-1.8, 2.7	<0.001 ^{a***}
p-value (visit_1 vs visit_4)		<0.001 ^{b***}				0.200 ^b			
Fat mass (kg)									
Visit_1	33	32.38 ± 4.43	33.52	25.32, 39.16	27	32.57 ± 5.34	33.61	19.36, 40.24	0.965 ^a
Visit_4	33	30.41 ± 5.33	31.62	20.86, 38.22	27	32.96 ± 5.03	34.21	20.65, 41.23	0.063 ^a
Change	33	1.97 ± 1.44	1.37	-0.46, 6.6	27	-0.39 ± 1.31	-0.57	-2.55, 2.42	<0.001 ^{a***}
p-value (visit_1 vs visit_4)		<0.001 ^{b***}				0.136 ^b			
Lean mass (kg)									
Visit_1	33	39.86 ± 9.77	37.94	27.31, 56.87	27	36.82 ± 7.86	32.73	26.84, 50.27	0.251 ^a
Visit_4	33	39.05 ± 9.72	38.13	26.62, 58.77	27	36.95 ± 7.87	32.45	27.3, 50.07	0.369 ^a
Change	33	0.81 ± 1.20	0.698	-1.89, 5.26	27	-0.13 ± 0.97	0.08	-1.68, 2.88	0.0018 ^{a***}
p-value (visit_1 vs visit_4)		<0.001 ^{b***}				0.499 ^b			
Lean mass/fat mass ratio									
Visit_1	33	1.49 ± 0.49	1.4	0.9, 2.6	27	1.39 ± 0.53	1.1	0.9, 2.9	0.472 ^a
Visit_4	33	1.55 ± 0.56	1.3	0.9, 2.6	27	1.36 ± 0.47	1.1	0.9, 2.5	0.166 ^a
Change	33	-0.06 ± 0.09	-0.04	-0.3, 0.1	27	0.03 ± 0.09	0.02	-0.1, 0.4	<0.001 ^{a***}
p-value (visit_1 vs visit_4)		<0.001 ^{b***}				0.053 ^b			

CGA: chlorogenic acid.

Change = Visit_1 - Visit_4.

^aIndependent t-test.^bPaired t-test (visit_1 vs visit_4).**p* < 0.05.***p* < 0.01.****p* < 0.001.

Subsequently, the waist/hip ratio was significantly changed (*p* < 0.001) in the CGA-7 group (0.01 ± 0.02) compared to placebo (-0.001 ± 0.01).

Effect of CGA-7 on serum lipid profile

Table 5 shows the changes in the mean levels of serum lipids. The total cholesterol level of the subjects in the CGA-7 group was significantly (*p* < 0.001) reduced from baseline (185.53 ± 14.17) to the end of study (178.97 ± 12.36). However, the change in cholesterol levels was not significant compared to placebo. Serum triglyceride level was significantly decreased in the CGA-7 group (124.11 ± 15.22 at baseline to 116.03 ± 9.23; *p* < 0.01). The mean change in triglycerides was significant compared to placebo (*p* < 0.05). CGA-7 treatment markedly reduced the LDL-c from baseline (128.33 ± 10.5) to the end of study (120.27 ± 9.91; *p* < 0.001). Interestingly, it was observed that there was significant reduction of LDL-c among the subjects in the placebo group (*p* < 0.05). CGA-7 group also showed considerable increase in HDL-c (*p* < 0.05) compared to baseline. However, the changes in LDL-c and HDL-c were not significant compared to placebo.

Effect of CGA-7 on blood biochemical parameters

CGA-7 ingested for 12 weeks at 500 mg/day did not significantly alter the serum biochemical markers of liver function compared to placebo (Table 6). The changes in plasma HbA1c levels were insignificant in CGA-7 group while it was found to be significantly increased (*p* < 0.05) in placebo group from baseline (5.80 ± 0.63) to the end of treatment (6.62 ± 1.00). The changes in the HbA1c from baseline to the end of treatment were significant between the groups (*p* < 0.01). Liver function markers such as AST and ALT were insignificantly changed in the treatment groups. Interestingly, the ALP level was significantly reduced in CGA-7 group compared to the baseline (*p* < 0.05). There was no significant change observed in the fasting blood glucose (FBG).

