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ORIGINAL COMMUNICATION

A novel soy-based meal replacement formula for weight loss among obese individuals: a randomized controlled clinical trial

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Objective: To assess the efficacy and safety of a low calorie soy-based meal replacement program for the treatment of obesity.
Design: A 12-week prospective randomized controlled clinical trial.
Setting: Outpatient weight control research unit.
Subjects: One hundred obese ($28 < BMI \leq 41$ kg/m^2) volunteers between the ages of 35 and 65 y. Seventy-four participants completed the trial.
Intervention: Participants were randomized to either the meal replacement treatment group ($n = 50$; 240 g/day, 1200 kcal/day) or control group ($n = 50$). Both groups at baseline received a single dietary counseling session and a pamphlet describing weight loss practices.
Main outcome measures: Weight, body fat, serum lipid concentrations.
Results: By intent-to-treat analysis, the treatment group lost significantly more weight than the control group (7.00 *vs* 2.90 kg; $P < 0.001$) and had a greater change in total (22.5 *vs* 6.8 mg/dl; $P = 0.013$) and LDL cholesterol (21.2 *vs* 7.1 mg/dl; $P < 0.009$). Among completers only, the treatment group again lost more weight (7.1 kg; $n = 37$ *vs* 2.9 kg; $n = 37$; $P = 0.0001$) and had a greater reduction in total cholesterol (26.1 mg/dl; $n = 37$ *vs* 6.7 mg/dl; $P = 0.0012$) and a greater change in LDL cholesterol (21.6 *vs* 5.5 mg/dl; $P = 0.0025$). (For any given degree of weight loss, the reduction in LDL cholesterol was significantly greater in the treatment group.) Treatment was well tolerated and no serious side effects were detected.
Conclusions: Use of this soy-based meal replacement formula was effective in lowering body weight, fat mass and in reducing LDL cholesterol beyond what could be expected given the weight lost.
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Keywords: obesity; soy; randomized controlled clinical trial; cholesterol

Introduction

Obesity is a medically serious (Allison & Pi-Sunyer, 1995) and increasingly prevalent condition in the USA (Flegal *et al*, 1998). Pharmacotherapy has become an increasingly popular treatment for obesity in recent years (Allison *et al*, 2001). However, the number of FDA-approved agents is quite small. Moreover,

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Contributors: **DBA was involved in the design, oversight, analysis, and the drafting of the manuscript. GG assisted in the data analysis and the drafting of the manuscript. LGS and RM were involved in the execution of the study and data interpretation. JLK conducted preliminary data analysis and assisted in the drafting of the manuscript. KRF assisted with manuscript preparation, the interpretation of the data, and editing. SH and SBH were involved in the design and oversight of the study, as well as editing drafts of the manuscript.**
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the available agents are not always efficacious or well tolerated. Thus, there is a need to rigorously evaluate additional methods for weight loss (Dhurandhar & Allison, 2000).

Soy protein may have cholesterol and triglyceride lowering effects (Clarkson, 2002; Toshiaki *et al*, 2000). Furthermore, soy protein diets have reduced body fat in both rats and genetically obese mice (Lichenstein, 1998). In addition, high-fiber diets and phospholipids have also been shown to have beneficial effects on serum lipids. The formulation used in this study combines soy protein, soy fiber and soy phospholipids. This combination has been shown to be effective in reducing serum lipids in earlier open trials (Hoie *et al*, 1993; Hoie & Bruusgaard, 1995). However, the evidence supporting the use of soy protein-based diets as anti-obesity treatment for humans, both to promote weight reduction and to reduce cholesterol levels, in rigorously conducted clinical trials is limited. Our study offers a strong experimental test of the efficacy of one potential anti-obesity program involving a novel meal-replacement formula containing isolated soy protein, fiber, and phospholipids.

Methods

One hundred overweight/obese persons with body mass index (BMI; kg/m^2) between 28 and 41 (men, $n=20$ and women, $n=80$) between the ages of 35 and 65 were recruited to participate in this trial. Exclusion criteria were: weight loss >5 kg in the past 3 months, use of weight loss medication within the past 6 weeks, scores above the 90th percentile on the Brief Symptom Inventory (BSI, a screening measure of general psychological functioning; Derogatis & Melisaratos, 1983), presence of disease not believed to be at least partially the result of obesity and treatable by weight reduction, medical or psychological contraindications as determined by study investigators, or known hypersensitivity to any of the ingredients of the formula, including but not limited to, soy protein. Prior to participation and acceptance into the program, subjects were deemed medically fit for safe weight loss through a physical examination. This study was approved by the St Luke's Roosevelt Hospital Institutional Review Board.

