VOLUME 64. No. 4. APRIL 2003

# Effects of a Stimulant-Free Dietary Supplement on Body Weight and Fat Loss in Obese Adults: A Six-Week Exploratory Study

Derek E. Woodgate, MSc, 1,2 and Julie A. Conquer, PhD3

<sup>1</sup>NxCare Inc., Guelph, Ontario, Canada, and the Departments of <sup>2</sup>Human Biology and Nutritional Sciences and <sup>3</sup>Human Nutraceutical Research Unit, University of Guelph, Guelph, Ontario, Canada

#### **ABSTRACT**

**Background:** Obesity is a well-established risk factor for cardiovascular disease, diabetes, hyperlipidemia, hypertension, osteoarthritis, and stroke. Stimulants, such as ephedrine and caffeine and their herbal counterparts, have proved effective in facilitating body weight loss, but their use is controversial due to their undesired effects. Other nutraceuticals have shown moderate success in reducing body weight, whereas several other compounds have demonstrated little or no effect. Therefore, a tolerable and effective nutraceutical that can increase energy expenditure and/or decrease caloric intake is desirable for body weight reduction.

**Objective:** The primary purpose of this study was to assess the tolerability and effectiveness of a novel, stimulant-free, dietary supplement containing glucomannan, chitosan, fenugreek, *Gymnema sylvestre*, and vitamin C on body weight and fat loss and change in body composition in obese adults.

**Methods:** In this single-center, prospective, randomized, double-blind, placebo-controlled study conducted at the University of Guelph (Guelph, Ontario, Canada), obese adults (aged 20–50 years; body mass index [BMI], ≥30 kg/m²) were randomized to the treatment or placebo group. The treatment group received 6 capsules of a dietary supplement containing a proprietary blend of glucomannan, chitosan, fenugreek, G sylvestre, and vitamin C daily for 6 weeks, and the placebo group received 6 capsules of rice flour daily for 6 weeks. Body weight; percentage of body fat; absolute fat mass; lean body mass; BMI; upper abdominal, waist, and hip circumference; and anthropometric measurements were recorded at baseline and at study end. Patients completed daily dietary intake records on days 1 to 3 and days 40 to 42. They also completed weekly activity logs throughout the study.

**Results:** Twenty-four subjects (mean [SD] age, 37.0 [8.2] years [range, 21–48 years]; mean [SD] BMI, 35.7 [6.2] kg/m<sup>2</sup> [range, 28.9–50.9 kg/m<sup>2</sup>]) were assigned

Accepted for publication February 10, 2003.
Reproduction in whole or part is not permitted.

doi:10.1016/S0011-393X(03)00058-4 0011-393X/03/\$19.00 to the treatment group (8 women, 4 men) or the placebo group (9 women, 3 men). Two subjects (8.3%; 1 patient [8.3%] from each group) dropped out for personal reasons unrelated to the study. No significant changes in the consumption of total calories; the percentage of calories ingested as carbohydrates, fat, or protein; or activity levels were found in either group throughout the study. Compared with the placebo group, the treatment group lost significantly more body weight (-2.3 kg vs 0.0 kg; P < 0.01), percentage of body fat (-1.1% vs 0.2%; P < 0.05), and absolute fat mass (-2.0 kg vs 0.2 kg; P < 0.001). The treatment group also experienced a significantly greater reduction in upper abdominal circumference (-4.5 cm vs -0.7 cm), waist circumference (-4.1 cm vs 0.1 cm), and hip circumference (-2.9 cm vs 0.6 cm) compared with the placebo group (P < 0.05 for all). No significant changes in heart rate or blood pressure were found in either group. Both the treatment and the placebo were well tolerated.

**Conclusion:** Within the context of this study, the novel combination of glucomannan, chitosan, fenugreek, G sylvestre, and vitamin C results in significant body weight and fat loss in obese adults. (*Curr Ther Res Clin Exp.* 2003;64:248–262) Copyright © 2003 Excerpta Medica, Inc.

**Disclosure:** Derek E. Woodgate, MSc, is president and owner of NxCare Inc., which produces the dietary supplement containing glucomannan, chitosan, fenugreek, *Gymnema sylvestre*, and vitamin C (trade name Calorie-Care<sup>TM</sup>).

**Key words:** dietary supplement, glucomannan, chitosan, weight loss, body composition.

#### INTRODUCTION

Obesity, defined as an unhealthy amount of body fat, is now a well-established risk factor for cardiovascular disease, diabetes mellitus, hyperlipidemia, hypertension, osteoarthritis, and stroke. It is also strongly linked to an increased risk for morbidity and mortality, contributing to >280,000 deaths per year in the United States. Unfortunately, obesity has reached epidemic proportions in North America. Nearly one third of the US population are clinically obese, and more than half are overweight.  $^{5,6}$ 

Standard treatment options for obesity include reducing caloric intake and/or increasing energy expenditure. Caloric restriction has been shown to facilitate short-term body weight loss. However, it is often accompanied by an adaptive decrease in metabolic rate, making further body weight loss and/or maintenance difficult.<sup>7</sup>

Increased physical activity has been shown to be moderately successful in stimulating body weight loss and weight maintenance in obese individuals. However, adherence to behavioral changes, such as a structured exercise program, is generally poor, hindering the effectiveness of such programs. Specifically, >50% of individuals who initiate an exercise program discontinue within 6 months.