The haematological assessment revealed marginal variations in the haemoglobin, total cell count, red blood cell (RBC) count and the mean corpuscular haemoglobin concentration (MCHC, %) (Table 7). However, the data were not significant. CGA-7 group showed a significant increase in the platelet count (*p* < 0.01), mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH; *p* < 0.05)

Table 4. Summary of changes in anthropometric parameters during the study.

Visit	CGA-7				Placebo				p-value between groups
	N	Mean ± SD	Median	Min, Max	N	Mean ± SD	Median	Min, Max	
Waist circumference (cm)									
Visit_1	33	96.24 ± 6.89	97.0	80, 114	27	92.05 ± 5.68	93.0	80, 103	0.014 ^{a*}
Visit_4	33	94.79 ± 7.05	96.0	77, 114	27	92.17 ± 6.26	93.0	77, 103	0.138 ^a
Change	33	1.45 ± 1.44	1.0	-1, 6	27	-0.12 ± 1.56	0.0	-3, 3	<0.001 ^{a**}
p-value (visit_1 vs visit_4)		<0.001 ^{b**}				0.697 ^b			
Hip circumference (cm)									
Visit_1	33	103.56 ± 6.04	104.0	96, 132	27	101.18 ± 3.75	101.0	91, 111	0.081 ^a
Visit_4	33	102.98 ± 6.42	103.0	93.5, 132	27	101.14 ± 4.20	102.0	89, 111	0.203 ^a
Change	33	0.57 ± 1.21	0.0	-2, 5.5	27	0.05 ± 1.52	0.0	-2, 5.5	0.143 ^a
p-value (visit_1 vs visit_4)		0.011 ^{b*}				0.871 ^b			
Waist/hip ratio									
Visit_1	33	0.93 ± 0.05	0.9	0.8, 1.1	27	0.91 ± 0.05	0.9	0.8, 1	0.153 ^a
Visit_4	33	0.92 ± 0.05	0.9	0.8, 1.1	27	0.91 ± 0.05	0.9	0.8, 1	0.499 ^a
Change	33	0.01 ± 0.02	0.0	0, 0.1	27	-0.001 ± 0.01	0.0	0, 0	0.013 ^{a*}
p-value (visit_1 vs visit_4)		0.003 ^{b*}				0.622 ^b			

CGA: chlorogenic acid.

Change = Visit_1 - Visit_4.

^aIndependent t-test.^bPaired t-test (visit_1 vs visit_4).

*p < 0.05.

**p < 0.01.

***p < 0.001.

Table 5. Summary of mean changes in lipid profile during the study.

Visit	CGA-7				Placebo				p-value between groups
	N	Mean ± SD	Median	Min, Max	N	Mean ± SD	Median	Min, Max	
Total cholesterol (mg/dL)									
Visit_1	33	186.79 ± 13.94	186.0	158, 212	27	203.44 ± 74.36	186.0	164, 464	0.261 ^a
Visit_4	33	178.97 ± 12.36	180.0	152, 198	27	188.33 ± 22.89	185.0	162, 289	0.048 ^{a*}
Change	33	7.82 ± 8.14	9.00	-10, 24	27	15.11 ± 82.77	-3.00	-107, 302	0.652 ^a
p-value (visit_1 vs visit_4)		<0.001 ^{b**}				0.352 ^b			
Triglycerides (mg/dL)									
Visit_1	33	124.18 ± 15.85	122.0	94, 188	27	117.96 ± 12.81	116.0	96, 144	0.105 ^a
Visit_4	33	116.03 ± 9.23	114.0	98, 134	27	119.52 ± 13.14	119.0	97, 142	0.233 ^a
Change	33	8.15 ± 15.56	6.00	-17, 78	27	-1.56 ± 13.65	-1.00	-25, 24	0.014 ^{a*}
p-value (visit_1 vs visit_4)		0.005 ^{b**}				0.559 ^b			
LDL-c (mg/dL)									
Visit_1	33	128.79 ± 10.56	128.0	100, 146	27	127.44 ± 9.08	126.0	106, 144	0.604 ^a
Visit_4	33	120.27 ± 9.91	121.0	100, 138	27	121.70 ± 11.85	124.0	100, 148	0.612 ^a
Change	33	8.52 ± 8.35	8.00	-10, 24	27	5.74 ± 13.79	4.00	-31, 30	0.364 ^a
p-value (visit_1 vs visit_4)		<0.001 ^{b**}				0.040 ^{b*}			
HDL-c (mg/dL)									
Visit_1	33	44.52 ± 3.51	44.0	40, 52	27	44.52 ± 3.24	44.0	40, 52	0.997 ^a
Visit_4	33	46.09 ± 3.28	46.0	40, 52	27	44.59 ± 8.41	44.0	12, 58	0.351 ^a
Change	33	-1.58 ± 3.80	-2.00	-9, 7	27	-0.07 ± 9.66	-1.00	-17, 34	0.452 ^a
p-value (visit_1 vs visit_4)		0.023 ^{b*}				0.969 ^b			