Design

In this parallel two group design, the treatment group received the Scan Diet meal-replacement formula (see Figure 1 for details), instructions for its use, a single session of dietary counseling and a pamphlet describing good weight loss practices, and the control group received only the single session of dietary counseling and a pamphlet describing good weight loss practices.

The treatment group was instructed to follow a daily diet that consisted of five Scan Diet Shakes, four exchanges of fruit, four exchanges of vegetables and one fat exchange. They were given a copy of the *Nutricia Scan Diet Meal Plan* booklet (scandiet.com), describing the diet as outlined in Table 1, as well as a copy of The American Dietetic Association's (1995) booklet *Exchange Lists for Weight Management*. The control group was instructed to follow a 1200 kcal exchange system diet. This group was also given a copy of The American Dietetic Association's booklet *Exchange Lists for Weight Management*. The macronutrient breakdown of the treatment and control group diets are shown in Table 1.

Upon acceptance into the trial, subjects were randomized via computer-generated pseudo random numbers at a 1:1 allocation ratio to each of the groups. Each patient was followed for 12 weeks or until dropout. Based on previous results from weight loss trials, 12 weeks was believed to be sufficient to establish short-term efficacy for weight loss (Bray & Greenway, 1999).

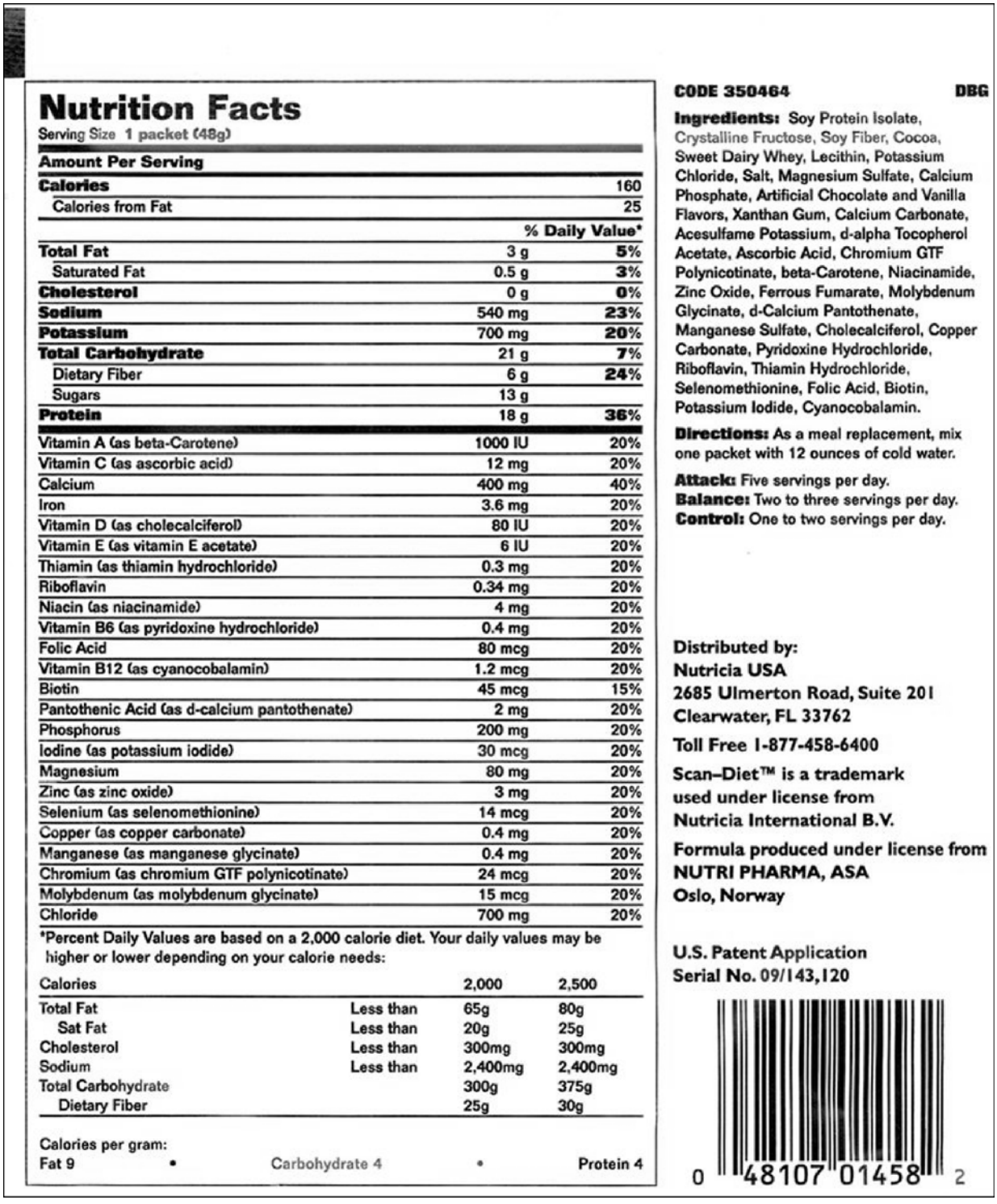
Patients were followed up at 4 week intervals and seen a total of four times, including baseline screening. At each visit, subjects in the treatment group were checked for compliance and supplied with sufficient meal replacement formula to last until the next scheduled visit, plus one additional week allowing for the possibility that patients might need to reschedule a clinic appointment. The control group was not checked for compliance and neither group was asked to keep food records. Written informed consent was obtained from each participant, and this study was approved by our institutional review board.

