Published by iambr.info/AMBR

Open Access Original Work

Single group, open-label, pilot study of weight loss formula designed to improve body composition by facilitating loss of body fat without concomitant loss of fat-free mass

Gilbert Kaats[1], Rich Scheckenbach[2], Debasis Bagchi[3], Robert B Leckie[1], Harry G Preuss[4]

To cite: Kaats G, Scheckenbach R, Bagchi D, Leckie RB, Preuss HG. Single group, open-label, pilot study of weight loss formula designed to improve body composition by facilitating loss of body fat without concomitant loss of fat-free mass. *Arch Med Biomed Res.* 2014;1(2):54-65.

Publication history
Received: April 1, 2014
Revised: May 1, 2014
Accepted: May 3, 2014

Correspondence to
Harry G Preuss;
preusshg@georgetown.edu

ABSTRACT

Efficacy and safety of a weight-loss formula (LeanSpa, Orange, CT) designed to increase metabolism, improve appetite, and influence hormonal balance positively in order to deplete excess body fat while preserving fat-free mass (FFM) and bone mineral density (BMD) was assessed in an open-label, single-group study. This was performed using conditions that closely resembled those under which consumers would most likely use the formula. The formula consisted of chromium, 5-hydroxytryptophan, iodine, natural caffeine, octopamine HCL and extracts of Garcinia cambogia, green tea, and acai berry. Efficacy, assessed in 20 over-weight adults enrolled in a 60-day regimen, focused on changes in dual energy x-ray absorptiometry--derived body composition and resting metabolic rates (RMR). Safety was assessed by analyses of a 40-item clinical chemistry panel, vital signs, and daily tracking reports of appetite control, adverse events, and self-reported quality of life. Over two-months, subjects lost an average of 3.8 lbs of body fat (P <0.0003) while gaining 1.3 lbs of fat-free mass (FFM) (P=0.054). BMD increased, but statistical significance was not reached. Total % body fat was reduced -1.7% (P=0.0017); and abdominal fat, by -1.7% (P=0.0035). At mid-study, RMR increased 7.5% (P=0.0165) and remained elevated until the end. While self-reported appetite control increased from baseline to end of study (P=0.042), no significant changes were found in blood pressure, resting heart rate, and daily self-ratings of adverse/positive effects. These results suggest the potential for formulas designed to have a multi-mechanistic effects (increase metabolism, aid eating control, better hormonal balance) to improve body composition by facilitating loss of excess body fat without concomitant adverse effects on FFM and BMD.

KEY WORDS: ***Weight Loss; Body Composition; Body Composition Improvement Index (BCI); Fat Loss; Fat-Free Mass; Bone Mineral Density; Resting Metabolic Rate; Eating Control; Multi-Mechanistic Approach***

INTRODUCTION

Excess body fat accumulation is an increasing burden on global healthcare resources.[1-5] In United States, treatment of obesity has been estimated to approach $70 billion per year[3]

and Americans have spent billions of dollars on diet products and programs over the past five decades in futile pursuit of an effective weight-control regimen. Over a decade ago, alarmed by these statistics, the US Department of Health and Human Services targeted a reduction in excess body weight as a national objective to be achieved by the year 2000.[4] However, data from the third National Health and Nutrition Examination Survey (NHANES)[6] indicate a striking increase in the prevalence of overweight in the United States — from 24% a decade ago to almost 66% currently—the largest 10-year increase since the study began in 1960 and almost four times the combined increases of the past half-century.

Two factors that may have contributed to the failure to meet the national objective are (1) the use of too narrowly focused, single mechanistic approaches to overcome fat accumulation; and (2) by an inappropriate use of scale weight and BMI changes as outcome measures instead of changes in body composition fat, fat-free mass (FFM) and bone mineral density (BMD). With regard to the first factor, the mechanisms for ameliorating fat accumulation are likely to require a multi-mechanistic approach including (1) controlling appetite, (2) increasing calorie burning, and (3) favorably influencing various hormonal shifts that occur over time.[7] Since many factors are involved in fat accumulation, it might be more appropriate to overcome overweight/ obesity via a multiple mechanistic approach, i.e., using products and procedures that overcome the different deleterious general mechanisms involved in excess fat accumulation.