CGA: chlorogenic acid; LDL-c: low-density lipoprotein-cholesterol; HDL-c: high-density lipoprotein-cholesterol.

Change = Visit_1 - Visit_4.

^aIndependent t-test.^bPaired t-test (visit_1 vs visit_4).

*p < 0.05.

**p < 0.01.

***p < 0.001.

Table 6. Summary of changes in blood biochemical parameters.

Visit	CGA-7			Placebo			p-value between groups
	N	Mean \pm SD	p-value (visit_1 vs visit_4)	N	Mean \pm SD	p-value (visit_1 vs visit_4)	
HbA1c							
Visit_1	33	5.94 \pm 0.81	0.419 ^a	35	5.87 \pm 0.69	0.011 ^{a*}	0.355 ^b
Visit_4	33	5.83 \pm 0.63		27	6.62 \pm 1.00		<0.001 ^{b***}
Change	33	0.109 \pm 0.77		27	-0.76 \pm 1.42		0.004 ^{b***}
AST (IU/L)							
Visit_1	36	28.03 \pm 3.26	0.782 ^a	35	28.19 \pm 3.57	0.493 ^a	0.836 ^b
Visit_4	33	27.88 \pm 2.99		27	27.70 \pm 2.49		0.809 ^b
Change	33	0.15 \pm 8.51		27	0.48 \pm 3.6		0.705 ^b
ALT (IU/L)							
Visit_1	36	32.82 \pm 3.23	1.000 ^a	35	32.37 \pm 3.76	0.147 ^a	0.520 ^b
Visit_4	33	32.82 \pm 2.72		27	33.33 \pm 2.76		0.471 ^b
Change	33	0.0 \pm 3.47		27	-0.96 \pm 3.35		0.282 ^b
ALP (IU/L)							
Visit_1	36	96.09 \pm 4.69	0.012 ^{a*}	35	90.44 \pm 16.98	0.409 ^a	0.157 ^b
Visit_4	33	93.36 \pm 5.04		27	93.11 \pm 5.28		0.851 ^b
Change	33	2.73 \pm 5.90		27	-2.67 \pm 16.51		0.086 ^b
Total bilirubin							
Visit_1	36	0.94 \pm 0.58	0.073 ^a	35	0.77 \pm 0.22	0.947 ^a	0.044 ^{b*}
Visit_4	33	0.75 \pm 0.16		27	0.77 \pm 0.22		0.591 ^b
Change	33	0.08 \pm 0.19		27	-0.004 \pm 0.29		0.176 ^b
Direct bilirubin							
Visit_1	36	0.25 \pm 0.08	0.572 ^a	35	0.26 \pm 0.08	1.000 ^a	0.943 ^b
Visit_4	33	0.25 \pm 0.06		27	0.25 \pm 0.07		0.569 ^b
Change	33	0.01 \pm 0.09		27	0.0 \pm 0.09		0.704 ^b
Fasting blood glucose (mg/dL)							
Visit_1	36	93.73 \pm 9.96	0.75 ^a	35	88.59 \pm 10.53	0.587 ^a	0.098 ^b
Visit_4	33	93.09 \pm 10.77		27	87.04 \pm 12.95		0.053 ^b
Change	33	0.64 \pm 11.37		27	1.56 \pm 14.69		0.786 ^b

CGA: chlorogenic acid; AST: aspartate transaminase; ALT: alanine transaminase; ALP: alkaline phosphatase.

Change = Visit_1 – Visit_4.

^aPaired t-test (visit_1 vs visit_4).

^bIndependent t-test.

