Safety and Efficacy of Banaba–*Moringa oleifera*–Green Coffee Bean Extracts and Vitamin D3 in a Sustained Release Weight Management Supplement

Sidney J. Stohs,[1]* Gilbert R. Kaats[2] and Harry G. Preuss[3]

[1]Creighton University, 7068 Maumee Valley Court, Frisco, TX 75034, USA
[2]Integrative Health Technologies, Inc., 5170 Broadway, San Antonio, TX, USA
[3]Department of Biochemistry, Georgetown University Medical Center, Washington, DC, USA

This 60-day, 30-subject pilot study examined a novel combination of ingredients in a unique sustained release (Carbopol matrix) tablet consumed twice daily. The product was composed of extracts of banaba leaf, green coffee bean, and *Moringa oleifera* leaf and vitamin D3. Safety was assessed using a 45-measurement blood chemistry panel, an 86-item self-reported Quality of Life Inventory, bone mineral density, and cardiovascular changes. Efficacy was assessed by calculating a body composition improvement index (BCI) based on changes in dual energy X-ray absorptiometry measured fat mass (FM) and fat-free mass (FFM) as well as between the study group (SG) and a historical placebo group. No changes occurred in any blood chemistry measurements. Positive changes were found in the Quality of Life (QOL) inventory composite scores. No adverse effects were observed. Decreases occurred in FM ($p = 0.004$) and increases in FFM ($p = 0.009$). Relative to the historical placebo group, the SG lost more FM ($p < 0.0001$), gained more FFM ($p = <0.0001$), and had a negative BCI of -2.7 lb. compared with a positive BCI in the SG of 3.4 lb., a 6.1 discordance ($p = 0.0009$). The data support the safety and efficacy of this unique product and demonstrate importance of using changes in body composition versus scale weight and BMI. © 2016 The Authors Phytotherapy Research Published by John Wiley & Sons Ltd.

Keywords: Moringa oleifera; green coffee bean extract; *Lagerstroemia speciosa* (banaba); vitamin D.

INTRODUCTION

Approximately two-thirds of the adult American population is either overweight or obese primarily because of a combination of inadequate physical exercise and adherence to unhealthy diets that are high in simple sugars and saturated fats (Vaughan *et al.*, 2014). Over the past 25–30 years, there has been an increase in total energy intake of approximately 570 kcal/day (Duffy and Popkin, 2011).

Numerous diseases are associated with excess weight including coronary artery disease and congestive heart failure, diabetes, hypertension and stroke, muscle wasting, almost all forms of cancer, depression, liver disease, and osteoporosis. As a consequence, large percentages of the population are attempting to lose weight at any given time. In spite of the fact that the health benefits of weight reduction are well known, weight loss via diet and exercise fails in most patients (Arbeeny, 2004; Ferraro *et al.*, 2015). Failure may occur in part because of the indices employed to assess outcomes. Body weight and body mass index (BMI) are commonly used as indicators of weight loss and weight gain. These indices do not differentiate between changes in body fat and lean muscle mass. For example, a 3 lb. loss of body fat with an equal gain in muscle mass will be recorded as no change in body weight when in reality two very beneficial effects were observed, namely, a loss of body fat and a gain in lean muscle mass.

Because of the lack of success in retaining weight loss, many patients turn to complementary and alternative approaches for the management of obesity (Esteghamati *et al.*, 2015). Although many dietary supplements have been designed to support weight management and weight loss, few supplements have been proven to be effective because either the ingredients are ineffective or the wrong indices to assess weight loss were used.

In the current study, the weight management product contains three active ingredients not previously used in combination in a unique sustained tablet delivery system designed to provide release of active ingredients for up to 6 h. The product is designed to improve body composition through the depletion of excess body fat while maintaining or increasing fat-free mass (FFM) without adverse effects on bone mineral density (BMD). In an unpublished pilot study, the product was found to improve eating control and helps maintain healthy blood sugar and lipid levels. Furthermore, the ingredients are believed to work in harmony via different and supporting mechanisms, ensuring a high degree of efficacy. The ingredients contained in this product and previous studies supporting these effects are described later.

* Correspondence to: Sidney J. Stohs, Dean Emeritus, Creighton University, 7068 Maumee Valley Court, Frisco, TX 75034, USA.
E-mail: sid.stohs9@gmail.com

Moringa oleifera leaves, seeds, bark, roots, sap, and flowers are widely used in traditional medicine, and the leaves and immature seed pods are used as food products in human nutrition (Mbikay, 2012). Leaf extracts exhibit the greatest antioxidant activity, and various safety studies in animals involving aqueous leaf extracts indicate a high degree of safety. No adverse effects were reported in association with human studies. Five human studies using powdered whole leaf preparations of *M. oleifera* have been published, which have demonstrated anti-hyperglycemic (anti-diabetic) and anti-dyslipidemic activities (Stohs and Hartman, 2015) that are highly supportive of weight management and weight loss. These activities have been confirmed using extracts as well as leaf powders in animal studies. A rapidly growing number of published studies have shown that aqueous, hydroalcoholic or alcoholic extracts of *M. oleifera* leaves possess a wide range of additional biological activities including antioxidant, tissue protective (liver, kidneys, heart, testes, and lungs), analgesic, anti-ulcer, anti-hypertensive, radioprotective, and immunomodulatory actions (Stohs and Hartman, 2015). A wide variety of polyphenols and phenolic acids as well as flavonoids, glucosinolates, and possibly alkaloids are believed to be responsible for the observed effects.