Compliance was checked to encourage and monitor use of the product. Meal replacement packets were counted followed by a standardized structured interview to determine compliance based on the work of Edlen-Nezin (1993). Specifically, we asked six questions (eg, 'Have you ever noticed that you miss using the formula at sometimes more than others?' 'Why do you think you sometimes miss using your formula?'), that were interposed with other questions not directly related to treatment compliance. These methods served as checks on treatment integrity (Peterson *et al*, 1982).

Measures

At each visit, patients had blood samples drawn, anthropometric measures, blood pressure and psychological wellness assessments. Laboratory assessment included standard blood work at initial screening (ie complete blood count and serum lipids). At every follow-up visit fasting blood was drawn to evaluate lipids and serum was stored for future analysis. Samples were analyzed by a commercial lab (Quest Diagnostics).

Body weight was measured within 0.1 kg using a standardized calibrated scale. Height was measured within 0.10 cm using a wall-mounted stadiometer. Body fat was measured through the use of a TANITA bio-impedance analyzer (TBF 305; Heymsfield *et al*, 1996) and waist circumference was taken with a non-distensible tape measure according to published guidelines (Lohman *et al*, 1988). Blood pressure was measured after at least 5 min rest using a standard mercury sphygmomanometer and appropriately sized cuffs according to the guidelines of the American Heart Association (Frolich *et al*, 1988).



Nutrition Facts

Serving Size 1 packet (48g)

Amount Per Serving		
Calories		160
Calories from Fat		25
		% Daily Value*
Total Fat	3 g	5%
Saturated Fat	0.5 g	3%
Cholesterol	0 g	0%
Sodium	540 mg	23%
Potassium	700 mg	20%
Total Carbohydrate	21 g	7%
Dietary Fiber	6 g	24%
Sugars	13 g	
Protein	18 g	36%
Vitamin A (as beta-Carotene)	1000 IU	20%
Vitamin C (as ascorbic acid)	12 mg	20%
Calcium	400 mg	40%
Iron	3.6 mg	20%
Vitamin D (as cholecalciferol)	80 IU	20%
Vitamin E (as vitamin E acetate)	6 IU	20%
Thiamin (as thiamin hydrochloride)	0.3 mg	20%
Riboflavin	0.34 mg	20%
Niacin (as niacinamide)	4 mg	20%
Vitamin B6 (as pyridoxine hydrochloride)	0.4 mg	20%
Folic Acid	80 mcg	20%
Vitamin B12 (as cyanocobalamin)	1.2 mcg	20%
Biotin	45 mcg	15%
Pantothenic Acid (as d-calcium pantothenate)	2 mg	20%
Phosphorus	200 mg	20%
Iodine (as potassium iodide)	30 mcg	20%
Magnesium	80 mg	20%
Zinc (as zinc oxide)	3 mg	20%
Selenium (as selenomethionine)	14 mcg	20%
Copper (as copper carbonate)	0.4 mg	20%
Manganese (as manganese glycinate)	0.4 mg	20%
Chromium (as chromium GTF polynicotinate)	24 mcg	20%
Molybdenum (as molybdenum glycinate)	15 mcg	20%
Chloride	700 mg	20%

*Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:

		2,000	2,500
Calories			
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate		300g	375g
Dietary Fiber		25g	30g

