Blocking Carbohydrate Absorption and Weight Loss: A Clinical Trial Using Phase 2™ Brand Proprietary Fractionated White Bean Extract

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Abstract

Background: Phase 2™ starch neutralizer brand bean extract product ("Phase 2") is a water-extract of a common white bean (*Phaseolus vulgaris*) that has been shown *in vitro* to inhibit the digestive enzyme alpha-amylase. Inhibiting this enzyme may prevent the digestion of complex carbohydrates, thus decreasing the number of carbohydrate calories absorbed and potentially promoting weight loss. Methods: Fifty obese adults were screened to participate in a randomized, double-blind, placebo-controlled study evaluating the effects of treatment with Phase 2 versus placebo on weight loss. Participants were randomized to receive either 1500 mg Phase 2 or an identical placebo twice daily with meals. The active study period was eight weeks. Thirty-nine subjects completed the initial screening process and 27 subjects completed the study. Results: The results after eight weeks demonstrated the Phase 2 group lost an average of 3.79 lbs (average of 0.47 lb per week) compared with the placebo group, which lost an average of 1.65 lbs (average of 0.21 lb per week), representing a difference of 129 percent (p=0.35). Triglyceride levels in the Phase 2 group were reduced an average of 26.3 mg/dL, more than three times greater a reduction than observed in the placebo group (8.2 mg/dL) (p=0.07). No adverse events during the study were attributed to the study medication. Conclusion: Clinical trends were identified for weight loss and a decrease in triglycerides, although statistical significance was not reached. Phase 2 shows potential promise as an adjunct therapy in the treatment of obesity and hypertriglyceridemia and further studies with larger numbers of subjects are warranted to conclusively demonstrate effectiveness.

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Introduction

Obesity is a dangerous and highly prevalent condition in the United States. Almost 61 percent of the U.S. population is either overweight (defined as a Body Mass Index (BMI) >25 kg/m^2) or obese (defined as a BMI >30 kg/m^2). Obesity increases the risk of several co-morbidities, including degenerative arthritis, obstructive sleep apnea, dyslipidemia, hypertension, diabetes mellitus, and coronary artery disease. In addition to health risks, obese individuals have lower quality of life evaluation scores (SF12) than their non-obese counterparts.[1] Fortunately, obesity is treatable and there is strong evidence that even modest weight loss

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(5% of body weight) significantly decreases the risk of these diseases, especially diabetes and cardiovascular disease.

Pharmacological treatments are currently available for obesity, including serotoninergic agents (dexfenfluramine, fluoxetine), noradrenergic agents (sibutramine) and lipase inhibitors (orlistat). While each of these drugs has been shown to be effective as an adjunct to dietary modification and exercise, their utility is limited by side effects that include cardiac valvular disease, hypertension, seizures, sexual dysfunction, and fecal incontinence.[2]

The general public uses many other methods for weight loss, including non-prescription weight loss products (herbs, vitamins, and nutritional supplements) and meal replacement preparations. Scientifically rigorous studies have not been performed on these products, and in many cases safety and efficacy take a back seat to marketing.

The Phase 2™ starch neutralizer brand bean extract product ("Phase 2") is a water extract of a common white bean (*Phaseolus vulgaris*) that has been shown *in vitro* to inhibit the digestive enzyme alpha-amylase.[3-6] Phase 2 was previously sold as Phaseolamin 2250, purportedly referring to 1 g of the product blocking 2,250 starch calories. Alpha-amylase, secreted in saliva and by the pancreas, is responsible for breaking down starch to simple sugars that are absorbed in the small intestine. Blocking this digestive enzyme may prevent the digestion of complex carbohydrates, allowing them to pass through the digestive system. The end result of blocking alpha-amylase would logically be a decrease in the number of calories absorbed, potentially promoting weight loss.

Acute and chronic (90 day) animal toxicity studies to date have demonstrated no clinical or pathological toxicity associated with ingestion of Phase 2.[7,8]

A 2003 double-blind, placebo-controlled clinical trial (n=60) of Phase 2 versus placebo for weight loss documented a 4.0-percent loss of body weight compared with 0.47 percent in the placebo group after 30 days ($p < 0.05$). In addition, the experimental group demonstrated a 10.45-percent reduction of body fat.[9]

An earlier controlled crossover study (n=10) of Phase 2 versus placebo in normoglycemic individuals measured pre- and postprandial glucose levels.[10] The glucose levels of the Phase 2 group returned to baseline 20 minutes earlier than the placebo group. In addition, the area under the plasma glucose versus time curve (a measure of glucose absorption and metabolism) was 57-percent lower with Phase 2. These results suggest less glucose is absorbed in subjects taking Phase 2 and the absorbed glucose is cleared from the bloodstream more rapidly.