With regard to the second factor, using scale weight changes to assess weight loss ignores the importance of determining the kind, not amount, of weight change. The typical approach to weight loss through caloric restriction not only can lead to fat loss, but also often depletion of metabolically active lean tissue and lowering bone mineral density (BMD). These last two counter-productive outcomes could frequently offset the benefits of fat depletion.[7,8] Therefore, instead of using scale weight and BMI as outcome measures, we used a body composition improvement (BCI) index to reflect a safe and efficacious weight loss. The BCI is calculated by scoring losses of fat and gains in fat-free mass (FFM) (muscle and bone mineral) as positive treatment outcomes, and gains of fat and losses of lean as negative outcomes. The BCI is the sum of these calculations. The higher is the BCI, the safer and more effective is the weight loss intervention.

The purpose of this study was to examine the safety and efficacy of a novel formula designed to create positive changes in mechanisms affecting body composition. Safety was assessed with baseline-ending changes in: a 43-test clinical chemistry profile of blood, vital signs, FFM, an 84-item self-reported quality of life inventory, and daily self-reports of adverse effects and discomfort. Efficacy was assessed through baseline-ending measures of body composition (Fat mass, FFM and BMD) and self-reported appetite and food intake control.

MATERIALS AND METHODS

Methods, Materials and Procedures

Methods

This study employed an open-label, single-arm study design to create conditions that closely resembled those in which consumers were likely to use the formula. Twenty overweight adults with an average BMI of 30.5 kg/m^2±1.1 (SEM) (range 22.9 kg/m^2 to 38.8 kg/m^2) were enrolled for a 60-day study period after all participants gave written informed consent in compliance with the Helsinki Declaration and as approved by the researchers' ethics committee. In conjunction with giving written consent and after reviewing the study requirements, risks and benefits with a research technician, subjects were provided with a copy of the study's

Informed Consent (IC) and were asked to review it with their personal physicians to ensure they had no medical conditions that would preclude their participation. Subjects subsequently executed a signed IC and were asked to take the product for three days to ensure there way no immediate adverse reactions. After completion of the brief "run-in" period, subjects were asked to fast for at least 12 hours before completing the baseline tests of: (1) a Total Body DXA, (2) vital signs, (3) an 84-item Quality of Life Inventory (QOL), (4) resting metabolic rate (RMR), and (5) a 43-chemistry blood test panel. Blood was drawn at a Lab Corps Service Center of the subject's choice (www.labcorp.com). Throughout the study period, subjects completed daily self-reports of energy levels, eating control, mood changes and adverse reactions. At mid-study (30 days) subjects completed a second RMR measurement and QOL inventory. At the end of study, subjects completed the same five tests performed at baseline.

Materials

A single serving of the formula contained 200 mcg of chromium polynicotinate, 50 mcg iodine as potassium iodine, and 2020 mg of a proprietary blend of Garcinia extract (*Garcinia cambogia* fruit), Green Tea extract (*Camillia sinensis* leaf), Acai Berry extract (*Euterpe oleracea* fruit), Natural Caffeine (*Coffea arabica* fruit), 5-hydroxytryptophan (*Griffonia simplicifolia* seed) and octopamine HCL. Subjects were asked to take 2 tablets with approximately eight ounces of fluid 30-45 minutes prior to each of their three daily meals.

Procedures

Prior to beginning the study, a random sample of the product was sent to an independent laboratory (Exova Laboratories, Portland, OR) for analysis of the ingredients and potential contaminants. The analysis revealed that the ingredient amounts were within the label claims, and no evidence was found of bacterial contaminants such as Salmonella, Listeria, *E. coli*, yeast, or mold and lead.

To measure the effects of a single serving on RMR, subjects received one of two challenges with V-8 juice, one half (n=10) containing one serving of the active formula, the other (n=10) containing only the V-8 juice. The contents of the administered fluid were blinded to both the subject and the technician. After remaining at rest for 45 minutes, subjects received a second RMR measurement and completed measurements of blood pressure, resting heart rate and a self-report of their mood, appetite, and energy level.