Banaba (*Lagerstroemia speciosa* L.) extracts and decoctions have been used for many years in folk medicine to support weight management and regulate blood sugar levels, with the first published research study being reported in 1940. The hypoglycemic and weight management effects of banaba have been attributed to both corosolic acid (Fig. 1) as well as ellagitannins, which are hydrolysable polymers of ellagic acid (Fig. 2). Studies have been conducted in various animal models, human subjects, and *in vitro* systems using water-soluble banaba leaf extracts, corosolic acid-standardized extracts, and purified corosolic acid and ellagitannins (Stohs *et al.*, 2012).

Corosolic acid exhibits anti-hyperlipidemic, antioxidant, anti-inflammatory, antifungal, antiviral, anti-neoplastic, and osteoblastic activities in addition to its insulin-like effects. The beneficial effects of banaba and corosolic acid with respect to various aspects of glucose and lipid metabolism as well as weight management appear to involve multiple mechanisms, including enhanced cellular uptake of glucose, impaired hydrolysis
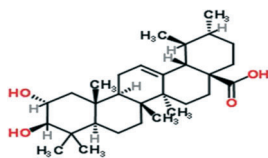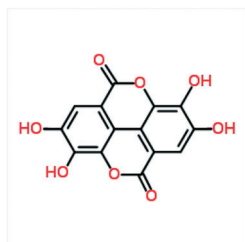
of sucrose, and starches, decreased gluconeogenesis, and regulation of peroxisome proliferator-activated receptor-mediated lipid metabolism (Stohs *et al.*, 2012). No adverse effects have been reported in animal studies or controlled human clinical trials. The highest dose of corosolic acid used to date has been 10 mg per day for 30 days and was without adverse effects (Stohs *et al.*, 2012). Tannins are the most abundant secondary metabolites in plants and are without adverse effects at exceedingly high doses. The oral lethal dose for 50% (LD50) of rats and mice of an ellagitannin has been reported to be greater than 1.5 g/kg body weight (Patel *et al.*, 2008).

Chlorogenic acid (Fig. 3) is the major polyphenolic compound present in coffee, and epidemiological studies have shown that high coffee consumption promotes weight loss and reduces the risk of type 2 diabetes. A number of human clinical trials have demonstrated the beneficial effects of green coffee bean extracts containing chlorogenic acid with respect to weight loss and weight management as well as regulation of blood glucose levels (Nardon *et al.*, 2007; Thom, 2007; Onakpoyo *et al.*, 2011). An increase in lean to fat mass (FM) has also been observed with no serious adverse effects being reported. Doses ranging from 180 to 1050 mg of green coffee extract containing approximately 45–50% chlorogenic acid have been used. Various studies in animals have demonstrated the weight loss effects of chlorogenic acid, and decreases in cholesterol, triglycerides, and plasma insulin and leptin levels have been reported.

Multiple mechanisms appear to be involved in these beneficial effects of chlorogenic acid and green coffee extract, including inhibition of the hepatic enzyme glucose-6-phosphatase, modulation of glucose absorption, inhibition of cholesterol and triglyceride biosynthesis, and antioxidant and chemoprotective properties (Onakpoyo *et al.*, 2011). Long-term exposure of human adipocytes has clearly shown that green coffee bean extract enhances the breakdown of fats and the release of free fatty acids (Flanagan *et al.*, 2014). These studies indicate that green coffee extracts containing chlorogenic acid are both effective and safe in weight management and blood glucose and lipid regulation and metabolism, factors essential for weight management.

The average daily intake of chlorogenic acid primarily from coffee consumption has been estimated to be about 150 mg per day, depending upon the kind of coffee and the amount consumed (Ludwig *et al.*, 2014; Grosso *et al.*, 2014). Chlorogenic acid appears to be exceedingly safe with an oral LD50 in mice greater than 2 g/kg (Perez-Vasquez *et al.*, 2014).

The tablets subjects consumed were composed of "Actives," a diluent, a modified release agent, and lubricant containing a swellable matrix system, "Carbopol 971P." In the body's aqueous gastrointestinal environment, the tablet swells significantly, increasing in size and geometry, and the Actives are released slowly over
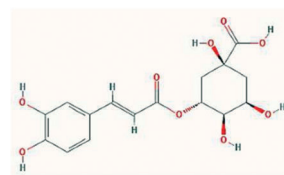

Figure 1. Corosolic Acid.

Figure 2. Ellagic Acid.

Figure 3. Chlorogenic Acid.

approximately 6 h by a process of diffusion through the polymer matrix that is essentially independent of pH. The hydrated polymer system is not rigid and is designed not to be broken.

The tablet also contains 500 IU of vitamin D. Vitamin D deficiency occurs in a majority of people in the United States. Many studies have reported an association between vitamin D and adipose tissue metabolism as well as the possible role of low levels of vitamin D in obesity (Cipriani *et al.*, 2014; Shanmugalingam *et al.*, 2014). Decreases in the BMI and FM have also been shown to occur in conjunction with vitamin D supplementation (Pathak *et al.*, 2014).