Methods

Subjects

Fifty obese adults were screened for this study. Randomized subjects (n=39; 35 females, 4 males) had a mean age of 36.5 years (range: 20-69; SD 12.19) and mean weight of 193.1 lbs (range 148-256; SD 26.95). There were no significant differences between the two groups. Entry criteria included subjects older than 18, a BMI (weight in kilograms divided by the square of height in meters) of 30-43 kg/m^2, adequate contraception in women of childbearing potential, and absence of any use of drugs to treat obesity. In addition, subjects were excluded if they had active eating disorders, history of seizures, or any significant gastrointestinal (including malabsorption), cardiac, renal, hepatic, psychiatric, or endocrine disorders, or a history or presence of drug abuse or excessive alcohol intake. Potential subjects whose baseline laboratory levels were abnormal (serum creatinine > 1.6 mg/dL; BUN > 28 mg/dL; AST > 57 IU/L (males), >39 IU/L (females); ALT > 72 IU/L (males), >52 IU/L (females); HbA1C > 6%) were also excluded from the study.

Intervention

Subjects were randomly allocated (using a random number generator at www.randomizer.org) to receive either 1500 mg Phase 2 or identical placebo twice daily with lunch and dinner for eight weeks. The product was taken with at least 8 oz of water. Subjects began a controlled high-fiber/low-fat diet at the beginning of

the study that provided 100-200 g of complex carbohydrate intake per day. Carbohydrate intake was recommended for the subjects on the basis of estimated daily maintenance carbohydrate requirement. Subjects were instructed to eat the majority of carbohydrates during lunch and dinner since those were the meals at which Phase 2 or placebo were taken. Dietary compliance was measured by requiring a daily diet diary, which was reviewed at each visit. Use of any drugs, herbs, or other nonprescription preparations for obesity were discontinued prior to the start of the study.

Measures

Objective Measures

Each participant was given a physical examination. Weight and bioelectrical impedance for body fat composition were also collected.

Subjective Measures

Each participant completed 10-point Likert scales for hunger, energy, and appetite control.

Bioassays

Standard metabolic spectrophotometric assays were run on a Hitachi model 717 for glucose, triglycerides, total cholesterol, basic metabolism, liver function, and kidney function (serum creatinine and BUN). HBA1C, hematology, and urinalyses were also conducted.

Apparati

Standard metabolic spectrophotometric assays were conducted on a Hitachi model 717. A Biodynamics 310e Body Fat Analyzer was used to determine body fat composition of study subjects.[11]

Design and Procedure

A randomized, double-blind, placebo-controlled study was conducted for eight weeks. Subjects participated in five group visits over the course of eight weeks; one baseline (week 0) and four clinical visits (weeks 2, 4, 6, and 8). Each subject signed a written, informed consent form before entry into the trial.

Baseline Visit

The initial screening visit included a medical history, physical examination, body weight evaluation, and fasting lab evaluations (see Bioassays section above).

Upon being determined eligible, subjects were randomized and given medication instructions and diet instruction from a registered dietician. The following clinical visit was scheduled two weeks from baseline.

Clinical Visits

Visit 2 (End of Week 2)

At the second visit, the weight of each participant was measured and bioelectrical impedance was performed for body fat composition. The initial 10-point subjective scales for hunger, appetite control, and energy were completed during this visit.

Visit 3 (End of Week 4)

During the third visit, the participants again had their weight measured and bioelectrical impedance was performed for body fat composition. Blood samples were collected for triglyceride and cholesterol analyses. Ten-point subjective scales for hunger, appetite control, and energy were again completed.

Visit 4 (End of Week 6)

The fourth visit involved weight measurement, performance of bioelectrical impedance for body fat composition, and completion of the 10-point subjective scales for hunger, appetite control, and energy.

Visit 5 (End of Week 8)

At the concluding visit, each participant had a final weight measurement and bioelectrical impedance for body fat composition tested. Blood samples were collected for basic metabolic panel, HbA1C, liver function tests, triglyceride, and cholesterol analyses, and the final 10-point subjective scales for hunger, appetite control, and energy were completed.