Subjects were subsequently provided with the test product for one month and began completing the daily tracking information. At the conclusion of the 4th week, after fasting for 12 hours, subjects returned to the Center and completed a mid-study RMR, and vital signs. At the conclusion of the 8th week, after fasting 12-hours, subjects returned to the Center and completed the same baseline test battery. Subjects were paid a "reporting fee" of $2.00 for each completed daily tracking form contingent upon completing the form within three days and completing all mid-study and end-of-study testing. Throughout the study, subjects were repeatedly reminded that the tracking fee was being paid irrespective of how much or how little of the product they actually consumed. They would be paid even for days when they failed to take the product. The purpose of this procedure was to encourage candid reporting of product usage to allow dose-related comparisons at the end of the study.

Subjects were also advised that the product they were taking was designed to improve body composition by adding or preserving lean while depleting body fat. They were instructed that they would be paid an incentive fee that would double their tracking fee if they achieved a positive change in body composition as

reflected in their Body Composition Improvement (BCI) index. They were told that the BCI was calculated by scoring all gains in lean and losses of fat as positive outcomes and, conversely, losses in lean and gains of fat as negative outcomes. The BCI is the net result of these calculations. For example, a person who loses 8 lbs of scale weight, but did so by losing 2 lbs of fat and 6 lbs of lean would have a BCI of -4 lbs, an outcome opposite to what might be suggested by the 8 lb scale weight loss. This outcome measure was designed to discourage subjects from relying too heavily on scale weight changes and to avoid procedures that led to rapid weight loss typically at the expense of depleting lean mass.

Specific Testing

Body Composition

The DXA test provides a three-compartment model of body composition: fat mass, free fat mass (FFM) and bone mineral density (BMD). Measurements were made using a constant potential energy source at 78 kVp and a K-edge filter (cerium) to achieve a congruent, stable, dual-energy beam with effective energies of 40 and 70 keV. The unit performs a series of transverse scans moving from head to toe at one mm intervals; the scan area was approximately 60 cm x 200 cm. Data were collected for about 120 pixel elements (5 X 10 mm) per transverse. Total body measurements were typically completed in ~10 minutes with a scan speed of 16 cm/sec or in ~20 minutes with a scan speed of eight cm/sec. The R-value (ratio of low to high-energy attenuation in soft tissue) ranged from 1.20 to 1.47.

Clinical Chemistry Profile of Blood

In order to provide an additional measure of safety, after fasting for 12 hours, subjects had venous blood samples drawn at a local drawing station of their choice. Blood samples were collected in EDTA (one mg per milliliter) and were centrifuged within four hours, the plasma was separated, and the plasma sample shipped at 4°C to a central laboratory. Analyses were made by routine clinical procedures.

RMR, BP and RHR Measurements

After remaining seated in an isolated area for 10-15 min., participants completed measurements of their blood pressure, resting heart-rate and resting metabolism using Micro Life's MedGem® Indirect Calorimeter (Microlife Medical Home Solutions, Golden, CO. 80401). The MedGem® is a hand-held, self-calibrating calorimeter that measures oxygen consumption (VO2) to determine resting metabolic rate (RMR). In conjunction with the study, test-retest reliabilities of the instrument were measured on 41 subjects from test-retest periods ranging from 1-17 days between tests. Test-retest measurements were measured over four time intervals with the following correlation coefficients: same day = 0.87, 6 days = 0.87, 11 days = 0.97 and a second set of measurements over 17 days = 0.97 with an average coefficient over all test periods of 0.902.

Tracking Forms

All participants completed weekly tracking forms recording appetite control, energy levels, positive and negative side effects, actual amounts of the supplement taken, estimates of daily caloric intake and daily activity levels as described elsewhere.[8]

Statistical Analyses

The effects of treatment were analyzed either using Student's t-test (paired analyses) or one-way analysis of variance. All statistical testing was two-sided with P values ≤ 0.05 deemed significant. All statistical analyses were carried out with SAS (version 8.2) software (SAS Institute, Cary, North Carolina).