For these reasons, many health care practitioners and obese individuals are turning to pharmaceuticals and nutraceuticals to treat obesity. Current pharmaceutical approaches focus on methods to reduce food intake, either via the central nervous pathways or via the gastrointestinal tract. New drugs include sibutramine, a selective serotonin and norepinephrine reuptake inhibitor that elicits dose-dependent body weight reduction in obese individuals,  $^{14}$  and orlistat, a specific inhibitor of gastric and pancreatic lipase activity that reduces gastrointestinal fat absorption by  $\sim\!30\%$  and also has demonstrated efficacy in achieving body weight loss in obese individuals.  $^{15}$  Unfortunately, sibutramine exhibits common adverse events (eg, dry mouth, insomnia, anorexia, constipation) in 10% to 20% of users.  $^{16,17}$  Likewise, orlistat has been accompanied by adverse events (eg, fecal urgency, oily spotting, fatty stools, flatus and discharge, increased defecation, fecal incontinence) in 10% to 30% of participants.  $^{18,19}$ 

Stimulants, such as ephedrine and caffeine, and their herbal counterparts, ma huang and guarana, have proved effective in facilitating body weight loss.  $^{20-22}$  However, their use is controversial due to their ability to cause undesired effects, including tremors, insomnia, nervousness, dry mouth, palpitations, tachycardia, hypertension, and mood-altering effects.  $^{20,21,23-25}$  Other nutraceuticals, such as green tea and certain fibers, have shown moderate success in reducing body weight,  $^{26,27}$  whereas several other compounds (eg, hydroxycitric acid) have demonstrated little or no effect.  $^{28}$  Therefore, a tolerable and effective nutraceutical that can increase energy expenditure and/or decrease caloric intake is desirable for weight reduction.

This study investigated the effects of a stimulant-free dietary supplement on body weight and fat loss in healthy, overweight adults. This supplement was standardized to contain a novel blend of glucomannan, chitosan, fenugreek, Gymnema sylvestre, and vitamin C. It is believed that dietary fibers such as glucomannan may provoke body weight and fat loss by acting as a bulking agent, thereby increasing satiety and reducing caloric intake, ingestion rate, and nutrient absorption. 29-33 Chitosan is a unique, indigestible, nonplant fiber that may aid in body weight loss by reducing fat absorption in the intestinal tract. The addition of ascorbic acid to chitosan has been shown to improve the ability of chitosan to bind to dietary fats and inhibit their digestion. 34,35 Other herbal compounds, such as fenugreek and G sylvestre, also may induce body weight and/or fat loss in humans through several mechanisms. Among the various constituents found in fenugreek seeds, their fiber and amino acid components have been shown to exhibit blood glucose-lowering activity.<sup>36</sup> The leaf of G sylvestre has been shown to inhibit body weight gain in rats fed a high-fat diet<sup>37</sup> and to significantly decrease fat digestibility.<sup>38</sup>

Although the findings on the effectiveness of these compounds in promoting body weight and fat loss are scarce, a theoretic basis exists for their use as weight loss agents. Thus, the primary objective of this trial was to assess the tolerability and effectiveness of a novel, stimulant-free nutraceutical in reducing

body weight and fat and changing body composition. In addition to the assessment of the potential for this product to aid in body weight loss of obese subjects, the influence of this nutraceutical on upper abdominal, waist, and hip circumference; heart rate; and blood pressure was investigated. Waist circumference and body fat percentage were of particular interest because some reports<sup>34–43</sup> indicate that they are better predictors of cardiovascular disease than either body mass index (BMI) or waist-to-hip ratio.

## SUBJECTS AND METHODS Subjects

Adult volunteers were recruited from the Guelph (Ontario, Canada) community through an advertisement in a local newspaper. Approval for this study was granted by the Human Ethics Committee of the University of Guelph (Guelph, Ontario, Canada), and written informed consent was obtained from each participant.

Men and women aged 20 to 50 years with a BMI  $\geq$ 30 kg/m² were eligible to participate. Exclusion criteria included a history of cardiac disease, diabetes mellitus, hypertension (blood pressure >160/>100 mm Hg), or psychiatric disorders; use of monoamine oxidase inhibitors; pregnancy or lactation; thyroid disease; use of other dietary aids or enrollment in a weight loss program; and allergy to any of the ingredients used in the treatment.

#### **Study Protocol**

In this single-center, prospective, double-blind, placebo-controlled study, subjects were randomized to the treatment group or the placebo group by drawing cards containing randomization codes. Every 2 capsules of the dietary supplement\* were standardized to contain a proprietary blend of glucomannan, chitosan, fenugreek, G sylvestre, and vitamin C, weighing 1395 mg. The treatment and placebo capsules (rice flour) were indistinguishable in size, color, weight, and appearance. The treatment and control groups were asked to consume 2 capsules of the supplement 3 times a day, 1 hour before meals. To help ensure compliance, participants were asked to record the number of capsules taken at the end of each week and to return any unused capsules at the completion of the study. Each group consumed the capsules for a period of 6 weeks. Subjects were instructed to continue their regular diet and exercise patterns. They also received instructions on how to properly complete the daily dietary intake record; and they were asked to complete these records on 2 occasions for periods of 3 days (days 1-3 and days 40-42). The records were analyzed by Food Processor (Salem, Oregon). Subjects also completed a weekly activity log and side effect questionnaire.