METHODS

A total of 30 subjects were enrolled and executed an informed consent form approved by Solutions' Institutional Review Board. A total of 28 subjects completed the study per protocol. One subject completed the baseline tests but failed to start the study for personal reasons unrelated to the product or protocol. Another subject reported insufficient compliance data. This subject's data were excluded from the final analyses. The remaining 28 subjects consumed the weight loss product supplement described in Table 1 (CraveCheck SR™, AdvoCare International, Plano, TX, USA) twice daily – before 8:00 AM and between 3:00 and 5:00 PM in the afternoon – thereby providing release of active ingredients for approximately 12 h.

Using a procedure described by Kaats and Preuss (2013) to encourage candid reporting, instead of paying an "incentive fee" for their participation, subjects were paid a daily "tracking fee" of $5.00 per day ($300 total), provided they reported their daily product usage in a "timely manner," within 48 h after the end of each study day. Using this procedure, the emphasis was placed on candid reporting of product usage and effects to avoid penalizing subjects for not taking the product.

Safety. To assess safety, fasting blood samples were drawn, and the 45-measurement blood chemistry/hematology panel shown in Table 2 was completed at the beginning, mid-point, and end of the 60-day study period. Tests were conducted by an independent testing

Table 1. Supplement Product Facts

Supplement facts		
Serving size: 2 tablets		
Servings per container 30		
	Amount per serving	% Daily value
Green coffee bean extract (45–50% chlorogenic acid)	300 mg	†
Moringa Oleifera leaf extract	200 mg	†
Banaba leaf extract (2% corosolic acid)	100 mg	†
Vitamin D3	500 IU	125

†, no percent daily values established.

Table 2. The blood chemistry panel

Total cholesterol	Alkaline phosphatse	Lymphocytes
HDL cholesterol	ALT	MCH
Non-HDL cholesterol	AST	MCHC
Chol/HDL ratio	Basophils	MCV
LDL cholesterol	Bilirubin, total	Monocytes
Triglycerides	Bun/creatine ratio	Neutrophils
Cardio CRP	Calcium	Platelet count
Glucose	Carbon dioxide	Potassium
Absolute basophils	Chloride	Protein, total
Absolute eosinophils	Creatinine	RDW
Absolute lymphocytes	Eosinophils	Red blood cell count
Absolute monocytes	Globulin	Sodium
Absolute neutrophils	GFR	TSH w/reflex T-4, free
Albumin	Hematocrit	Urea nitrogen (BUN)
Albumin/globulin ratio	Hemoglobin	White blood cell count

HDL, high density lipoprotein; LDL, low density lipoprotein; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentrate; MCV, mean corpuscular volume; TSH, thyroid stimulating hormone; GFR, glomerular filtration rate; RDW, red cell distribution width.

laboratory, Quest Diagnostics, at drawing stations of the subjects' choosing. All test results were sent directly to the principal investigator and provided to subjects at the end of the study period. All 28 subjects completed the three blood tests as per protocol. Additionally, comparisons were also made between baseline-ending changes in the study group and the historical placebo group of similar subjects who had also completed the same baseline-ending blood tests over the same study period.

Assessing positive or negative outcomes in the first eight blood tests shown in Table 2 is simply a matter of comparing changes in the respective means using a traditional Student's *t*-test. However, assessing changes in the remaining tests required different analyses. Unlike the eight continuous variables, increases or decreases in the remaining measures could reflect either positive or adverse effects depending upon whether or not the changes in the subject's measurements went from "normal" to "abnormal" or vice versa. Measurements that were in either the normal or abnormal ranges on test 1 or remained in the same ranges on test 2 were deemed irrelevant with regard to safety concerns. Measurements that were in the abnormal range on test 1, but were normal on test 2, were assumed to reflect a positive change. Conversely, measurements that were in the normal range on test 1, but were subsequently in the abnormal range on test 2, were deemed to reflect a negative change or an adverse effect. The appropriate analyses were conducted for all 45 measurements and are shown in the Results section.

As additional measures of safety, subjects completed the 86-item Composite Quality of Life Inventory (QOL) shown in Table 3. Responses to all 86 items were averaged to obtain an overall score for adverse wellness.

The safety analysis also included assessment of changes in heart rates and the ankle–brachial index by conducting simultaneous brachial and ankle blood pressure measurements after the subject remained in a resting prone position for approximately 15 min while completing the dual energy X-ray absorptiometry (DEXA) body composition test.

