

BLOCKING CARBOHYDRATE ABSORPTION AND WEIGHT LOSS: A CLINICAL TRIAL USING A PROPRIETARY FRACTIONATED WHITE BEAN EXTRACT

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Background • A proprietary fractionated white bean extract of *Phaseolus vulgaris* has been shown in vitro to inhibit the digestive enzyme alpha-amylase. This may prevent or delay the digestion of complex carbohydrates, potentially resulting in weight loss.

Methods • A 4-week randomized, double-blind, placebo-controlled study of 25 healthy subjects consuming 1000 mg of a proprietary fractionated white bean extract or an identical placebo twice a day before meals in conjunction with a multi-component weight-loss program, including diet, exercise, and behavioral intervention, was conducted.

Results • Both groups reduced their weight and waist size significantly from baseline. The active group lost 6.0 lbs ($P=.0002$) and 2.2 in ($P=.0050$), and the placebo group lost 4.7 lbs ($P=.0016$) and 2.1 in ($P=.0001$). The differences between groups were not significant (weight $P=.4235$, waist size $P=.8654$). Through subsequent exploratory analysis to investigate group

findings further, subjects were stratified by total dietary carbohydrate intake. This probative analysis revealed that the tertile of subjects who had consumed the most carbohydrates demonstrated significant reductions in both weight (8.7 lbs vs 1.7 lbs, $P=.0412$) and waist size (3.3 in vs 1.3 in $P=.0100$) compared with placebo subjects in the same tertile of carbohydrate intake.

Conclusion • Subjects who adhere to a program including dietary modification, exercise, and behavioral intervention can significantly reduce their weight and waist size in a short period of time. In an exploratory analysis of data, the tertile of subjects who ate the most carbohydrates experienced a significant reduction in both weight and waist size with the addition of the white bean extract compared to the placebo group of the same tertile of carbohydrate consumption. Longer studies with a larger pool of subjects are required to validate these findings. (*Altern Ther Health Med.* 2007;13(4):32-37.)

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As weight gain and obesity have become central in the minds of the public and health professionals alike, a dizzying array of nutritional supplement options for weight loss have become available. The vast majority of the products are either untested, useless, or, in some cases, unsafe.¹

One popular method of nutritional dieting is the low-carbohydrate diet, which has become mainstream through the efforts of Atkins and others. The ability to reduce effective carbohydrate intake through the inhibition of amylase has been researched for over 20 years, starting with unpurified white kidney bean products in the 1980s²⁻⁵ and more recently with purified water extracts. The central theory is that the digestion of carbohydrates begins with salivary amylase in the mouth and continues with pancreatic amylase in the gut. The ability to block these enzymes

may result in a decrease in the digestion of complex carbohydrates into mono- and disaccharides, which are then absorbed by the gut and stored in skeletal tissue and in the liver as glycogen or stored in adipose tissue after conversion to triglycerides and fatty acids.⁶

The white bean extract is a water extract of a common white bean (*Phaseolus vulgaris*). *Phaseolus vulgaris* has been shown in vitro to inhibit the digestive enzyme alpha-amylase.^{2,7,9} This white bean extract has undergone acute and chronic (90-day) animal toxicity studies, which have not demonstrated any clinical or pathological toxicity associated with ingestion of white bean extract.¹⁰

Prior to this study, human clinical trials were conducted on the starch-neutralizer bean extract product. Four studies have been conducted. Two of these studies generated internal company data that remain unpublished,^{11,12} though the internal reports indicated that between-group differences were found. Two other studies have been conducted. One study (the only published study to date) showed a trend toward weight reduction but did not reach statistical significance,¹³ and one study did not show any difference between the placebo and active group.¹⁴

The cited studies tested the white bean extract as a single

component in a weight loss trial. This pilot study was conducted to determine whether the extract would be a useful component in a short-term, multifaceted weight loss program including diet, exercise, and behavior modification.

METHODS

This study was conducted in accordance with good clinical practices, which encompass the International Conference on Harmonisation and Helsinki Declaration. A randomized, double-blind, placebo-controlled trial was performed to determine if the addition of 1000 mg of the white bean extract twice a day to a multi-component weight loss program would demonstrate a significant difference in weight loss, waist size, hip size, triglycerides, fasting glucose, total cholesterol, appetite control, hunger, energy level, and percentage of body fat. The study sample was 25. It is acknowledged that the sample size was less than that required by a power calculation based on earlier data. However, funding from the sponsor could support only a small sample size in this pilot study due to the multi-factorial nature of the study.