<sup>\*</sup>Trademark: Calorie-Care™ (NxCare Inc., Guelph, Ontario, Canada).

Subjects reported to the laboratory on 2 occasions—baseline and week 6—and were weighed wearing only essential clothing after they had fasted for 3 hours and voided. At both visits, total body weight was assessed using a calibrated medical scale (Health-O-Meter®, Continental Scale Corp., Chicago, Illinois) accurate to 0.1 kg. Body composition was determined using bioelectric impedance (Bodystat 1500®, Bodystat Inc, Tampa, Florida). In addition, height, blood pressure (Dinamap Plus, Johnson & Johnson, New Brunswick, New Jersey), resting heart rate (Dinamap Plus), and circumference of the upper abdomen, waist, and hips were measured at each visit. Measurements at baseline and week 6 were taken at approximately the same time of day by the same investigator.

#### **Statistical Analysis**

Statistical analyses were done using the SAS system (SAS Institute Inc., Cary, North Carolina). The data were tested for normality using a normal quantile plot. An unpaired t test was used to assess between-group differences in baseline characteristics and the delta change scores from baseline to week 6. Differences between pretreatment and posttreatment dietary intake; body weight; percentage of body fat; absolute fat mass; lean body mass; BMI; upper abdominal, waist, and hip circumference; anthropometric measurements; and activity level were analyzed using a paired t test. All data are reported as mean (SD).  $P \le 0.05$  was considered statistically significant.

#### **RESULTS**

Twenty-four obese adults (mean [SD] age, 37.0 [8.2] years [range, 21–48 years]; mean [SD] BMI, 35.7 [6.2] kg/m² [range, 28.9–50.9 kg/m²]) were assigned to the treatment group (8 women, 4 men) or the placebo group (9 women, 3 men). No significant differences in age; body weight; percentage of body fat; absolute fat mass; lean body mass; BMI; or upper abdominal, waist, or hip circumference were found between the 2 groups at baseline (Table I). No significant difference in blood pressure was found between the 2 groups, but the mean resting heart rate was significantly lower in the placebo group (P < 0.05).

Two subjects (8.3%; 1 patient [8.3%] from each group) dropped out for personal reasons unrelated to the study, leaving 11 subjects (7 women, 4 men) in the treatment group and 11 (8 women, 3 men) in the placebo group.

Mean caloric intake and percentage of calories ingested as carbohydrates, fat, protein, and alcohol are shown in Table II. No significant differences in any of these variables at baseline were found between the treatment and placebo groups. Furthermore, supplementation with either placebo or the dietary supplement had no significant effect on mean total caloric intake or mean percentage of calories ingested as carbohydrates, fat, or protein. However, mean (SD) alcohol intake decreased in the treatment group from 5.1% (5.1%) to 3.2% (4.8%) of total calories ingested after 6 weeks (P < 0.05 vs baseline).

Table I.	Baseline	characteristics	of the stud	y subjects	(N = 22).	(Values ar	re expressed as
mean [SI	D] unless	otherwise spec	cified.)				

Characteristic	Treatment Group $(n = 11)$	Placebo Group (n = 11)	
- Characteristic	(11 11)	(11 11)	
Age, y	35.4 (8.6)	38.5 (7.9)	
Sex, no. (%) of subjects			
Women	7 (63.6)	8 (72.7)	
Men	4 (36.4)	3 (27.3)	
Body weight, kg	101.0 (20.8)	91.6 (16.8)	
Body fat, %	39.4 (10.3)	40.0 (5.9)	
Absolute fat mass, kg	40.2 (16.1)	36.4 (7.6)	
LBM, kg	60.8 (15.2)	55.2 (13.1)	
BMI, kg/m <sup>2</sup>	36.8 (7.7)	34.6 (4.4)	
UAC, cm	106.4 (11.7)	100.0 (10.9)	
WC, cm	111.8 (15.3)	103.5 (13)	
HC, cm	125.3 (14.6)	120.3 (6.3)	

LBM = lean body mass; BMI = body mass index; UAC = upper abdominal circumference; WC = waist circumference; HC = hip circumference.

Twenty-two participants (92%) completed the study, with 93% (8%) and 96% (4%) (P < 0.05) compliance with the dosing regimen in the treatment and placebo groups, respectively.

Body composition (mean body weight; percentage of body fat; absolute fat mass; lean body mass; BMI; and upper abdominal, waist, and hip circumference) at baseline and week 6 are shown in Table III. The decrease in mean body weight was significantly higher in the treatment group compared with the placebo group ( $-2.3~{\rm kg}$  vs  $0.0~{\rm kg}$ ; P < 0.01). The treatment group also achieved a significant reduction in mean percentage of body fat compared with the placebo group (-1.1% vs 0.3%; P < 0.05). In addition, the treatment group lost significantly more absolute fat mass compared with the placebo group ( $-2.0~{\rm kg}$ )

**Table II.** Dietary analysis (total calories and percentage of total calories ingested as carbohydrates, fat, protein, and alcohol). (Values are expressed as mean [SD].)