RESULTS

Initial RMR Testing

As shown in **Table 1**, a within-group Student's t-test reveals that the placebo

group experienced the expected and statistically significant (P=0.0424) decrease in RMR from baseline, since they continued their fasting state. Conversely, the RMR in the treatment group significantly increased from baseline (P=0.0050), and the "over-placebo" increase was even greater (P=0.0005). The average % decrease in the placebo group from baseline was -5.7% and the average % increase from baseline RMR in the treatment group was +9.4% -- a difference between the two groups of 15.1%. Only two of the ten control subjects showed an increased RMR above baseline, while all ten subjects receiving formula showed an increase 45 minutes from baseline to the end of the study.

Table 1: Acute Testing of Resting Metabolic Rate (RMR) in Subjects Receiving the Test Formulation or Placebo

	Placebo	Formula
Average Baseline Reading	1,342±64	1,271±83
45 Minutes after Challenge	1,265+50	1,391+93
Average Delta	-77	+119
Per Cent Change	-5.7%	+9.4%

P values relative to baseline range from 0.0424 to 0.0050. N = 10 for both groups. Data are shown as mean ± SEM. Results emanate from single dose of formula.

Subjects

Seventeen of the 20 subjects completed the study. Two subjects withdrew during the first month complaining of restlessness and difficulty in sleeping, even though no evidence of increased heart rate or heart palpitations was noted. With further questioning, both mentioned that they were sensitive to caffeine and had been warned previously to avoid it. The third dropout was hospitalized by her private physician for elective surgery unrelated to anything occurring in the study.

Long-term RMR Testing

Table 2 provides comparisons of RMR and vital signs at the 30-day mid-study and 60-day end-of-study. While the average RMR at mid-study and end-of-study were greater than the average beginning baseline RMR of the 17 subjects completing the study, only the difference between baseline and mid-study was statistically significant (P=0.017). At the midpoint the RMR was 7.5% higher than the initial baseline with 12 of the 17 subjects showing an increase. After two months, the RMR increased an average of 4.0% with an increase occurring in only 10 of the 17 subjects. As in baseline testing, there were no statistically significant differences in systolic and diastolic BP and RHR between baseline, mid-study and end-of-study.

Complete Blood Count

Table 3 depicts the various parameters in a complete blood count (CBC) at the beginning and end of the study. While the average white count (WBC) decreased significantly and the red count (RBC) increased significantly, these changes occurred with the normal clinical range.

Clinical Chemistry Profile of Blood

Table 4 depicts the blood chemistries at the beginning and end of the study. While total protein, albumin, globulin, HDL, AST, and ALT increased significantly, these increases occurred within the normal range.

Self-Reported Quality of Life

Table 5 shows changes in a sum of the 84 self-reported adverse health conditions. These data suggest that taking the formula led to statistically significant positive changes from: baseline to mid-study, mid-study to end-of-study, and baseline to end-of-study. Partitioning the effects of the 15 items on Dysfunction Eating Behaviors sub-scale, reveals

positive changes from baseline to mid-study, mid-study to end-of-study, and baseline to end-of-study. However, only the changes from baseline to end-of-study reached statistical significance.

Changes in Body Composition

A total of 12 of the 17 completing subjects reduced their scale weight by 2.5 lbs or more ($p<0.004$). This reduction occurred in spite of gaining an average of 1.3 lbs of FFM ($p=0.054$), because of a concomitant average loss of 3.8 lbs of body fat ($p<0.0003$). Since these FFM gains and fat losses were both considered positive outcomes, the total improvement in body composition, or BCI, was 5.1 lbs, a positive treatment outcome more than double the outcome if one used only scale weight. Abdominal fat was significantly reduced from 45%±1.7 (SEM) to 43.5%±1.9 (SEM), ($p=0.004$). Although BMD actually increased from baseline, this increase failed to reach statistical significance.