Calories per gram:
Fat 9 • Carbohydrate 4 • Protein 4

CODE 350464 **DBG**

Ingredients: Soy Protein Isolate, Crystalline Fructose, Soy Fiber, Cocoa, Sweet Dairy Whey, Lecithin, Potassium Chloride, Salt, Magnesium Sulfate, Calcium Phosphate, Artificial Chocolate and Vanilla Flavors, Xanthan Gum, Calcium Carbonate, Acesulfame Potassium, d-alpha Tocopherol Acetate, Ascorbic Acid, Chromium GTF Polynicotinate, beta-Carotene, Niacinamide, Zinc Oxide, Ferrous Fumarate, Molybdenum Glycinate, d-Calcium Pantothenate, Manganese Sulfate, Cholecalciferol, Copper Carbonate, Pyridoxine Hydrochloride, Riboflavin, Thiamin Hydrochloride, Selenomethionine, Folic Acid, Biotin, Potassium Iodide, Cyanocobalamin.

Directions: As a meal replacement, mix one packet with 12 ounces of cold water.

Attack: Five servings per day.
Balance: Two to three servings per day.
Control: One to two servings per day.

Distributed by:
Nutricia USA
2685 Ulmerton Road, Suite 201
Clearwater, FL 33762

Toll Free 1-877-458-6400

Scan–Diet™ is a trademark used under license from Nutricia International B.V.

Formula produced under license from NUTRI PHARMA, ASA Oslo, Norway

U.S. Patent Application Serial No. 09/143,120

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Figure 1 Scan Diet label.

Table 1 Macronutrient diet for the treatment and control groups

Exchange/food group	*Protein*	*Carbohydrates*	*Fat*	*Energy*
		treatment group		
5 Scan Diet shakes	90 g	75[c] g	15 g	800 kcals
4 fruits	0 g	60 g	0 g	240 kcals
4 vegetables	8 g	20 g	0 g	100 kcals
1 fat	0 g	0 g	5 g	45 kcals
Total	98 g	155 g	20 g	1185 kcals
Percentage of daily diet[a]	33%	52%	15%	
		Control group[b]		
5 starches	15 g	75 g	2.5 g	382.5 kcals
4 lean meats	28 g	0 g	12 g	220 kcals
5 vegetables	10 g	25 g	0 g	125 kcals
3 fruits	0 g	45 g	0 g	180 kcals
2 milk (nonfat)	16 g	24 g	0 g	180 kcals
3 fat	0 g	0	15 g	135 kcals
Total	69 g	169 g	29.5 g	1222.5 kcals
Percentage of daily diet[c]	23%	56%	21%	

[a]Percentage of daily diet composed of respective macronutrients.
[b]Diet prescribed derived from the American Dietetic Association (ADA) exchange lists.
[c]After removal of dietary fibers.

Side effects and adverse events were assessed by a standardized interview/questionnaire, the Monitoring of Side Effects Scale (MOSES; Kalachnik, 1985). Each of the 70 items is answered on a five-point Likert-type scale ranging from 0 = not present to 4 = severe.

Power analysis

To calculate power, we assumed, based on prior research we have conducted, a within-group weight loss standard deviation of $\sim$3.5 kg over a 12 week period. Under these assumptions, if one allocates subjects equally to treatment and control conditions, then 60 complete subjects (30 per group) provide over 80% power to reject the null hypothesis at a two-tailed α of 0.05 if the between-group difference is as small as 2.7 kg. The value of 2.7 kg was deemed suitable in planning this study because it represented a rate of weight loss of approximately $\frac{1}{2}$ lb a week for 12 weeks, which we thought would be a minimum acceptable weight loss for subjects consuming a liquid protein diet. Using a conservative estimate, based on our previous research, of a 40% post-randomization attrition rate, a total of 100 subjects were randomized into the study.

Data analysis

The primary analysis was an 'intention-to-treat' (ITT) analysis (ie data from all subjects were analyzed regardless of whether those subjects complied with or remained in treatment; Lachin, 2000; Committee for Proprietary Medicinal Products, 1997). Missing data due to dropouts were handled via multiple imputation as described by Schafer (1997). Specifically, the missing data points were computed from a probability model obtained from observed values. As a form of sensitivity analysis, we also conducted analyses with only those subjects completing the 12-week trial ('completers only').