	Treatment Group $(n = 10)$		Placebo Group (n = 10)	
Parameter	Days 1–3	Days 40-42	Days 1–3	Days 40-42
Total calories, kcal	2165.1 (930.0)	1945.2 (835.2)	2267.5 (701.2)	1783.0 (498.5)
Carbohydrate, %	52.5 (7.6)	56.2 (10.3)	47.8 (9.6)	48.8 (8.2)
Fat, %	26.8 (9.7)	24.8 (8.7)	34.3 (8.2)	31.1 (4.3)
Protein, %	15.4 (4.7)	16.1 (5.5)	16.0 (4.1)	17.6 (6.1)
Alcohol, %	5.1 (5.1)	3.2 (4.8)*	1.7 (2.5)	2.5 (4.0)

<sup>\*</sup>P < 0.05 versus baseline.

Table III.	Body	composition.	(Values	are	expressed	as	mean	[SD]	.)
I UDIC III.	Dody	COHIDOSHIOH.	( values	uic	CAPICSSCU	us	IIICUII	וטטו	.,

	Treatment Group (n = 11)			Placebo Group (n = 11)*		P Delta Changes Between
Parameter	Baseline	Week 6	Baseline	Baseline	Week 6	Groups
Body weight, kg	101.0 (20.7)	98.7 (20.7)	< 0.005	91.6 (16.8)	91.6 (17.5)	< 0.01
Body fat, %	39.4 (10.3)	38.3 (11.1)	< 0.005	40.0 (5.9)	40.2 (6.2)	< 0.05
Absolute fat						
mass, kg	40.2 (16.1)	38.2 (16.4)	< 0.005	36.4 (7.6)	36.6 (7.9)	< 0.001
LBM, kg	61.0 (15.2)	60.5 (15.5)	NS	55.2 (13.1)	55.0 (13.6)	NS
BMI, kg/m <sup>2</sup>	36.8 (7.7)	35.9 (7.5)	< 0.05	34.6 (4.4)	34.6 (4.6)	< 0.01
UAC, cm	107.7 (11.7)	103.2 (12.0)	< 0.005	100.0 (10.9)	99.3 (11.0)	< 0.05
WC, cm	111.8 (15.3)	107.7 (14.1)	< 0.05	103.5 (13.0)	103.6 (11.9)	< 0.05
HC, cm	125.3 (14.6)	122.4 (14.4)	< 0.005	120.3 (6.3)	119.7 (6.4)	< 0.05

LBM = lean body mass; BMI = body mass index; UAC = upper abdominal circumference; WC = waist circumference; HC = hip circumference.

vs 0.2 kg; P < 0.001) and experienced a significant reduction in BMI compared with placebo ( $-1.0~{\rm kg/m^2}$  vs 0.0 kg/m², respectively; P < 0.05). Neither group experienced a significant change in LBM. In terms of anthropometric measurements, the treatment group experienced a significant reduction in upper abdominal circumference ( $-4.5~{\rm cm~vs}-0.7~{\rm cm}$ ), waist circumference ( $-4.1~{\rm cm}$  vs 0.1 cm), and hip circumference ( $-2.9~{\rm cm~vs}-0.6~{\rm cm}$ ) compared with the placebo group (all P < 0.05). Because 1 subject (9.1%) in the treatment group had an initial BMI of 50.9 kg/m², statistics were performed with and without this subject's data to determine whether the results were skewed. After performing the statistics without this subject's data, all significant results remained significant (Table IV). Therefore, this patient's data were included in all analyses.

Table V lists the body weight for each participant at baseline and week 6. Every subject in the treatment group lost body weight.

Heart rate and blood pressure data are shown in Table VI. No significant changes in heart rate or blood pressure were found.

Activity records confirmed no significant differences in activity levels between the groups.

Adverse events reported by subjects are shown in Table VII. Two subjects (18.2%) in the treatment group and 2 (18.2%) in the placebo group reported adverse events, which included constipation, headache, and indigestion (1 subject [9.1%] each in the treatment group) and dry mouth, irritability, and nausea (1 subject [9.1%] each in the placebo group). None of these adverse events were considered treatment related.

<sup>\*</sup>No significant differences versus baseline were found.

**Table IV.** Body composition without data from the subject with a body mass index of 50.9 kg/m<sup>2</sup>. (Values are expressed as mean [SD].)

	Treatmer	nt Group (n =	10)		P Delta Changes	
			P vs	Placebo Gro	up (n = 11)	Between
Parameter	Baseline	Week 6	Baseline	Baseline	Week 6	Groups
Body weight, kg	98.4 (19.9)	96.5 (20.3)	< 0.005	91.6 (16.8)	91.6 (17.5)	< 0.01
Body fat, %	37.8 (9.2)	36.6 (10.0)	< 0.005	40.0 (5.9)	40.2 (6.2)	< 0.01
Absolute fat						
mass, kg	37.0 (12.9)	35.3 (13.9)	< 0.005	36.4 (7.6)	36.6 (7.9)	< 0.001
LBM, kg	61.3 (15.9)	61.2 (16.2)	NS	55.2 (13.1)	55.0 (13.6)	NS
BMI, kg/m²	35.4 (6.4)	34.7 (6.7)	< 0.005	34.6 (4.4)	34.6 (4.6)	< 0.01
UAC, cm	106.4 (11.7)	102.1 (12.0)	< 0.005	100.0 (10.9)	99.3 (11.0)	< 0.05
WC, cm	110.4 (15.3)	106.1 (13.7)	< 0.05	103.5 (13.0)	103.6 (11.9)	< 0.05
HC, cm	122.6 (12.3)	119.9 (12.5)	< 0.05	120.3 (6.3)	119.7 (6.4)	< 0.05

LBM = lean body mass; BMI = body mass index; UAC = upper abdominal circumference; WC = waist circumference; HC = hip circumference.