Efficacy was assessed by calculating a body composition improvement index (BCI) based on changes in DEXA-measured FM and FFM derived from the DEXA scans

Table 3. Overall problems with quality of life

Please report problems occurring over the last 30 days

0 = NOT a problem 1 = a MINOR problem 2 = a MAJOR problem 3 = a SEVERE problem

1 Headaches	⓪①②③	30 Feeling weak	⓪①②③	59 Sleepy throughout the day	⓪①②③
2 Irritable bowel syndrome	⓪①②③	31 Eating too rapidly *	⓪①②③	60 Difficulty in making decisions	⓪①②③
3 Arthritis	⓪①②③	32 Eating after being full *	⓪①②③	61 Feeling restless	⓪①②③
4 Premenstrual syndrome	⓪①②③	33 Embarrassed about overeating *	⓪①②③	62 Getting more tired than usual	⓪①②③
5 Recurring sinus infections	⓪①②③	34 Depressed over eating habits *	⓪①②③	63 Blaming myself too often	⓪①②③
6 Tension fatigue syndrome	⓪①②③	35 Depressed about my weight *	⓪①②③	64 Causing problems for others	⓪①②③
7 Recurrent Anxiety	⓪①②③	36 Difficult to Stop Eating *	⓪①②③	65 Worrying About My Faults	⓪①②③
8 Recurrent depression	⓪①②③	37 Worrying about the future	⓪①②③	66 Wondering if life is worth living	⓪①②③
9 Insomnia	⓪①②③	38 Unable to concentrate	⓪①②③	67 Suicidal thoughts and worries	⓪①②③
10 Low self-esteem	⓪①②③	39 Forgetfulness	⓪①②③	68 Decreasing interest in people	⓪①②③
11 Binge eating *	⓪①②③	40 Bad temper or quick to anger	⓪①②③	69 Decreasing interest in activities	⓪①②③
12 Chronic tension	⓪①②③	41 Indigestion	⓪①②③	70 Difficulty in sitting or standing still	⓪①②③
13 Lack of energy	⓪①②③	42 Diabetes	⓪①②③	71 Often fidgety	⓪①②③
14 Food allergies	⓪①②③	43 Vomiting	⓪①②③	72 More tired than usual	⓪①②③
15 Feeling under stress	⓪①②③	44 Heartburn	⓪①②③	73 Generalized depression	⓪①②③
16 Cancer	⓪①②③	45 Esophageal reflux	⓪①②③	74 Difficulty in finishing activities	⓪①②③
17 Prostate problems	⓪①②③	46 Control over my appetite *	⓪①②③	75 Feeling sad too much of the time	⓪①②③
18 Overeating *	⓪①②③	47 Ability to relax	⓪①②③	76 Dieting too often	⓪①②③
19 Stomach pain	⓪①②③	48 Heart disease	⓪①②③	77 Difficulty in staying with a diet	⓪①②③
20 Back pain	⓪①②③	49 Fibromyalgia	⓪①②③	78 Difficulty in getting up in the morning	⓪①②③
21 Pain in arms, legs or joints	⓪①②③	50 Difficulty in falling asleep	⓪①②③	79 Eating too much between meals *	⓪①②③
22 Menstrual pain or problems	⓪①②③	51 Awakening during the night	⓪①②③	80 Eating too much during meals *	⓪①②③
23 Chest pain	⓪①②③	52 Feeling sad	⓪①②③	81 Getting tired too often	⓪①②③
24 Dizziness	⓪①②③	53 Waking up too early	⓪①②③	82 Preoccupied with gloomy thoughts	⓪①②③
25 Diarrhea	⓪①②③	54 Sleeping too much	⓪①②③	83 Thinking too much about death	⓪①②③
26 Irregular heartbeat	⓪①②③	55 Unintentional weight gain *	⓪①②③	84 Slowing down of my thinking	⓪①②③
27 Shortness of breath	⓪①②③	56 Unintentional weight loss	⓪①②③	85 Unhappy too much of the time	⓪①②③
28 Constipation	⓪①②③	57 Inability to concentrate	⓪①②③	86 Difficult to stop eating once I start *	⓪①②③
29 Stomach gas or indigestion	⓪①②③	58 Satisfied with my life	⓪①②③		

*Problems with eating control sub-scale.

shown in the graphics later. All DEXA measurements were performed using a GE Lunar's DEXA DPX-IQ Bone Densitometer (Madison, WI, USA) with software version DPX-IQ X-Ray Bone Densitometer with SmartScan™ Version 4.7e. All tests used in this study were conducted by a certified technician using the same DEXA technology for baseline and ending measurements

Although scale weight and the BMI are often used to assesses changes in weight loss interventions and treatment plans, these measures report only changes in total body mass, not the kind of mass (fat and FFM) that was lost or gained. Because the BMI is a ratio of height to weight, and height rarely changes in studies involving adults, as a measure of change, the BMI and scale weight are identical and correlate 1.00. Thus, scale weight and the BMI can be used interchangeably with regard to a measure of change. However, using a DEXA scan to assess changes also provides measurements of the kind of weight, FM, and FFM that was lost or gained – measurements that can be used independently or combined as a BCI index. The BCI is the net result of scoring losses of FM and gains of FFM as positive outcomes and gains of FM and losses of FFM as negative outcomes. The BCI is the net result of combining these positive and negative outcomes. Previous research has found significant differences between the conclusions one would draw about the success or failure of weight loss interventions and treatment plans as opposed to using an index of BCI (Opala *et al.*, 2006; Kaats *et al.*, 2006).

Although included in FFM, because most weight loss interventions often deplete BMD, changes in baseline, mid-study, and ending BMD measurements are also reported. Decreases in BMD could also be considered a measure of safety as well as efficacy. To partition out the potential effects of changes in physical activity, subjects wore a research-quality pedometer during their waking hours and recorded their daily step totals.