Table 1. Weight Loss in Pounds

Weight loss	Week 2	Week 4	Week 6	Week 8
Phase 2™	1.87	1.93	2.29	3.79
Placebo	1.05	0.14	0.75	1.65

Table 2. Triglyceride Levels (mg/dL)

Triglyceride level	Week 0	Week 4	Week 8	Change
Phase 2™	152.6	145.3	126.3	26.3 (17.2%)
Placebo	146.9	144.6	138.7	8.2 (5.6%)

Results

Participation

Of a total of 50 subjects who initially were screened, 39 subjects were randomized and 27 completed the study. Twenty randomized subjects received Phase 2 and 19 received placebo. Fourteen Phase 2 subjects and 13 placebo subjects completed the study. New subjects were not recruited to replace dropouts and an intent-to-treat analysis was performed.

Weight Loss

The study results after eight weeks demonstrated the Phase 2 group lost an average of 3.79 lbs (an average of 0.47 lb per week) compared with the placebo group, which lost an average of 1.65 lbs (an average of 0.21 lb per week) (Table 1). The difference is 129 percent with a two-tailed p-value = 0.35. Similar trends were seen at two, four, and six weeks.

Triglyceride Levels

Triglyceride levels in the Phase 2 group decreased an average of 26.3 mg/dL, more than three times greater a reduction than the 8.2 mg/dL drop observed in the placebo group (p=0.07) (Table 2).

Secondary Outcomes

Several secondary outcomes were measured during the study. For each secondary measure, however, no clinically or statistically significant differences were identified between the active and placebo groups (Tables 3 and 4).

Adverse Events

No adverse events occurred that were believed to be due to the active product. Abdominal pain, bloating, and gas were experienced by one placebo subject, and one Phase 2 subject complained of an increased incidence of tension headaches while in the active phase of the trial.

Safety Data

Safety data was obtained at time 0 and week 8. These data included creatinine as a marker of kidney function; electrolytes including sodium, chloride, and calcium; carbon dioxide; and AST/ALT as markers of liver function. There were no clinically significant changes in any of these markers across either of the groups.

Discussion

The data from this study provides preliminary evidence through positive trends that Phase 2 may be effective in reducing both weight and triglyceride levels. Positive secondary outcome

Table 3. Secondary Outcomes

Outcome	Phase 2™ baseline	Phase 2™ at eight weeks	Phase 2™ change	Placebo baseline	Placebo at eight weeks	Placebo change	P Values
Body Fat (%)	38.7 %	38.2 %	-0.5 %	41 %	41 %	0 %	>0.05
Energy Level (10-pt scale)	4.8	6.2	+1.4	6.0	5.9	-0.1	>0.05
Appetite Control (10-pt scale)	4.7	5.1	+0.4	5.7	5.4	-0.3	>0.05
Hunger (10-pt scale)	4.8	5.1	+0.3	5.4	5.1	-0.3	>0.05
HbA1c	5.54 mg/dL	5.16 mg/ dL	-0.38 mg/dL	5.47 mg/dL	5.21 mg/dL	-0.26 mg/dL	>0.05
Total Cholesterol	194 mg/dL	200 mg/dL	+6.45 mg/dL	194 mg/dL	200 mg/dL	+6.18 mg/dL	>0.05

Table 4. Additional Secondary Outcomes – Waist and Hip Measurements

Changes from Baseline (in)		2 weeks	4 weeks	6 weeks	8 weeks
Change in Waist Measurements	Phase 2™	-1.27 in	-0.67 in	-1.29 in	-1.46 in
	Placebo	-0.85 in	-0.96 in	-1.08 in	-1.08 in
	p Values	>0.05	>0.05	>0.05	>0.05
Change in Hip Measurements	Phase 2™	+0.32 in	+0.43 in	+0.32 in	+ 0.32 in
	Placebo	-0.17 in	-0.21 in	-0.52 in	-0.57 in
	p Values	>0.05	>0.05	>0.05	>0.05

trends, including an increase in energy and a decrease in body fat, were also seen. While none of these trends reached statistical significance, they are clinically relevant and provide a good framework on which future research can be conducted.

While weight loss is an important end point in obesity treatment, the primary concern in the medical management of obesity is morbidity and mortality risk reduction by improving the underlying cardiovascular and metabolic risk factors, including high blood pressure, atherogenic dyslipidemia, and insulin resistance. A widely held view is that modest (approximately 5%) intentional weight loss is associated with significant improvements in obesity-related cardiovascular and metabolic abnormalities.[2,12-14] If the results from this study can be replicated in the future, then the Phase 2 product might play a role in this risk factor reduction by assisting with modest weight loss over time. A number of cardiovascular risk factors were measured directly and it was found the reduction of triglycerides by Phase 2 approached statistical significance (p=0.07). None of the other secondary endpoints, including total cholesterol and HbA1c, showed improvement.