#### DISCUSSION

This is the first study to investigate the combined effects of glucomannan, chitosan, fenugreek, *G sylvestre*, and vitamin C on body weight and fat loss and body composition in humans. In this study, this stimulant-free dietary supplement significantly reduced total body weight, percentage of body fat, absolute fat mass, and waist circumference compared with placebo.

**Table V.** Body weight (kg) of each study subject (N = 22).

Treatme	ent Group (n =	11)	Placeb	o Group (n = 1	1)
Subject No.	Baseline	Week 6	Subject No.	Baseline	Week 6
1	81.5	81.2	2	87.0	87.5
3	103.9	99.1	4	80.2	80.4
5	127.0	120.9	6	79.5	80.2
7	128.0	127.3	8	86.5	85.4
9	73.0	69.8	10	109.5	111.0
11	85.5	84.5	12	122.4	122.0
13	113.0	112.5	14	90.5	92.2
15	108.0	104.6	16	116.0	117.2
17	80.8	77.7	18	70.7	69.0
19	125.7	125.0	20	78.4	75.6
21	84.4	82.8	22	86.8	86.5

Table VI. Mean (SD) heart rate (HR) and blood pressure (BP).

	Treatmen (n =	•		Group : 11)
Parameter	Baseline	Week 6	Baseline	Week 6
HR, bpm BP, mm Hg	77.1 (12.8) 125/76 (20/11)	73.0 (9.1) 127/79 (15/9)	67.2 (7.0) 125/73 (13/11)	73.0 (11.3) 117/74 (17/10)

Although we were investigating the effects of a proprietary nutraceutical blend on body weight and fat loss, our results agree with studies<sup>27,44–47</sup> using many of these compounds individually. Dietary fibers are well documented to possess various physiologic and biomechanical properties that may aid in body weight loss. Amorphophallus konjac, otherwise known as glucomannan, is a dietary fiber consisting of repeating units of B-1,4 p-glucose, and p-mannose and is reported to be the most water-soluble fiber (97%), expanding up to 200 times its original volume when combined with water. 48 It is believed that dietary fibers, including glucomannan, may provoke body weight loss by acting as bulking agents, thereby increasing satiety and reducing caloric intake, ingestion rate, and nutrient absorption. <sup>29–33</sup> Glucomannan is a highly viscous fiber, more so than pectin and 5-fold more than guar gum. 49 Due to this high viscosity, glucomannan has been reported to decrease the postprandial increase in blood glucose and insulin levels.<sup>50</sup> The viscosity of glucomannan can vary greatly depending on its purity and manner of preparation. It is believed that the higher the viscosity, the more profound the effect on blood glucose and insulin levels, <sup>49</sup> although this theory is controversial. It is hypothesized that the viscosity of glucomannan prolongs the absorption of macronutrients, thereby reducing the postprandial response rather than causing malabsorption.<sup>51</sup> An animal study<sup>52</sup> has shown that glucomannan can form a gel around food particles, causing carbohydrates and lipids to be absorbed at a slower rate. Treatment with

**Table VII.** Adverse events reported by the study subjects (no. [%] of study subjects) during the 6-week supplementation period.

	Treatment Group $(n = 11)$	Placebo Group $(n = 11)$
Constipation	1 (9.1)	0
Headache	1 (9.1)	0
Indigestion	1 (9.1)	0
Dry mouth	0	1 (9.1)
Irritability	0	1 (9.1)
Nausea	0	1 (9.1)
Total events	3	3

glucomannan also has been shown to increase insulin sensitivity in patients with type 2 diabetes mellitus in as little as 3 weeks.  $^{53}$  Obesity often is associated with hyperglycemia and poor insulin sensitivity.  $^{54}$  Research by Walsh et al  $^{44}$  showed that supplementation with 1 g of glucomannan 3 times per day resulted in body weight loss comparable to that found in our trial.

Chitosan, a deacetylated derivative of chitin that is found in the exoskeleton of shrimp and crabs, is a unique, indigestible, nonplant fiber that may aid weight loss by reducing fat absorption in the intestinal tract. Whether chitosan can cause weight loss is inconclusive, as results vary from no effects<sup>55</sup> on body weight loss to mild<sup>27</sup> or moderate effects. <sup>45–47</sup> The unique positive charge of chitosan allows it to bind to negatively charged lipids and form a chitosan–fat gel 4- to 5-fold its original weight, causing the lipids to be trapped and excreted. <sup>56,57</sup> The addition of ascorbic acid to chitosan has been shown to improve the latter's ability to bind to dietary fats and inhibit their digestion. <sup>34,35</sup> This synergistic effect is attributed to the ability of ascorbic acid to reduce the viscosity of chitosan in the stomach, increase the oil-holding capacity of chitosan, and reduce the likelihood of trapped fat escaping the chitosan gel. <sup>35</sup>