RESULTS

Blood chemistries. Table 4 provides the mean values for baseline, mid-study, and ending for the eight continuous variable measurements with P values for comparisons between tests 1 (baseline), 2 (mid-study), and 3 (ending). No statistically significant changes were found in any of these within-group paired *t*-tests comparisons with respect to total cholesterol, high density lipoprotein (HDL), triglycerides, low density lipoprotein (LDL), LDL:HDL ratio, non-HDL triglycerides, C-reactive protein, and glucose.

Analyses of the remaining 37 blood chemistry measurements required different statistical analyses because increases or decreases could reflect a positive effect, a negative effect, or no effect depending upon what impact the intervention had relative to changes in the "normal" or "abnormal" ranges for the test. As shown

Table 4. Blood chemistry changes from baseline, mid-study, and ending

TC	TotC	HDL	TRIG	LDL	Ratio	Non-HDL TC	CRP	Gluc
Baseline	201.3	59.86	124	116.7	3.532	141.4	2.328	94.214
Mid-study	201.5	58.93	125.1	117.5	3.589	142.5	2.377	93.25
Ending	198	57.43	127	115.2	3.625	140.6	3.246	94.357
1–2 P values =	0.965	0.534	0.870	0.788	0.467	0.747	0.928	0.422
1–3 P values =	0.298	0.068	0.592	0.534	0.200	0.736	0.077	0.910
2–3 P values =	0.404	0.320	0.813	0.485	0.661	0.579	0.056	0.279

TotC, total cholesterol; HDL, high density lipoprotein; TRIG, triglycerides; LDL, low density lipoprotein; CRP, C-reactive protein; Gluc, glucose.

in Fig. 4, 93.7% of the study group had scores in the "normal" range at baseline and remained in the "normal" range on the ending test. Another 2.6% were abnormal at baseline and remained abnormal on the ending test. A total of 1.3% were abnormal at baseline and became normal on the ending test. And finally, 2.4% were normal on the baseline test but were abnormal on the ending test. Thus, 97.6% of the scores remained unchanged or improved. The remaining 2.4% suggesting potentially adverse effects could also be due to statistical artifacts as the result of chance occurrences in taking the 37 measurements. These data are consistent with the findings from the eight continuous variables that, with respect to blood chemistries, there is no evidence of adverse effects. These data were also compared with a random sample of 5000 similar subjects in the investigator's Longitudinal Database of Medical Biomarkers who had completed the same blood tests during a variety of studies. The average change from normal to abnormal was 4.14% – a percentage significantly ($p = <.001$) higher than the same changes found in this study.

The secondary measure of safety was to examine changes in subject responses to the Quality of Life Inventory and sub-scales shown in Table 3 previously. All subjects completed the inventory at baseline, mid-study, and at the end of the study. When completing these items, respondents reported the severity of problem for them by selecting 0 = No Problem, 1 = A Minor Problem, 2 = A Major Problem, or 3 = A Severe Problem.

Thus, the lower the scores on these scales, the lesser the problem or the greater the improvement during the study period. Results of these analyses are shown in Table 5. As shown in the composite overall scale and all sub-scales, there are consistent improvements from baseline to mid-study and to end-of-study. All of these improvements average ~36% and were statistically significant.

Final safety measures were potential changes in heart rates as well as ankle/brachial blood pressures and the ankle brachial index. These data are shown in Table 6. As shown, ankle and brachial blood pressures were lowered from baseline to end-of-study, although only the changes in the ankle systolic and diastolic reached statistical significance ($p = 0.0335$ and $p = 0.0346$, respectively). However, from a safety standpoint, changes in the resting blood pressures support the safety of the product. No changes were observed with respect to heart rates.

Efficacy. Although the QOL could be classified as a measure of efficacy, the primary outcome measure used in this study was the body composition improvement (BCI©) index that is the net result or sum of scoring gains of FFM and reductions of FM as positive treatment outcomes, and, conversely, losses of FFM and gains of FM as negative treatment outcomes. As shown in Table 7, while there was no significant change in
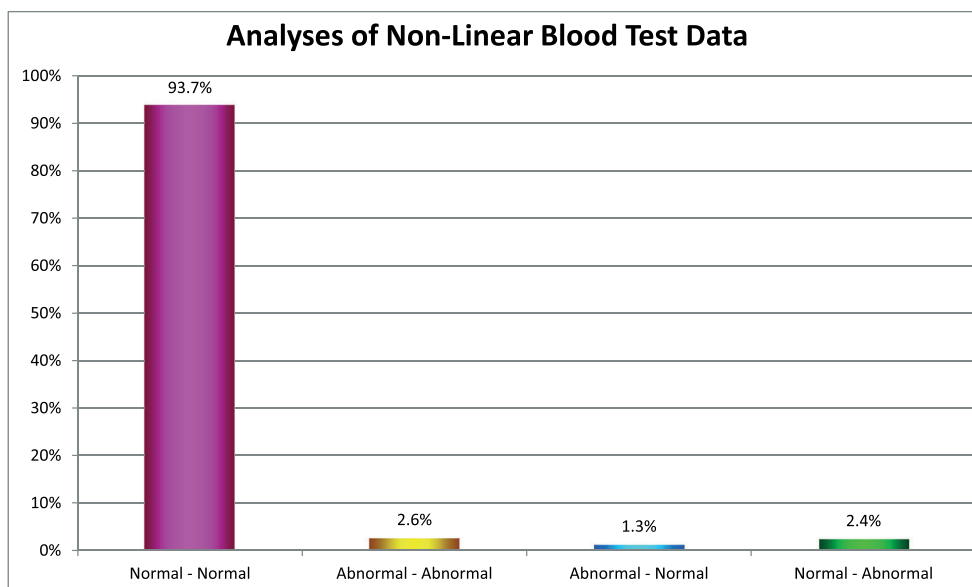
Figure 4. Analyses of non-linear blood test data.