Data were analyzed using analysis of covariance (ANCOVA) at each subsequent visit. Change from baseline (visit 1) of a subject's response was the dependent variable and the corresponding baseline response was a covariate. We did not detect any treatment $\times$ baseline interactions, nor did we find other covariates (eg race, age, etc) that were significant in explaining the variation in the dependent variable. We also analyzed changes in cholesterol and its sub-fractions using a linear regression model that included corresponding weight change as a covariate, the purpose being to determine if there were cholesterol reductions after adjusting for changes in weight. All analyses were performed with S-plus 2000.

Results

Baseline characteristics

One-hundred and twenty-one obese subjects were screened, and 100 were randomized, 40 women and 10 men to each group. Differences between groups on measured baseline characteristics did not reach significance (see Table 2). Seventy-four percent of subjects in the treatment and control groups (37/50 per group) completed the trial (see Figure 2).

Treatment effects

Weight loss. The change in weight at each assessment is shown in Table 3. ITT analyses showed that weight loss was greater in the treatment group at each assessment, significantly so at week 12 ($P = 0.001$). Among completers only,

Table 2 Measured baseline subject characteristics[a]

Characteristic	*Treatment group* ($n=50$)	*Control group* ($n=50$)
Age (y)	50.4 (8.9)	50.0 (8.0)
Weight (kg)	92.1 (14.8)	91.4 (14.0)
Body mass index (BMI, kg/m^2)	35.1 (7.9)	33.5 (3.5)
Total body fat mass (%)	42.1 (6.3)	43.1 (5.7)
Fat mass (kg)	38.9 (9.1)[b]	39.5 (8.7)
Waist circumference	101.2 (10.7)[c]	100.1 (9.6)[b]
Total cholesterol (mg/dl)	204.0 (38.7)	206.6 (35.0)[b]
LDL cholesterol (mg/dl)	126.3 (36.2)	130.1 (35.5)[b]
HDL cholesterol (mg/dl)	54.7 (15.5)	52.5 (12.2)[b]
Diastolic blood pressure (mmHg)	76.2 (7.9)[b]	77.6 (7.3)[b]
Systolic blood pressure (mmHg	115.6 (15.6)[b]	119.7 (15.0)[b]

[a]Values are mean and standard deviation.
[b]One subject missing from analysis.
[c]Two subjects missing from analysis.

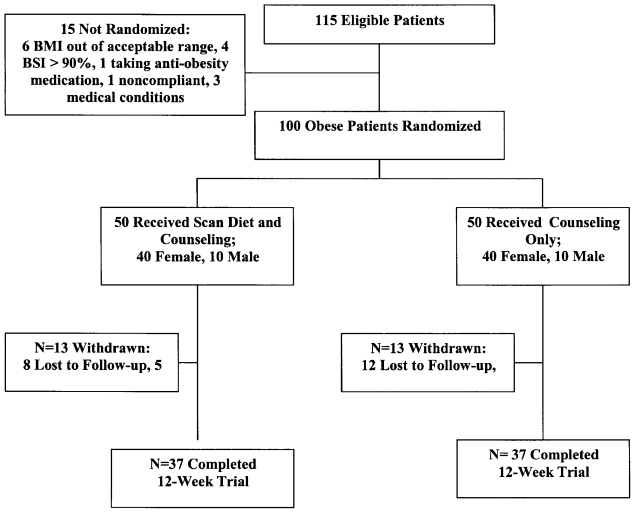

Figure 2 Study CONSORT (Begg *et al*, 1996) flow chart.

the treatment group had mean weight losses of 3.4 kg (95% confidence intervals (95% CI) 2.6, 4.1), 5.7 kg (95% CI 4.4, 7.0), and 7.1 kg (95% CI 5.4, 8.8) at weeks 4, 8 and 12, respectively, whereas the corresponding weight losses for the control group were 2.1 kg (95% CI 1.4, 2.8), 2.5 kg (95% CI 1.5, 3.4), and 2.9 kg (95% CI 1.8, 4.0; Ps $=0.0142$, <0.0001, and <0.0001, respectively).