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$.

compared to baseline. The changes in haematological parameters were insignificant compared to placebo.

No adverse (AE) or serious adverse events (SAEs) were recorded during the study. The measurement of vital signs revealed no significant changes from baseline to the end of study among the subjects in either group (data not shown). These observations and the data clearly suggest that CGA-7 at the tested dose was well tolerated.

Discussion

Green coffee beans are valued as functional ingredients with several health benefits including weight loss.²² This study was conducted to scientifically validate the weight loss properties of a standardized green coffee bean extract containing seven isomers of CGAs. Here we have documented the

efficacy of CGA-7 in reducing the risk of obesity among the healthy overweight individuals. In a randomized placebo-controlled clinical trial, we have evaluated the effect of a 12-week ingestion of 500 mg/day CGA-7, on the primary outcome measures such as body weight, BMI, lean mass/fat mass ratio and body fat percentage in overweight subjects. The secondary outcome of the study included measurement of lipid profile, anthropometric parameters and the tolerability assessment of the extract using biochemical and haematological measures.

To precisely validate the functionality of the extract, we have used the DEXA analysis as a reliable method for obtaining body composition data.²³ DEXA analyses were performed at the baseline and after 12-week treatment. CGA-7 at 500 mg/day dose significantly reduced the body weight and BMI compared to placebo. As expected, the body fat percentage

Table 7. Summary of changes in blood haematological parameters.

Visit	CGA-7			Placebo			p-value between groups
	N	Mean \pm SD	p-value (visit_1 vs visit_4)	N	Mean \pm SD	p-value (visit_1 vs visit_4)	
Haemoglobin (g/dL)							
Visit_1	33	14.85 \pm 0.01	0.101 ^a	27	15.11 \pm 1.11	0.697 ^a	0.475 ^b
Visit_4	33	15.13 \pm 0.71		27	15.21 \pm 0.74		0.657 ^b
Change	33	-0.28 \pm 0.96		27	-0.10 \pm 1.37		0.557 ^b
Total cell count ($\times 10^3$ cells/mm³)							
Visit_1	33	7.50 \pm 0.86	0.073 ^a	27	7.29 \pm 0.72	0.692 ^a	0.729 ^b
Visit_4	33	7.22 \pm 0.79		27	7.23 \pm 0.47		0.958 ^b
Change	33	0.27 \pm 0.84		27	0.06 \pm 0.72		0.295 ^b
Red blood cell count (millions/mm³)							
Visit_1	33	4.97 \pm 0.49	0.140 ^a	27	5.17 \pm 0.41	0.722 ^a	0.197 ^b
Visit_4	33	5.14 \pm 0.39		27	5.20 \pm 0.41		0.522 ^b
Change	33	-0.17 \pm 0.64		27	-0.04 \pm 0.54		0.396 ^b
Platelet count (lakhs/mm³)							
Visit_1	33	3.33 \pm 0.36	0.004 ^{a**}	27	3.39 \pm 0.36	0.120 ^a	0.661 ^b
Visit_4	33	3.56 \pm 0.39		27	3.53 \pm 0.39		0.813 ^b
Change	33	-0.23 \pm 0.42		27	-0.14 \pm 0.44		0.407 ^b
MCV (fL)							
Visit_1	33	82.61 \pm 3.53	0.041 ^{a*}	27	83.33 \pm 3.89	0.543 ^a	0.350 ^b
Visit_4	33	84.58 \pm 3.63		27	84.00 \pm 3.76		0.550 ^b
Change	33	-1.97 \pm 5.31		27	-0.66 \pm 5.62		0.360 ^b
MCH (pg)							
Visit_1	33	28.20 \pm 0.98	0.017 ^{a*}	27	28.59 \pm 1.13	0.054 ^a	0.079 ^b
Visit_4	33	28.84 \pm 0.98		27	29.10 \pm 1.06		0.328 ^b
Change	33	-0.65 \pm 1.47		27	-0.51 \pm 1.30		0.705 ^b
MCHC (%)							
Visit_1	33	32.64 \pm 0.82	0.109 ^a	27	32.89 \pm 0.79	0.272 ^a	0.128 ^b
Visit_4	33	32.98 \pm 0.86		27	33.12 \pm 0.83		0.544 ^b
Change	33	-0.34 \pm 1.19		27	-0.23 \pm 1.08		0.715 ^b

CGA: chlorogenic acid; MCV: mean corpuscular volume; MCH: mean corpuscular haemoglobin; MCHC: mean corpuscular haemoglobin concentration. Change = Visit_1 - Visit_4.