Table 5. Analyses of self-reported problems with quality of life

Measurement	Overall problems with quality of life (items 1–86)	Problems with QOL (items 1–51 only)	Problems with eating control (items shown with *)	Problems with depression (items 52–86)
Baseline	0.2262	0.2522	0.3854	0.2098
Mid-study	0.1649	0.1747	0.2901	0.1561
End-of-study	0.1459	0.1601	0.2782	0.1318
% improvement baseline-ending	35.5%	36.5%	27.8%	37.2%
Baseline/ending P values =	<0.0001	<0.0001	<0.0001	0.0002

QOL, quality of life.

Table 6. Baseline-ending changes in blood pressures

Resting blood pressures	(Chg) baseline-ending	P-values
Arm systolic BP	−2.32	0.3701
Arm diastolic BP	−1.18	0.4197
Heart rate	1.43	0.4435
Ankle systolic BP	−4.61	0.0335
Ankle diastolic BP	−3.71	0.0346
Ankle heart rate	2.11	0.2198
Ankle/brachial index	−0.02	0.2429

Chg, Change.

baseline-ending scale weight (-0.2 lb., $p = 0.718$), there were statistically significant decreases in FM ($p = 0.004$) and increases in FFM ($p = 0.009$) resulting in a BCI of 3.4 lb. There were also no significant changes in baseline-mid-study and baseline ending BMD ($p = 0.735$).

As shown in Fig. 5, all of the comparisons between the active study group and the historical placebo group were statistically significant. It is also worth noting that a within-group repeated measures t-test found a statistically significant scale weight loss of -3.6 lb. ($p < 0.0001$) while the -0.2 lb.. scale weight loss in the active study group was statistically insignificant ($p = 0.716$). Additionally, a between-groups t-test also found that the scale weight loss in the placebo group was statistically greater than that of the active group ($p < 0.0001$).

A total of 94.5% of the study subjects complied with the study protocol based on the compliance procedures that encouraged candid reporting. There were no significant changes in BMD found between baseline to mid-study to end-of-study. An analysis of the pedometer-monitored physical activity levels revealed no significant relationship between physical activity levels and improvements in body composition.

Table 7. Baseline, mid-study and ending

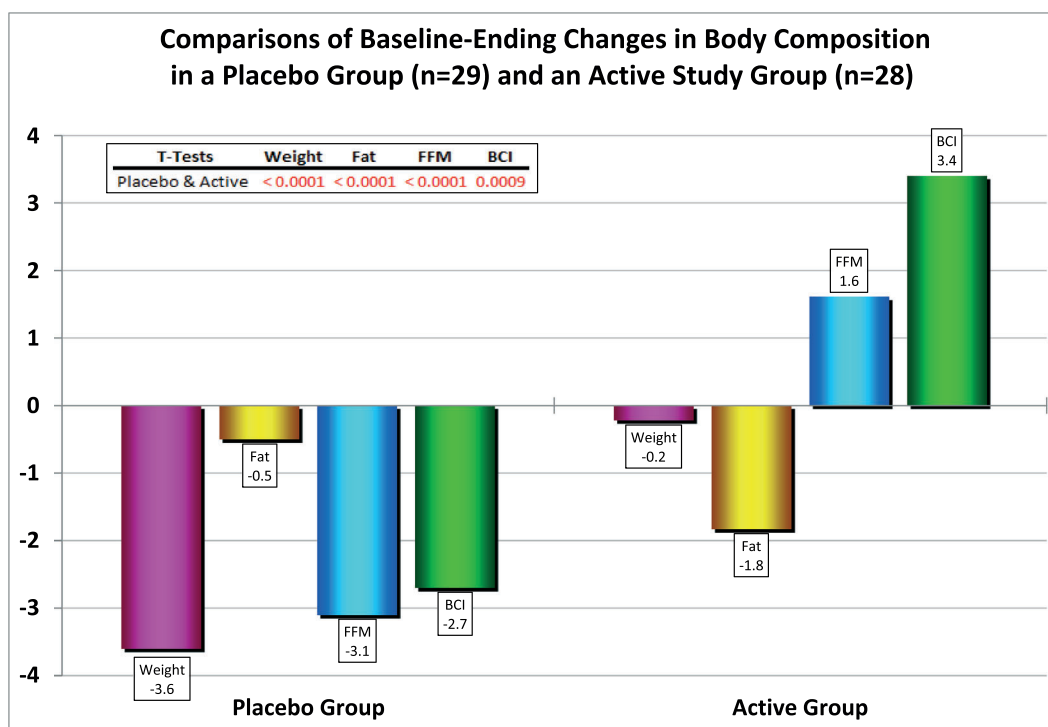|	Changes in body composition			
	BMD	Wgt	Fat	FFM
Baseline	1.187	180.1	79.3	100.8
Mid-study	1.186	180.9	78.3	102.6
Changes	−0.001	0.8	−1.0	1.8
Ending	1.188	179.9	77.5	102.4
Changes	0.001	−0.2	−1.8	1.6
Within Gp	0.735	0.718	0.004	0.009

BMD, bone mineral density; FFM, fat-free mass.