Fat mass. Table 3 also shows the ITT analysis of change in both body fat percentage (BF%) and fat mass in both the treatment and control groups. With regard to BF%, there were no significant differences between the groups at any of

Table 3 Intention-to-treat analysis: change, mean (standard deviation), on study outcomes at each assessment

		Group		
Outcome	*Study period*	*Treatment, Mean (s.d.)*	*Control, Mean (s.d.)*	*P-value*
Weight (kg)	4 weeks	−3.5 (3.8)	−2.7 (4.5)	0.379
	8 weeks	−5.5 (5.7)	−3.0 (4.9)	0.058
	12 weeks	−7.0 (4.6)	−2.9 (3.3)	0.001
Total body fat mass (%)	4 weeks	−0.5 (3.0)	−0.3 (2.0)	0.743
	8 weeks	−0.6 (3.5)	−0.5 (4.2)	0.864
	12 weeks	−1.5 (3.6)	−0.2 (4.8)	0.255
Fat mass (kg)	4 weeks	−1.8 (3.3)	−1.5 (3.0)	0.377
	8 weeks	−3.0 (4.1)	−1.7 (3.9)	0.011
	12 weeks	−4.3 (4.0)	−1.4 (4.8)	0.003
Waist circumference	4 weeks	−3.2 (4.0)	−2.9 (4.0)	0.553
	8 weeks	−5.4 (4.5)	−3.9 (8.3)	0.324
	12 weeks	−6.0 (4.2)	−2.9 (3.7)	0.003
Total cholesterol (mg/dl)	4 weeks	−35.5 (36.8)	−13.1 (27.8)	0.002
	8 weeks	−30.8 (23.0)	−10.6 (20.4)	0.0001
	12 weeks	−22.5 (30.2)	−6.8 (24.7)	0.013
LDL cholesterol (mg/dl)	4 weeks	−32.9 (23.0)	−7.7 (20.4)	<0.0001
	8 weeks	−24.8 (22.5)	−8.3 (18.1)	<0.0001
	12 weeks	−21.2 (23.5)	−7.1 (19.1)	0.009
HDL cholesterol (mg/dl)	4 weeks	−4.6 (8.7)	−1.5 (7.0)	0.062
	8 weeks	−4.4 (8.1)	−1.4 (6.6)	0.055
	12 weeks	−1.5 (7.8)	−0.5 (10.6)	0.657
Diastolic blood pressure (mmHg)	4 weeks	−2.0 (8.2)	0.8 (7.7)	0.094
	8 weeks	−1.1 (9.4)	0.7 (7.3)	0.336
	12 weeks	−1.3 (11.0)	0.9 (6.6)	0.246
Systolic blood pressure (mmHg)	4 weeks	−1.4 (12.4)	−3.0 (13.5)	0.570
	8 weeks	−0.3 (10.4)	−0.8 (12.4)	0.858
	12 weeks	−4.8 (28.4)	−1.5 (12.3)	0.527

the assessments. However, the treatment group had a significantly greater loss of fat mass at weeks 8 and 12 compared with controls. The findings were virtually identical when the analyses were restricted to completers only (data not shown).

Blood pressure. The ITT analysis revealed that there were no significant differences in the magnitude of change on either diastolic or systolic blood pressure between the two groups (Table 3). The findings were identical in analyses that included only completers.

Cholesterol. Compared to controls, the treatment group had a significantly greater reduction in total cholesterol at each assessment in both ITT and completer-only analyses (Table 3). Interestingly, the reduction in total cholesterol remained significant in the treatment group compared with controls even after accounting for weight loss. With regard to LDL cholesterol, the treatment group had a significantly greater change than controls at each visit in both ITT and completer-only analyses (see Figure 3). The weight change by treatment interaction term was not statistically significant ($\alpha = 0.05$) and was omitted from the model. The different intercepts, therefore, represent the effect of treatment on LDL change after adjusting for weight change. The intercepts were significantly different ($P = 0.0316$). Specifically, from baseline to visit 4 the treatment group had a 12.41 mg/dl (95% CI 1.09, 23.73) greater reduction on LDL than did controls ($P = 0.031$), even after accounting for weight loss. When baseline LDL is included as a covariate, the results are virtually the same (ie 12.63 mg/dl (95% CI 2.63, 22.63) reduction, $P = 0.013$). The LDL values observed at weeks 8 and 12 were marginally significantly different from that observed at week 4 ($P = 0.059$ and $P = 0.045$, respectively), suggesting some diminution of effect over time for LDL cholesterol. The reasons for this are unclear, but may relate to factors such as reduced compliance over time, the initial

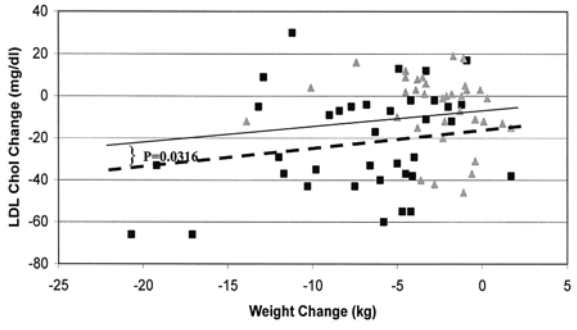

Figure 3 LDL cholesterol change by weight change: treatment *vs* control (completers only). Treatment (Scan Diet) group: black squares and black dashed line. Control group: gray triangles and gray solid line. Although the *x*-axis of this figure extends below the point to include of all the available data, we do not mean to imply that we can make confident statements that involve weight losses greater than 15 kg.