Other herbal compounds, such as fenugreek and *G sylvestre*, also may induce body weight and/or fat loss through various mechanisms. Fenugreek is an annual herb cultivated in southern Europe, northern Africa, and India.<sup>58</sup> Among the constituents of fenugreek seeds, their fiber and amino acid components have been shown to exhibit glucose-lowering activity. In a study involving patients with type 1 diabetes mellitus, defatted fenugreek seed powder was found to significantly reduce fasting plasma glucose levels and to improve scores on the glucose tolerance test.<sup>36</sup> The fiber found in fenugreek has been shown to reduce the rate of diffusion toward the absorptive mucosal surface and thus alter glucose absorption. In addition, the soluble fiber fraction increases the viscosity of the gastric contents, increases the thickness of the unstirred layer in the small intestine, and inhibits the uptake of cholesterol and bile acids.<sup>59</sup> Thus, fenugreek may aid in body weight loss by improving blood glucose control.

The leaf of G sylvestre is another herb that has been shown to exhibit antihyperglycemic effects in animals.  $^{60}$  It has also been shown to inhibit weight gain in rats fed a high-fat diet $^{37}$  and to significantly decrease fat digestibility.  $^{38}$  Therefore, it is feasible that the addition of G sylvestre to a combination of glucomannan, chitosan, and fenugreek may have an additive or synergistic effect on lipid absorption, glucose control, and, ultimately, weight loss.

The studies herein\* suggest that the individual compounds used in this dietary supplement may induce body weight loss by altering the timing or absorption of macronutrients. Thus, it is possible that the significant fat loss in the treatment group can be attributed to a shift in lipid metabolism and/or absorption, potentially by improved blood glucose control. It also may be attributed to a reduction in caloric intake, although our results do not support this.

<sup>\*</sup>References 27, 34, 35, 37, 38, 44-47, 50, 51-53, 59.

We hypothesized that the blend of glucomannan, chitosan, fenugreek, *G sylvestre*, and vitamin C in the dietary supplement we studied would have a synergic effect, possibly due to increased gel formation, resulting in delayed digestion and prolonged transit time in the stomach. Prolonged transit time theoretically would allow chitosan to bind an increased amount of fat and could possibly result in a greater percentage of lipids being trapped and malabsorbed. Furthermore, the glucomannan in this supplement may increase satiety and insulin sensitivity, and reduce caloric intake. Therefore, this novel combination of fibers may both reduce caloric intake and lipid absorption, leading to body weight loss. Although the exact mechanism by which the nutraceutical combination used in our study induces body weight loss is unclear, results in vitro<sup>35</sup> and in animal studies <sup>37,38,52,57,59</sup> suggest that the individual compounds may be capable of delaying glucose absorption, eliciting lipid malabsorption, reducing caloric intake, and improving insulin sensitivity.

To further examine in humans the therapeutic potential and mechanism of body weight loss of the dietary supplement in this study, future trials should investigate substrate oxidation, insulin sensitivity, fat malabsorption, fasting lipid levels, and 24-hour energy expenditure. The present trial assessed the effectiveness of a novel dietary supplement over a relatively short time period. Thus, future trials should investigate the long-term effects of this supplement on body weight loss and maintenance.

#### **CONCLUSION**

Within the context of this study, the novel combination of glucomannan, chitosan, fenugreek, *G sylvestre*, and vitamin C results in significant body weight and fat loss in obese adults.

#### **ACKNOWLEDGMENT**

The authors would like to thank NxCare Inc. (Guelph, Ontario, Canada) for donating Calorie-Care<sup>TM</sup> and for their input in the study design.

Derek E. Woodgate, MSc, is president and owner of NxCare Inc., which produces the dietary supplement containing glucomannan, chitosan, fenugreek,  $Gymnema\ sylvestre$ , and vitamin C (trade name Calorie-Care<sup>TM</sup>).

#### **REFERENCES**

- 1. National Task Force on the Prevention and Treatment of Obesity. Overweight, obesity, and health risk. *Arch Intern Med.* 2000;160:898–904.
- 2. Must A, Spadano J, Coakley E, et al. The disease burden associated with overweight and obesity. *JAMA*. 1999;282:1523–1529.
- 3. Allison DB, Fontaine KR, Manson JE, et al. Annual deaths attributable to obesity in the United States. *JAMA*. 1999;282:1530–1538.