Table 2: Testing of Resting Metabolic Rate (RMR) in Subjects Receiving the Test Formulation at 1 and 2 Months

	Baseline	1 Month	2 Month
Average RMR Reading (kcal/day)	1,322±59.8	1421±71.0	1375±52.1
Average Delta (kcal/day)		+99	+53
Per Cent Change		+7.5%	+4.0%
P value relative to baseline		0.0165*	0.249
# positive		12/17	10/17
Systolic BP (mm Hg)	120±4.5	121±3.1	120±4.2
Diastolic BP (mm Hg)	77±3.0	76+±1.9	76+±3.0
Resting Heart Rate (beats/min)	66±2.6	69±3.5	67±2.2

Average values were obtained from a total number of 17 subjects. Data are expressed as mean ± SEM of 17 subjects. Results emanate from three daily doses of formula. Readings were taken 45 minutes after serving of formula.

Table 3: Complete Blood Count (CBC)

Parameter	RBC	Hct	Hgb	MCV	MCH	MCHC	WBC	Platelets
Normal	3.8-5.1	34-44	11.5-15.0	80-98	27-34	32-36	4.0-10.5	140-415
Baseline	4.4	39.8	13.4	89.8	30.2	33.7	7.2	264.2
Ending	4.6	41.1	13.8	89.4	30.1	33.7	6.5	267.4
Change	0.2	1.4	0.5	-0.4	-0.1	0.0	-0.7	3.2
P value	0.000	0.004	0.003	0.00	0.17	0.88	0.039	0.76

Average values were obtained from a total number of 17 subjects. RBC = red blood cell count values are expressed as million cells/ ml, while Hct represents hematocrit (%).

Table 4: Clinical chemistry profile of blood

Parameter	Normal Range	Baseline	Ending	Change	P value
Glucose*	65-99	94.3	95.7	1.4	0.49
BUN*	5-26	13.0	12.8	-0.2	0.55
Creatinine*	0.57-1.0	0.8	0.8	0.0	0.07
Sodium#	135-145	139.5	139.9	0.4	0.41
Potassium#	3.5-5.2	4.1	4.2	0.1	0.12
Chloride#	97-108	102.4	101.8	0.6	0.32
CO2#	20-32	22.6	22.5	-0.1	0.92
Calcium*	8.7-10.2	9.1	9.3	0.2	0.18
Total Protein@	6-8.5	6.8	7.2	0.4	0.002
Albumin@	3.5-5.5	4.2	4.4	0.2	0.019
Globulin@	1.5-4.5	2.6	2.8	0.2	0.002
Total Bilirubin*	0-1.2	0.6	0.5	0.0	0.0
Alk Phos>	25-150	78.1	77.9	-0.1	0.97
AST>	0-40	21.6	28.6	6.9	0.001
ALT>	0-55	24.6	27.7	3.1	0.04
Total Cholesterol*	100-199	197.3	200.4	3.1	0.92
Triglycerides*	0-149	160.8	149.3	-11.5	0.80
HDL*	>39	50.8	54.8	4.0	0.05
VLDL*	5-40	28.5	25.6	-2.9	0.71
LDL Cholesterol*	0-99	117.1	114.0	-3.1	0.14
CRP^	0-3.0	5.48	4.39	-1.09	0.54

*Average values are depicted for 17 finishing subjects. Values are *mg/dl, or #mEq/L, @g/dl or ^mg/L with exception of >AST, ALT and Alk Phos that are in units. BUN = blood urea nitrogen, CO2 = CO2 content, Alk Phos = alkaline phosphatase, AST = aspartate aminotransferase, ALT = alanine aminotransferase, CRP = C reactive protein.*

Table 5: Quality of life

Testing Time	Adverse Health Conditions	Adverse Eating Behavior
1. Baseline	0.155	0.196
2. Mid-study	0.137	0.148
3. Ending	0.106	0.102
p value 1 vs. 2	0.000	0.073
p value 1 vs. 3	0.000	0.042
p value 2 vs. 3	0.004	0.502

Adverse health conditions and adverse eating behavior were determined at three time points (baseline, mid-study and end point). p values <0.05 are significantly different.