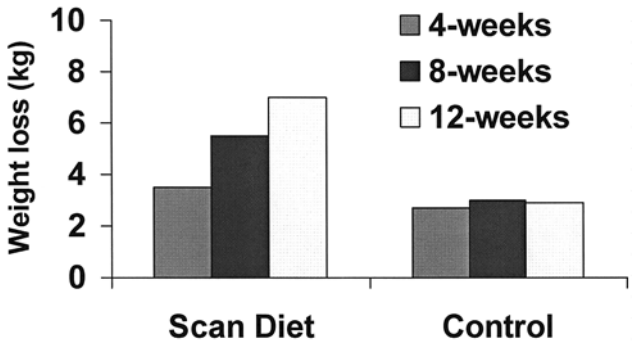

Figure 4 Weight change for the Scan Diet and control group over the course of the trial.

effects of energy restriction on cholesterol, or the slowing of weight loss over time.

On HDL cholesterol, the ITT analysis revealed no significant differences between the groups. However, among completers-only, the treatment group had a greater reduction in HDLs at weeks 8 and 12 of the study (*P*s = 0.0019, and 0.0287, respectively).

Waist circumference. The ITT analysis revealed that, compared to controls, the treatment group had a significantly greater reduction in waist circumference at week 12 (Table 3). Among completers-only, however, the treatment group had significantly greater reductions at weeks 8 and 12 (*P*s = 0.0007 and 0.0002, respectively).

Adverse effects

Table 4 provides data on each adverse effect that was significant at the nominal 0.05 α level for at least one post-randomization time point. As shown, although there were some differences, especially on gas/indigestion, the Scan Diet was generally well tolerated. However, five subjects withdrew from the study due to adverse events (three due to diarrhea, one due to diarrhea and nausea, one due to gastric reflux, and one because of generic 'symptoms unbearable'). No serious side-effects were observed.

Discussion

The group using the Scan Diet (ie treatment group) experienced significantly greater reductions in weight, fat mass and waist circumference over the 12 week trial than did controls. Furthermore, total and LDL serum cholesterol were changed to a greater extent than expected given the amount of weight loss (Anderson & Konz, 2001; Dattilo & Kris-Etherton, 1992), suggesting that soy protein, phospholipids, fibre, or other elements may reduce serum cholesterol independent of weight loss (Bosello *et al*, 1988). Other weight loss methods, specifically weight loss medications such as

Table 4 Adverse events, as assessed by the monitoring of side effects system (MOSES)

MOSES item[a]	*Study period*	*Treatment, mean*	*Control, mean*	P-*value*
7. Appetite: decreased/anorexia	4 weeks	1.29	0.42	0.0103
	8 weeks	0.76	0.53	0.1971
	12 weeks	0.89	0.46	0.1588
9. Constipation	4 weeks	0.82	0.45	0.2722
	8 weeks	0.49	0.39	0.2383
	12 weeks	0.51	0.24	0.0446
10. Diarrhea	4 weeks	0.71	0.12	0.0089
	8 weeks	0.84	0.13	0.0010
	12 weeks	0.27	0.11	0.1151
11. Drooling/salivation	4 weeks	0.24	0.00	0.0404
	8 weeks	0.03	0.00	0.3238
	12 weeks	0.03	0.03	1.0000
13. Gas/indigestion	4 weeks	2.12	0.42	<0.001
	8 weeks	1.65	0.32	<0.001
	12 weeks	1.59	0.51	0.0009
16. Taste: abnormal/metallic	4 weeks	0.49	0.00	0.0015
	8 weeks	0.30	0.00	0.0054
	12 weeks	0.30	0.00	0.0223
39. Lethargy/no movement	4 weeks	0.17	0.03	0.6791
	8 weeks	0.16	0.00	0.0778
	12 weeks	0.19	0.00	0.0426
41. Sleep: excessive	4 weeks	0.41	0.00	0.0138
	8 weeks	0.11	0.11	0.9891
	12 weeks	0.11	0.08	1.0000
63. Urinary: enuresis/nocturesis	4 weeks	0.41	0.00	0.0404
	8 weeks	0.14	0.08	0.9849
	12 weeks	0.16	0.11	1.0000
69. Weight: gain	4 weeks	0.22	0.15	0.3066
	8 weeks	0.03	0.29	0.0496
	12 weeks	0.08	0.14	0.9545
70. Weight: loss	4 weeks	1.71	0.88	0.0051
	8 weeks	1.54	0.92	0.0443
	12 weeks	1.30	0.62	0.0208