- 4. Cummings S, Parham ES, Strain GW. Position of the American Dietetic Association: Weight management. *J Am Diet Assoc*. 2002;102:1145–1155.
- 5. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: Prevalence and trends, 1960–1994. *Int J Obes Relat Metab Disord*. 1998:22:39–47.
- Schaefer DC, Cheskin LJ. Update on obesity treatment. Gastroenterologist. 1998;6: 136–145.
- 7. Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. *N Engl J Med.* 1995;332:621–628.
- 8. DiPietro L, Kohl HW 3rd, Barlow CE, Blair SN. Improvements in cardiorespiratory fitness attenuate age-related weight gain in healthy men and women: The Aerobics Center Longitudinal Study. *Int J Obes Relat Metab Disord.* 1998;22:55–62.
- 9. Ross R, Dagnone D, Jones PJ, et al. Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men: A randomized, controlled trial. *Ann Intern Med.* 2000;133:92–103.
- 10. Ross R, Freeman JA, Janssen I. Exercise alone is an effective strategy for reducing obesity and related comorbidities. *Exerc Sport Sci Rev.* 2000;28:165–170.
- 11. Ross R, Janssen I. Is abdominal fat preferentially reduced in response to exercise-induced weight loss? *Med Sci Sports Exerc.* 1999;31:S568–S572.
- 12. Sopko G, Leon AS, Jacobs DR Jr, et al. The effects of exercise and weight loss on plasma lipids in young obese men. *Metabolism*. 1985;34:227–236.
- 13. Dishman RK. The measurement conundrum in exercise adherence research. *Med Sci Sports Exerc.* 1994;26:1382–1390.
- 14. Hanotin C, Thomas F, Jones SP, et al. Efficacy and tolerability of sibutramine in obese patients: A dose-ranging study. *Int J Obes Relat Metab Disord*. 1998;22:32–38.
- 15. McNeely W, Benfield P. Orlistat. Drugs. 1998;56:241-249.
- 16. McNeely W, Goa KL. Sibutramine. A review of its contribution to the management of obesity. *Drugs*. 1998;56:1093–1124.
- 17. Bray GA, Blackburn GL, Ferguson JM, et al. Sibutramine produces dose-related weight loss. *Obes Res Relat Metab Disord*. 1999;7:189–198.
- 18. Sjostrom L, Rissanen A, Andersen T, et al, for The European Multicentre Orlistat Study Group. Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. *Lancet*. 1998;352:167–172.
- 19. Davidson MH, Hauptman J, DiGirolamo M, et al. Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat. *JAMA*. 1999;281:235–242.
- 20. Daly PA, Krieger DR, Dulloo AG, et al. Ephedrine, caffeine and aspirin: Safety and efficacy for treatment of human obesity. *Int J Obes Relat Metab Disord*. 1993;17 (Suppl 1):S73–S78.
- 21. Boozer CN, Nasser JA, Heymsfield SB, et al. An herbal supplement containing Ma Huang-Guarana for weight loss: A randomized, double-blind trial. *Int J Obes Relat Metab Disord*. 2001;25:316–324.
- 22. Astrup A, Toubro S, Cannon S, et al. Thermogenic synergism between ephedrine and caffeine in healthy volunteers: A double-blind, placebo-controlled study. *Metabolism*. 1991;40:323–329.
- 23. Sprual M, Ravussin AM, Fontvieille R, et al. Reduced sympathetic nervous system activity. A potential mechanism predisposing to body weight gain. *J Clin Invest*. 1993;92:1730–1735.

- 24. Bray GA, Ryan D. Drugs used in the treatment of obesity. *Diabetes Rev.* 1997;5:83–100.
- 25. Astrup A, Toubro S, Cannon S, et al. Caffeine: A double-blind, placebo-controlled study of its thermogenic, metabolic, and cardiovascular effects in healthy volunteers. *Am J Clin Nutr.* 1990;51:759–767.
- 26. Dulloo AG, Duret C, Rohrer D, et al. Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am J Clin Nutr.* 1999;70:1040–1045.
- 27. Schiller RN, Barranger E, Schauss AG, Nichols E. A randomized, double-blind, placebo-controlled study examining the effects of a rapidly soluble chitosan dietary supplement on weight loss and body composition in overweight and mildly obese individuals. *JAMA*. 2001;4:34–41.
- 28. Kovacs EM, Westerterp-Plantenga MS, Saris WH. The effects of 2-week ingestion of (-)-hydroxycitrate and (-)-hydroxycitrate combined with medium-chain triglycerides on satiety, fat oxidation, energy expenditure and body weight. *Int J Obes Relat Metab Disord*. 2001;25:1087–1094.
- 29. Birketvedt GS, Aaseth J, Florholmen JR, Ryttig K. Long-term effect of fibre supplement and reduced energy intake on body weight and blood lipids in overweight subjects. *Acta Med.* 2000;43:129–132.
- 30. Evans E, Miller DS. Bulking agents in the treatment of obesity. *Nutr Metab.* 1975;18: 199–203.
- 31. Blackwood AD, Salter J, Dettmar PW, Chaplin MF. Dietary fibre, physicochemical properties and their relationship to health. *J R Soc Health*. 2000;120:242–247.
- 32. Heaton KW. Food fibre as an obstacle to energy intake. Lancet. 1973;2:1418–1421.
- 33. Van Itallie TB. Dietary fiber and obesity. Am J Clin Nutr. 1978;31:S43–S52.
- 34. Kanauchi O, Deuchi K, Imasato Y, Kobayashi E. Increasing effect of a chitosan and ascorbic acid mixture on fecal dietary fat excretion. *Biosci Biotech Biochem*. 1994;58:1617–1620.
- 35. Kanauchi O, Deuchi K, Imasato Y, et al. Mechanism for the inhibition of fat digestion by chitosan and for the synergistic effect of ascorbate. *Biosci Biotech Biochem*. 1995;59:786–790.
- 36. Sharma RD, Raghuram TC, Rao NS. Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes. *Eur J Clin Nutr.* 1990;44:301–306.
- 37. Shigematsu N, Asano R, Shimosaka M, Okazaki M. Effect of long term-administration with *Gymnema sylvestre* R. BR on plasma and liver lipid in rats. *Biol Pharm Bull*. 2001;24:643–649.
- 38. Shigematsu N, Asano R, Shimosaka M, Okazaki M. Effect of administration with the extract of *Gymnema sylvestre* R. Br leaves on lipid metabolism in rats. *Biol Pharm Bull*. 2001;24:713–717.
- 39. Booth ML, Hunter C, Gore CJ, et al. The relationship between body mass index and waist circumference: Implications for estimates of the population prevalence of overweight. *Int J Obes Relat Metab Disord*. 2000;24:1058–1061.
- 40. Dobbelsteyn CJ, Joffres MR, MacLean DR, Flowerdew G, for the Canadian Heart Health Surveys Research Group. A comparative evaluation of waist circumference, waist-to-hip and body mass index as indicators of cardiovascular risk factors. The Canadian Heart Health Surveys. *Int J Obes Relat Metab Disord*. 2001;25:652–661.
- 41. Ledoux M, Lambert J, Reeder BA, Despres JP, for the Canadian Heart Health Surveys Research Group. A comparative analysis of weight to height and waist to hip circumference indices as indicators of the presence of cardiovascular disease risk factors. *CMAJ.* 1997;157(Suppl 1):S32–S38.