Table 6: Changes in body proportions over two months

Parameter	Initial	Final	Delta	p Value	Proportion
Body Weight (lbs)	171.2±6.5	168.7±6.5	-2.5	0.004	12/17 -
Fat Mass (lbs)	73.0±4.4	69.2±4.5	-3.8	0.000	14/17 -
Abdominal Fat (%)	45.0±1.7	43.5±1.9	-1.7	0.004	15/17 -
Free Fatty Mass (lbs)	98.1±3.7	99.5±3.7	+1.3	0.054	12/17 +
BMD (g/cm^2)	1.1889±0.019	1.1916±0.019	+0.003	0.410	10/17 +
BCI (lbs)		5.1±1.3			15/17 +

Data are shown as mean ± SEM. Body weight (lbs), fat mass (lbs), abdominal fat (%), fat free mass (lbs), and BCI (g/cm2) changes are shown in the "delta" column either as "-" indicating loss and as "+" indicating gain over the period. p values <0.05 are significantly different.

DISCUSSION

There is little disagreement that the overweight state and obesity are serious and growing global problems. As the former U.S. surgeon-general Richard Carmona concluded, obesity is America's "terrorist within", the ultimate cost of which will dwarf 9/11 or any other terrorist attempt unless we reverse the current trend.[9] Extrapolating from the current trend, a recent study projected that by 2030 over 86% of Americans will be overweight or obese and by 2048 virtually all Americans will be overweight or obese.[10] Much of this has been attributed to the recent increased uptake of table sugar and high fructose corn syrup.[11,12]

Excess weight has been increasingly reported as a major risk factor for a number of degenerative diseases and has been hypothesized to play a major role in the "diabetic epidemic."[13] For example, a presentation at the American Medical Association's "National Summit on Obesity" suggested that excess body weight is a major accelerator of over 40 diseases, including the most common forms of cancer.[14] Another study reported that women with BMIs above 40, as compared to those with BMIs below this level, are at increased risk of dying from

14 different forms of cancer and 6.25 times more likely to dies from uterine cancer.[15] Another study suggests that the incidence of sudden death unexplained at post mortem examination is 40 times higher in the severely obese than in the general population.[16] Data from the Nurses Health Study confirmed the relationship between excess weight and mortality and demonstrated that the lowest mortality rates were in women who weighed 15% below the US average.[1,17] Thus, not only the obese, but women of average or slightly above-average weight are at greater risk compared with their leaner peers.

One shortcoming of the above cited studies and many others is the reliance on scale weight and BMI instead of using an index of body composition improvement outcome measures in the assessment of the risk factors and health consequences associated with overweight and obesity. While BMI typically correlates ~0.67% with measured body fat, this suggests that scale weight accounts for only about one-third of the relationship between BMI and body fat. Since the BMI is a weight/height ratio and height remains constant during most studies, changes in BMI are virtually identical to scale weight changes. But, as discussed above, what appears to be successful scale weight loss could result from a negative outcome on body composition. In fact, lean and bone are typically depleted with weight loss and severely depleted in pathologies such as anorexia. Conversely, a gain in scale weight could be the result of a depletion of excess fat, but increases of lean that exceed the amount of fat lost. The deficiencies in using scale weight and/or the BMI as outcome measures has been reported in a number of studies.[18-21] In fact, the title of one author's study, "Beyond BMI: The Value of More Accurate Measures of Fatness and Obesity in Social Science Research" captures the weakness of using the BMI as the primary outcome measure.[20]

There is widespread agreement that loss of excess fat is a positive treatment outcome and that gain of fat is a negative treatment outcome. There is also widespread agreement that loss of metabolically active FFM is a negative treatment outcome and gain of FFM is a positive treatment outcome. Because a gain in FFM is associated with an increased metabolic rate and could facilitate long-term weight control, the relative value of gaining a pound of FFM versus losing a pound of fat needs to be determined. However, notwithstanding the absence of this determination, it is our view that changes in body composition, as reflected in a BCI index, is a more precise outcome measure of the safety and efficacy of weight control interventions than scale weight or BMI. The challenge for the weight loss industry is to validate claims of the safety and efficacy of weight loss interventions, technologies or products that have been based on studies supporting positive BCIs, a challenge virtually ignored in contemporary weight loss claims.