^aPaired *t*-test (visit_1 vs visit_4).

^bIndependent *t*-test.

**p* < 0.05.

***p* < 0.01.

****p* < 0.001.

and fat mass were significantly reduced in the CGA-7 groups. Lean mass and lean mass to fat mass ratio were markedly increased in the extract-treated group compared to placebo. More recently, Roshan et al. reported in a randomized, placebo-controlled trial the beneficial attributes of a standardized green coffee bean extract containing 46% of CGA. The authors reported significant decline in the anthropometric indices, glycemia and appetite after 8-week administration of 800 mg/day green coffee bean extract. The study consisted of patients diagnosed with metabolic syndrome. On the contrary, this study included healthy subjects and the body compositions are derived from DEXA analysis. Furthermore, the duration of this study was for 12 weeks. The secondary outcomes such as waist and hip circumference, waist to hip ratio and blood lipid parameters were significantly varied in the CGA-7-treated subjects as compared to placebo. These

significant changes in secondary outcome are evident may be due to multiple evaluations during the study.

Previously, the anti-obesity property of CGA have been reported by several clinical studies. In a crossover study, green coffee bean extract was administered to the subjects at high (350 mg three times a day) and low (250 mg twice a day) doses for 6 weeks with a 2-week washout period between the treatments.²⁴ This study concluded that the extract was more efficacious in reducing the weight than the FDA-approved drugs. The limitations of this study included the crossover design and the shorter duration of treatment. In another study, 50 overweight subjects aged 19–75 years were randomly allocated to receive a green coffee bean extract (Svetol) in capsule form for 60 days.²⁵ The investigators reported a significant change in body weight and BMI compared to placebo (*p* < 0.001). However, in this study, the blinding of the

intervention is not clearly stated. Furthermore, the safety aspects of the extracts are not described. The limitations of previous studies were considered in designing this study.

We have demonstrated that the weight loss effects of CGA consumption is largely a function of reduction in body fat percentage and lipid metabolism. These results are in line with our previous findings on the mechanism of action of CGA-7 in HFD model rats.²¹ There are several other preclinical studies reporting the lipid lowering effects of CGA.^{26–28}

Importantly, the ingestion of CGA-7 did not induce any AE or SAEs throughout the study. The safety of the extract was further confirmed by the analysis of biochemical and haematological parameters and measurement of vital signs. It was observed that majorly the blood biochemical parameters including the markers of hepatic toxicity did not alter significantly upon administration of CGA-7. There was a significant reduction in the ALP of CGA-7 group. Increased level of ALP is an important blood marker of hepatic damage.²⁹ In our study, CGA-7 did not increase the ALP and hence the significant change cannot be considered as indication of toxicity. Assessment of haematological parameters further confirmed the safety of CGA-7. There were significant changes observed in some of the parameters such as platelet count, MCV and MCH of the CGA-7 group compared to baseline. However, the observed values were still in the normal ranges.

The limitations of our study include the short duration of treatment, smaller sample size and inclusion of single study site. Appetite biomarkers were not included in the study. Further studies are required to elucidate the long-term benefits of green coffee bean supplementation.

Conclusion

Collectively, the data from this study further support the anti-obesity properties of CGAs from green coffee beans. Importantly, the study comprehensively documents the efficacy of green coffee beans alongside the safety for consumption as a functional food ingredient.

Author contributions

Both the authors have read and approved the manuscript. K.S.P. contributed to conceptualization, review and editing of the article; H.V.S. contributed to protocol design, study monitoring and coordination, and writing – original draft preparation.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Both the authors are employed by Vidya Herbs Pvt Ltd, and hence declare potential conflicts of interest.

Ethical approval

Ethical approval for this study was obtained from Institutional Ethics Committee – Sri Kalabyraveshwara Swamy Ayurvedic

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Informed consent

Written informed consent was obtained from all subjects before the study.

Trial registration

CLINICAL TRIAL REGISTRY–INDIA: CTRI/2017/04/008295.

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Supplemental material

Supplemental material for this article is available online.

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