[a]Higher values indicative of greater symptom severity. MOSES items that produced a two-tailed *P*-value using a Wilcoxon rank-sum test (Mann–Whitney) ≤ 0.05 on at least one subsequent visit. For the treatment group, there were 9, 13 and 13 missing responses for weeks 4, 8 and 12, respectively. For controls, there were 17, 12 and 13 missing responses.

orlistat, have also been shown to reduce lipids more than would be expected on the basis of weight loss alone (Davidson *et al*, 1999).

This study has several strengths including: its randomized nature (Allison *et al*, 1997), the use of ITT analysis and the use of more sophisticated and statistically sound multiple imputation approach instead of the more commonly used but less than optimal last observation carried forward approach. In addition, we actively collected data on a large number of side effects through a standardized protocol rather than passively receiving spontaneous reports of adverse events as many studies of dietary supplements do.

This study also has limitations. First, the study was of only 12 weeks in duration. Thus, we could not evaluate the long-term effects of the treatment on study outcomes. Second, because of the duration of the study, many of the subjects were still in a dynamic phase of negative energy balance. It is known that negative energy balance can influence certain metabolic variables (including HDL cholesterol), independent of, and sometimes in the opposite direction of the effects expected with weight loss (Dattilo & Kris-Etherton, 1992). Third, 25% of the participants did not complete the trial. Fourth, compliance was not checked in the control group and food records were not kept in either study group. Fifth, the study was designed and powered to detect weight loss, and common easily observable side effects. Therefore, this study, while effective in showing short-term safety, cannot rule out the possibility of rare adverse effects or events that might occur with long-term use. However, given that this product and similar versions have been widely used in the US and in Europe since 1989 without apparent adversity minimizes concerns in this regard.

In this randomized controlled trial, we showed that the soy-based low calorie diet (Scan Diet) reduces body weight, total and LDL cholesterol. In this regard, we are currently following the treatment group from this study for one year and have a second 9 month randomized-controlled trial

underway. Soy protein, perhaps due to its isoflavone content, may have benefits in reducing the bone loss (Potter *et al*, 1998), alleviating symptoms of menopause (Eden, 2001), and reducing visceral adiposity (Tchernof *et al*, 1998), as well as possibly improving glucose tolerance (Hermansen *et al*, 2001; Lavigne *et al*, 2000), and systemic arterial compliance (Clarkson, 2002).

Of course, it should be noted that this study did not prove that it is the soy components of the treatment that produced the additional benefit with respect to the LDL cholesterol reduction. That is because the treatment and control group differed with respect to other characteristics besides soy component ingestion (eg receiving a meal replacement formula, counseling, differential monitoring of compliance), the effect could be attributable to other components of the treatment program to which they were assigned. Nevertheless, the randomized nature of the study does provide evidence that assignment to the Scan Diet program may have produced this effect and past research on soy components makes it quite plausible that they are critical factors in producing the observed results. Possible mechanisms by which soy might reduce LDL cholesterol include: phytoestrogen (genistein and daidzein) content, fiber components, and phosphatidylcholine (Friedman *et al*, 2001; Hecker, 2001; Tsourounis, 2001).

Future research should address these questions in the context of weight loss studies. In such studies, the Scan Diet could be compared to an equicaloric control in a blinded fashion. Finally, the high protein content of the formula used herein may have beneficial effects on satiety (Westerterp-Plantenga *et al*, 1999) as may the high fiber content (Alfieri *et al*, 1995). This speculation is consistent with the greater reduction in appetite reported by the treatment group at the four week time point (Table 4). Rigorous studies addressing the satiating efficiency (Kissileff, 1988) of this formula relative to equi-energetic controls may, therefore, be useful.

In conclusion, a soy protein meal replacement formula, the Scan Diet, was shown to be an effective treatment for weight loss and fat mass reduction, as well as an effective cholesterol-reducing agent, in obese subjects.

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