Consistent with this paradigm shift, the formula evaluated in this study was designed specifically to enhance body composition by using a combination of natural ingredients rather than a single natural ingredient to influence multiple mechanisms controlling appetite, increasing energy expenditure, and affecting a hormonal milieu favoring fat decrease, muscle gain and retention of bone density.[7,8] The ingredients in the formula were *Garcinia* extract, 5-hydroxytryptophan, green tea extract, natural caffeine, acai, octopamine and trivalent chromium. While we are aware that natural ingredient may have more than one effect on fat loss, as a first approximation we chose *Garcinia* and 5-hydroxytrytophan for appetite suppression; octopamine, green tea and caffeine for increased metabolism, and trivalent chromium for its metabolic effects favoring fat loss and muscle gain.[7] Overall, the average BCI in the present

study was 5.1 lbs and 15 of the completing 17 subjects showing a positive BCI. The statistically significant decrease in fat, increase in FFM, while maintaining BMD suggests the formula had a positive impact on body composition.

With regard to safety as measured by changes in the 43 blood tests, it is generally accepted that significant increases in cholesterol, LDL, triglycerides, glucose, and C-reactive protein; and decreases in HDL suggest a negative outcome and potential adverse effect. A comparison between baseline and ending means for these tests revealed that there were no statistically significant changes in any of these "uni-directional" test scores. However, evaluating changes in the remaining 37 chemistries is less straightforward, since they are "multi-directional" where both increases and decreases could be associated with either adverse or positive changes. Additionally, with 37 chemistries it is probable that some changes would be chance occurrences. Therefore, instead of using changes from baseline in these 37 chemistries, we compared the number of changes in scores that were in the "normal" (or acceptable) ranges at baseline with those that became abnormal by the end of the study. Since none of the scores in the normal range became abnormal by the end of the study, it was our conclusion that the absence of changes in blood chemistries supports product safety. Additional support for the safety of the formula is provided by the positive changes in the 86-item Quality of Life Inventory and the positive change in the Dysfunctional Eating Behavior sub-scale.

The obvious weakness of this study is the absence of an RCT control group. Additionally, the "incentive" fee paid for improvements in the BCI may have introduced an artificial motivational adherence bias that had little to do with the effects of the supplement. The latter also points out a weakness in the extent to which the incentive fee may have added a degree of compliance unlike "real world" considerations.

In our view the strengths of this study go beyond serving as a precursor for a larger study by addressing three factors that may have contributed to the chronic failures of weight loss studies. One factor is that the results suggest a potential benefit of using a multi-mechanistic, instead of a single-mechanistic, approach to overcome fat accumulation, appetite control, increased energy expenditure, and favorably influencing hormonal shifts. A second factor is that the study provides an example of how the using changes in scale weight or BMI, as opposed to changes in body composition, as an outcome measure can distort a study's conclusions. In this study, using the insignificant change in scale weight as an outcome measure masked the positive changes that occurred in body composition through gains of lean and depletion of fat as reflected by the body composition improvement index, or BCI. Using the BCI as the outcome measure will also point out the adverse effects a weight loss intervention can have if it results in depletion of metabolically active lean mass—an effect masked by using weight loss or BMI as an outcome measure.[22,23] A third factor is the procedure of paying subjects for candid "reporting" of their adherence instead of "incentive" payments for compliance or adherence. It is our view that this procedure is not only more ethical, but will encourage more candid reporting of adherence that can provide valuable information for "dose-related" analyses.

Author affiliations

[1]Integrative Health Technologies, Inc., San Antonio, Texas 78209, USA

[2]Breakthrough Nutrition LLC, Sequim WA 98382, USA

[3]University of Houston, Department of Pharmacological & Pharmaceutical Sciences, Houston, TX 77204, USA

[4]Georgetown University Medical Center, Departments of Biochemistry, Medicine and Pathology, Washington DC, USA

Abbreviations: DXA: Dual Energy X-ray Absorptiometry; FFM: Fat Free Mass (Muscle tissue and bone minerals); BMD: Total Body Bone Mineral Density; RMR: Resting Metabolic Rate; BP: Blood Pressure; RHR: Resting Heart-Rate; QOL: Quality of Life; BMI: Body Mass Index; BCI: Body Composition Improvement index