DISCUSSION

The absence of any significant within-group changes between baseline, mid-study, and end-of-study in the 45-measurement blood chemistry panel, or in the between-group comparisons between the active group and the historical placebo groups, provides compelling support for the safety of the product. Additionally, the consistent and significant positive changes from baseline to mid-study and mid-study to end-of-study in the QOL composite scale and its sub-scales provide further evidence of product safety. Nor were any adverse effects found in the heart rates, resting brachial or ankle blood pressure measurements, or in the brachial/ankle index taken at baseline, mid-study, and end-of-study. Although both systolic and diastolic blood pressures decreased throughout the study, none of these decreases reached statistical significance.

With regard to efficacy, DEXA body composition measurements taken at baseline, mid-study, and end-of-study found statistically significant decreases in FM and increases in FFM resulting in a 3.4 BCI index over the 60 days of the study. The same statistically significant decreases in FM and increases in FFM were also found in comparisons of the study group with the historical placebo group. The subjects' 94.5% average compliance measurement also supports both the safety and efficacy of the product as does the absence of expected decreases in BMD often found in weight loss studies. An argument could also be made that the consistent and significant improvements found in the QOL and its sub-scales should also be viewed as supporting product efficacy. A study has demonstrated that corosolic acid, the active constituent in banaba leaf extracts, possesses osteoblastic activity that may explain the absence of bone mineral loss in the current study (Shim *et al.*, 2009).

Another important finding from this study is the illustration of the differences in the conclusions one would draw about the success or failure of a weight loss interventions using the BCI or scale weight/BMI. Fig. 2 presents a comparison of within-group or repeated measures changes in body composition between the placebo group and the active study group. The placebo group had a -3.2 lb. reduction in body weight that was significantly greater ($p < 0.0001$) than the non-significant -0.2 lb. weight loss found in the active group. Thus, one could conclude that the placebo group was a modestly successful intervention compared with the unsuccessful intervention of the active group. However, examination of changes in body composition as shown by the BCI

Figure 5. Comparisons of baseline-ending changes in body composition in a placebo group (*n* = 29) and an active study group (*n* = 28).

suggests an opposite outcome because the weight reduction experienced by the placebo group was the result of a −3.1 lb. loss of metabolically active FFM as compared with a 1.6 lb. gain in FFM found in the active group – a 4.7 lb. differential or discordance in changes in FFM.

Because muscle is the primary site at which calories are consumed, any loss of muscle results in a loss of thermogenic ability, while conversely, any gain in muscle enhances the ability to utilize fat as an energy source and decrease FM. The results of this study clearly demonstrate the ability of this unique product over the course of 60 days to increase FFM while decreasing FM, thus leading to a healthy outcome.

The strengths of this study lie in the use of widely recognized multiple measurements of safety and efficacy and the consistent and statistically significant findings between changes from baseline to mid-study and to end-of-study. The 94.5% compliance finding and the 93.3% completion rate of the subjects stand in stark contrast to the 30–40% dropout rates typically reported for weight loss studies. This study also underscores the importance of using the BCI as an outcome measure instead of changes in the BMI or scale weight. In this study, using changes in scale weight as an outcome measure would have led to a conclusion that the product was ineffective as a weight loss supplement – a conclusion in stark contrast to the conclusions one would draw by using changes in body composition, particularly the BCI. Questions could be raised about previous weight loss interventions whose safety and efficacy were rejected, or accepted, by using only changes in body mass as an outcome measure as opposed to using changes in FM, FFM, and BMD. This issue is clearly something that needs further exploration.

The weaknesses of the study are its relatively small number of subjects (*n* = 28), the failure to use an randomized controlled trial (RCT) protocol with a random selection of placebo subjects, and the relatively short study period (60 days).

CONCLUSIONS

The safety and efficacy of the unique weight management product used in this study contain a novel combination of active ingredients in a unique sustained tablet delivery system that provided release of active ingredients for up to 6 h. The results of this 60-day study demonstrated the product increased FFM while decreasing body fat (FM). The product was designed to suppress appetite, support weight management and weight loss, and help maintain healthy blood sugar and lipid levels. Furthermore, the ingredients are believed to work in harmony via different and supporting mechanisms, ensuring a high degree of efficacy.

The significance and consistency of the measurements of safety and efficacy in this study clearly warrant further study of this combination of ingredients. Additionally, the results obtained using BCI as opposed to body weight and BMI strongly indicate a need for general application of this technique and the need for further comparative studies.