There were several limitations of this study. The first and foremost was the small sample size, which occurred due to a combination of factors. These include an effect size power calculation based upon data from the only available literature at the time – a study reporting a striking difference between groups with a loss of four-percent body weight after only 30 days. Factors that may have contributed to the high dropout rate include the requirements of multiple blood draws and the slow weight loss effect of the product. Many subjects have expectations of losing several pounds a week. This study showed an average of 0.47 lb per week in the active group and 0.21 lb per week in the placebo group. Regardless of the reason, the overall number of completers was lower than hoped for. Given the statistical rigor of the study design, statistical significance was not reached. Future studies will be needed to definitively test this product. Preliminary calculations indicate a minimum of 150 completed subjects would be required to demonstrate a statistically meaningful result. This study can provide a good framework, however, for future studies to demonstrate conclusively whether Phase 2 can effectively contribute to the treatment of obesity.

Disclosures

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References

1. Hansen B. Emerging strategies for weight management. *Postgrad Med Special Report* 2001;June:3-9.
2. Hensrud DD. Pharmacotherapy for obesity. *Med Clin North Am* 2000;84:463-476.
3. Layer P, Zinsmeister AR, Di Magno EP. Effects of decreasing intraluminal amylase activity on starch digestion and postprandial gastrointestinal function in humans. *Gastroenterology* 1986;91:41-48.
4. Layer P, Rizza RA, Zinsmeister AR, et al. Effect of a purified amylase inhibitor on carbohydrate tolerance in normal subjects and patients with diabetes mellitus. *Mayo Clin Proc* 1986;61:442-447.
5. Bo-Linn GW, Santa Ana CA, Morawski SG, Fordtran JS. Starch-blockers – their effect on calorie absorption from a high-starch meal. *N Engl J Med* 1982;307:1413-1416.
6. Hollenbeck CB, Coulston AM, Quan R, et al. Effects of a commercial starch blocker preparation on carbohydrate digestion and absorption: *in vivo* and *in vitro* studies. *Am J Clin Nutr* 1983;38:498-503.

7. Jensen N, Everone C, Rosenberg M. A study of the survival, body weights, health status, and food consumption of mice when given varying concentrations of raw bean meal and bean extract which contain Phaseolamin. Unpublished Data. 1982.
8. Maheshwari R, Srimal R, Kuttan R. Chronic toxicity studies of Phaseolamin 2250. Unpublished Data. 2002.
9. Meiss DE, Ballerini R. Effectiveness of Phase 2™, a natural alpha-amylase inhibitor, for weight loss: a randomized double-blind, placebo-controlled study. Presented at Scripps Clinic Natural Supplements in Evidence-Based Practice Conference. January 18, 2003.
10. Vinson J. Investigation on the efficacy of Phaseolamin 2250, a purified bean extract from Pharmachem Laboratories. Unpublished Data. University of Scranton. 2001.
11. Lewy VD, Danadian K, Arslanian S. Determination of body composition in African-American children: validation of bioelectrical impedance with dual energy X-ray absorptiometry. *J Pediatr Endocrinol Metab* 1999;12:443-448.
12. Meyer BH, Muller FO, Grigoleit HG, Clur BK. Inhibition of starch absorption by tendamistate (an alpha amylase inhibitor). *S Afr Med J* 1983;64:284-285.
13. Anonymous. Clinically studied Phaseolamin 2250 for non-stimulant carb control. http://www.phaseolamin2250.com/catalog7.htm. Accessed October 19, 2001.
14. Goldstein DJ. Beneficial health effects of modest weight loss. *Int J Obes Relat Metab Disord* 1992;16:397-415.

Corrections to Bovine Colostrums: A Review of Clinical Uses; *Alternative Medicine Review* 2003;8(4):378-394.

The following credits were inadvertently omitted:

Figure 1.
Adapted from: Ebina T, Sato A, Umezu K, et al. Treatment of multiple sclerosis with anti-measles cow colostrum. *Med Microbiol Immunol (Berl*1984;173:87-93.

Figure 2.
Adapted from: Hagiwara K, Kataoka S, Yamanaka H, et al. Detection of cytokines in bovine colostrum. *Vet Immunol Immunopathol* 2000;76:183-190.