REFERENCES

1. Jia H, Lubetkin EI. Obesity-related quality-adjusted life years lost in the U.S. from 1993 to 2008. *Am J Prev Med*. 2010;39(3):220-7.
2. Finkelstein EA, Trogden JG, Cohen JW, Dietz W. Annual medical spending attributable to obesity: payer- and service-specific estimates. *Health AFF (Millwood)*. 2009;28(5):822-31.
3. Cawley J, Meyerhoefer C. The Medical Care Costs of Obesity: An Instrumental Variables Approach John Cawley and Chad Meyerhoefer NBER Working Paper No. 16467, October 2010 JEL No. D62,G22,H23,I1.
4. Public Health Service: Healthy People 2000. National Health Promotion and Disease Prevention Objectives. Washington, DC: US Department of Health and Human Services; 1990. Publication 90-50212.
5. Ryan DH, Kushner R. The state of obesity and obesity research. *JAMA*. 2010;304:1835-6.
6. National Health and Nutrition Examination Survey (NHANES). Accessed Nov 2010. Retrieved from: http://www.healthline.com/galecontent/national-health-and-nutrition-examination-survey-nhanes#ixzz16EGRV0G2.
7. Preuss HG, Gottlieb. The Natural Fat Loss Pharmacy. Broadway Books, New York, NY, 2007:1-260.
8. Kaats GR. Restructuring Body Composition: How the Kind Not the Amount of Weight Loss Defines a Pathway to Optimal Health. Taylor Publishing Company, Dallas TX, 2008.
9. US Department of Health and Human Services. The obesity crisis in America. Surgeon General's Web site. http://www.surgeongeneral.gov/news/testimony/obesity07162003.html. Accessed November 30, 2010.
10. Wang Y, Beydoun MA. The obesity epidemic in the United States--gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and meta-regression analysis. *Epidemiol Rev*. 2007;29:2-28.
11. Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systemic review and meta-analysis of randomized controlled trials and cohort studies. *BMJ*. 2013;346:e7492.
12. Raben A, Richelsen B. Artificial sweeteners: a place in the field of functional foods? Focus on obesity and related metabolic disorders. *Curr Opin Clin Nutr Metab Care*. 2012;15(6):597-604.
13. Eckel RH, Kahn SE, Ferranini E, Goldfine AB, Nathan DM, Schwartz MW, et al. Obesity and type 2 diabetes: what can be unified and what needs to be individualized? *J Clin Endocrinol Metab*. 2011;96(6):1654-63.
14. American Medical Association's National Summit on Obesity, Chicago, IL, 2004.
15. Adami HO, Trichopoulos D. Obesity and mortality from cancer. *N Engl J Med*. 2003;348(17):1623-4.
16. Chugh SS, Kelly KL, Titus JL. Sudden cardiac death with apparently normal heart. *Circulation*. 2000;102(6):649-54.
17. Allison DB, Fontaine KR, Manson JE, Stevens J, Vanitallie TB. Annual deaths attributable to obesity in the United States. *JAMA*. 1999;282(16):1530-8.
18. Gallagher D, Visser M, Sepulveda D, Pierson RN, Harris T, Heymsfield SB. How useful is body mass index for comparison of body fatness across age, sex, and ethnic groups? *Am J Epidemiol*. 1996;43(3):228-39.
19. Kragelund C, Omland T. A farewell to body-mass index? *Lancet*. 2005;366(9497):1589-91.
20. Burkhauser RV, Cawley J. Beyond BMI: the value of more accurate measures of fatness and obesity in social science research. *J Health Econ*. 2008;27(2):519-29.
21. Burkhauser RV, Cawley J, Schmeiser MD. The timing of the rise in U.S. obesity varies with measure of fatness. *Econ Hum Biol*. 2009;7(3):307-18.
22. Arnold DM, Burns KE, Adhikari NK, Kho ME, Meade MO, Cook DJ; McMaster Critical Care Interest Group. The design

and interpretation of pilot trials in clinical research in critical care. *Crit Care Med*. 2009;37:S69-74.

23. Kaats GR, Preuss HG. Challenges to the conduct and interpretation of weight loss research. In: Obesity. Epidemiology, Pathophysiology, and Prevention, 2nd edition, (Eds) Bagchi D, Preuss HG, CRC Press, Fl, 2012:833-52.