Conflict of Interest

S. J. S. and H. G. P. have served as consultants for AdvoCare International, the distributor of the product. Dr. Kaats has no conflict of interest.

REFERENCES

Arbeeny CM. 2004. Addressing the unmet medical need for safe and effective weight loss therapies. *Obesity Res* **12**: 1191–1196.

Cipriani C, Pepe J, Piemonte S, Colangelo L, Cilli M, Minisola S. 2014. Vitamin D and its relationship with obesity and muscle. *Int J Endocrinol* . DOI:10.1155/2014/841248.

Duffy KJ, Popkin BM. 2011. Energy density, portion size, and eating occasions: contributions to increased energy intake in the United States, 1977-2006. *PLoS Med* 8. DOI:10.1371/Jounral.pmed.1001050.

Esteghamati A, Mazaheri T, Rad MV, Noshad S. 2015. Complementary and alternative medicine for the treatment of obesity: a critical review. *Int J Endocrinol Metabol* **13**: . DOI:10.5812/ijem.19678.

Ferraro ZM, Patterson S, Chaput JP. 2015. Unhealthy weight control practices: culprit and clinical recommendations. *Clin Med Insights Endocrinol Diabetes* **8**: 7–11.

Flanagan J, Bily A, Rolland Y, Roller M. 2014. Lipolytic activity of Svetol, a decaffeinated green coffee bean extract. *Phytother Res* **28**: 946–948.

Grosso G, Stepaniak U, Topor-Madry R, Szafraniec K, Pajak A. 2014. Estimated dietary intake and major food sources of polyphenols in the Polish arm of the HAPIEE study. *Nutrition* **30**: 1398–1403.

Kaats GR, Preuss HG. 2013. Challenges to the conduct and interpretation of weight loss research. In Obesity: Epidemiology, Pathophysiology and Prevention (2nd ed.) (pp. 833–850). New York, NY: CRC Press.

Kaats GR, Michalek JE, Preuss HG. 2006. Evaluating efficacy of a chitosan product using a double-blinded, placebo-controlled protocol. *J Am Coll Nutr* **25**: 389–394.

Ludwig IA, Mena P, Calani L, *et al.*. 2014 Variations in caffeine and chlorogenic acid contents of coffees: what are we drinking? *Food Funct* **5**: 1718–1726.

Mbikay M. 2012. Therapeutic potential of *Moringa oleifera* leaves in chronic hyperglycemia and dyslipidemia: a review. *Front Pharmacol* **3**: 24.

Nardon K, Lemaire B, Lafay S. 2007. Green coffee extract Svetol® can manage weight: a review. *Agrofood* **18**: 37–39.

Onakpoyo I, Terry R, Ernst E. 2011. The use of green coffee extract as a weight loss supplement: a systematic review and meta-analysis of randomized clinical trials. *Gastroenterol Res Pract*. DOI:10.1155/2011/382852.

Opala T, Rzymski P, Pischel I, Wilczak M, Wozniak J. 2006. Efficacy of 12 weeks supplementation of a botanical extract-based weight loss formula on body weight, body composition and blood chemistry in healthy, overweight subjects – a randomized double-blind placebo-controlled clinical trial. *Eur J Med Res* **11**: 343–350.

Patel C, Dadhaniya P, Hingorani L, Sonu MG. 2008. Safety assessment of pomegranate fruit extract: acute and subacute toxicity studies. *Food Chem Toxicol* **46**: 2728–2735.

Pathak K, Soares MJ, Calton EK, Zhao Y, Hallett J. 2014. Vitamin D supplementation and body weight status: a systematic review and meta-analysis of randomized controlled trials. *Obes Res* **15**: 528–537.

Perez-Vasquez A, Castillejos-Ramirez E, Christians S, Mata AR. 2014. Development of a UHPLC-PDA method for the simultaneous quantification of 4-phenylcoumarins and chlorogenic acid in *Exostema caribaeum* stem bark. *J Nat Prod* **77**: 516–520.

Shanmugalingam T, Crawley D, Bosco C, *et al.* 2014. Obesity and cancer: role of vitamin D. *BMC Cancer* **14**: . DOI:10.1186/1471-2407-14-712.

Shim KS, Lee SU, Ryu SY, Min YK, Kim SH. 2009. Corosolic acid stimulates osteoblast differentiation by activating transcription factors and MAP kinases. *Phytother Res* **23**: 1754–1758.

Stohs SJ, Hartman MJ. 2015. Review of the safety and efficacy of *Moringa oleifera*. *Phytother Res* **29**: 796–804.

Stohs SJ, Miller H, Kaats GR. 2012. A review of the efficacy and safety of Banaba (*Lagerstromia speciosa* L.) and corosolic acid. *Phytother Res* **26**: 314–326.

Thom E. 2007. The effect of chlorogenic acid enriched coffee on glucose absorption in healthy volunteers and its effect on body mass when used long term in overweight and obese people. *J Int Med Res* **35**: 900–908.

Vaughan RA, Conn CA, Mermier CM. 2014. Effects of commercially available dietary supplements on resting energy expenditure: a brief review. *ISRN Nutr* . DOI:10.1155/2014/650264.