- 42. Reeder BA, Senthilselvan A, Despres JP, et al, for the Canadian Heart Health Surveys Research Group. The association of cardiovascular disease risk factors with abdominal obesity in Canada. *CMAJ*. 1997;157(Suppl 1):S39–S45.
- 43. Wei M, Gaskill SP, Haffner SM, Stern MP. Waist circumference as the best predictor of noninsulin dependent diabetes mellitus (NIDDM) compared to body mass index, waist/hip ratio and other anthropometric measurements in Mexican Americans—A 7-year prospective study. *Obes Res.* 1997;5:16–23.
- 44. Walsh DE, Yaghoubian V, Behforooz A. Effect of glucomannan on obese patients: A clinical study. *Int J Obes Relat Metab Disord*. 1984;8:289–293.
- 45. Macchi G. A new approach to the treatment of obesity: Chitosan's effects on body weight reduction and plasma cholesterol's levels. *Acta Toxicol Ther.* 1996;17:303–320.
- 46. Colombo P, Sciutto AM. Nutritional aspects of chitosan employment in hypocaloric diet. *Acta Toxicol Ther.* 1996;17:287–302.
- 47. Veneroni G, Veneroni F, Contos S, et al. Effect of a new chitosan dietary integrator and hypocaloric diet and hyperlipidemia and overweight in obese patients. *Acta Toxicol Ther.* 1996:17:53–70.
- 48. Kishida N, Okimasu S, Kamata T. Molecular weight and intrinsic viscosity of konjac glucomannan. *Agric Biol Chem.* 1978;42:1645–1650.
- 49. Jenkins DJ, Wolever TM, Leeds AR, et al. Dietary fibres, fibre analogues, and glucose tolerance: Importance of viscosity. *BMJ*. 1978;27:1392–1394.
- 50. Shima K, Tabata M, Tanaka A, Kumahara Y. Effect of dietary fiber (guar gum and konjac powder) on diabetic control. *Nutr Rep Int.* 1982;26:297–302.
- 51. Doi K. Effect of konjac fibre (glucomannan) on glucose and lipids. *Eur J Clin Nutr.* 1995;49(Suppl 3):S190–S197.
- 52. Kiriyam S, Morisaki H, Yoshido A. Changes in hypocholesterolemic activity in rats by various konnyaku powder treatments. *Agric Biol Chem.* 1970;34:641–643.
- 53. Vuksan V, Jenkins DJ, Spadafora P, et al. Konjac-mannan (glucomannan) improves glycemia and other associated risk factors for coronary heart disease in type 2 diabetes. A randomized controlled metabolic trial. *Diabetes Care*. 1999;22:913–919.
- 54. Garvey WT, Hermayer KL. Clinical implications of the insulin resistance syndrome. *Clin Cornerstone*. 1998;1:13–28.
- 55. Pittler MH, Abbot NC, Harkness EF, Ernst E. Randomized, double-blind trial of chitosan for body weight reduction. *Eur J Clin Nutr.* 1999;53:379–381.
- 56. Nauss JL, Thompson JL, Nagyvary J. The binding of micellar lipids to chitosan. *Lipids*. 1983:18:714–719.
- 57. Deuchi K, Kanauchi O, Imasato Y, Kobayashi E. Decreasing effect of chitosan on the apparent fat digestibility by rats fed on a high-fat diet. *Biosci Biotech Biochem*. 1994;58:1613–1616.
- 58. Sauvaire Y, Ribes G, Baccou JC, Loubatieeres-Mariani MM. Implication of steroid saponins and sapogenins in the hypocholesterolemic effect of fenugreek. *Lipids*. 1991;26:191–197.
- 59. Stark A, Madar Z. The effect of an ethanol extract derived from fenugreek (*Trigonella foenum-graecum*) on bile acid absorption and cholesterol levels in rats. *Br J Nutr.* 1993;69:277–287.

60. Chattopadhyay RR. Possible mechanism of antihyperglycemic effect of *Gymnema sylvestre* leaf extract, part I. *Gen Pharmacol.* 1998;31:495–496.

### Address correspondence to:

Julie A. Conquer, PhD Human Nutraceutical Research Unit J.T. Powell Building University of Guelph Guelph, Ontario Canada N1G 2W1 E-mail: jconquer@uoguelph.ca

262