Sample Generation

Participants were identified through mass community recruitment. The inclusion criteria for the study were as follows: (1) age >18 and <40 at screening; (2) body mass index (BMI) ≥ 23 kg/m² and ≤ 31 kg/m² at screening; (3) agreement to maintain diet, exercise, and behavioral modification guidelines while participating in the study; (4) agreement to periodic follow-up; and (5) females' agreement to use appropriate birth control methods during the active study. Exclusion criteria included the following: (1) use of any drugs, herbs, or other non-prescription preparations for obesity within 4 weeks of screening, including but not limited to sibutramine, orlistat, Fen-phen (Wyeth, Madison, NJ), Metabolife products (Ideasphere Inc, American Fork, Utah), diuretics, etc; (2) abnormal electrocardiogram (EKG), complete blood count (CBC), metabolic panel, or physical examination; (3) an active eating disorder; (4) severe hepatic or renal disease; (5) history of seizures, alcohol abuse, chronic malabsorption, diverticulosis, or diverticulitis; (6) diagnosis of coronary artery disease, congestive heart failure, stroke, arrhythmia, or uncontrolled hypertension; (7) pregnancy or lactation; (8) inability to understand or follow the study protocol; (9) diagnosis of significant psychiatric disease or depression; and (10) known sensitivities to the product.

Screening

Prior to participating in any study-related procedures, including clinical screen, potential subjects read and signed a Southern California University of Health Sciences Institutional Review Board-approved consent form. A clinical screening followed, including an EKG, blood work (comprehensive metabolic panel, which included serum electrolytes, liver, and kidney function tests, lipid panel, and CBC including differential), and physical by a medical doctor. Subjects fasted from midnight the night prior to a blood draw until they had attended morning lab. A cardiologist read the EKG results

to rule out any abnormalities prior to study participation, as the study required an exercise component. The participants also met individually with a registered dietician, a certified physical trainer, and a behavioral psychologist before the initiation of the study to determine if there were any reasons that compliance with the various aspects of the study would not be possible.

Study Interventions

After this screening period, participants were randomly allocated to receive either the proprietary fractionated white bean extract or identical placebo in a double-blind manner. Assessors and participants were blinded to group assignment. Two people dropped out after having been randomized. One withdrew from the study before receiving any product, and another withdrew after receiving product but without ingesting it or following other protocol requirements. These people are not included in the data analysis.

The white bean extract was administered in the form of a 500-mg capsule. The product is a water extract of the white kidney bean *Phaseolus vulgaris*. Non-genetically modified organism (GMO) whole white kidney beans were ground and then extracted for 4 hours. The liquid was filtered and concentrated under vacuum. The extract was filtered again and then pasteurized before being spray dried. The product was in capsule form and was supplied by Pharmachem Labs, Kearny, NJ.

A capsule of identical appearance, texture, taste, and smell was used as the placebo. Participants were advised to take 2 capsules (1000 mg) at the beginning of breakfast and lunch each day. No other drugs, herbs, or non-prescription products for obesity were allowed during the study.

An intensive dietary intervention included weekly personal meetings with a registered dietician, during which instructions were reiterated and prepared food was provided for the 2 meals per day when the extract or placebo was taken. Participants in the study were monitored throughout the trial by use of a daily diet record, which was evaluated by a registered dietician to determine whether participants consumed carbohydrates within the range indicated in the protocol. Other dietary factors such as fats, protein, fiber, and so forth, were monitored as well. Participants in both groups were supplied with supplemental foods that met the diet parameters to facilitate compliance and avoided diet restrictions that could produce a financial burden for participants. Breakfast and lunch were provided on a daily basis, and dinners were prepared along dietary guidelines by participants. Participants were instructed to maintain a daily caloric intake of 1800 calories. Additionally, they received an exercise regimen that instructed them to exercise for at least 30 minutes 4 times a week.

Exercise periods were supervised by a personal trainer to monitor activity to produce equivalency in effort among subjects for this component. Subjects were assessed on their baseline visit by the trainer and during weeks 2, 3, and 4 of the study were monitored to make sure that effort was stable despite the possibility of habituation to the initial routine. This trial supervision was includ-

ed to eliminate as much bias as possible in the exercise component between groups and intra-individually over time in the trial.

Finally, subjects participated in weekly group behavioral therapy sessions led by a licensed psychologist to address personal eating issues that potentially may have led to noncompliance to the protocol.

Outcome Measures and Data Collection

The primary outcome measure was weight loss. The secondary outcome measures included body composition (determined by bioelectrical impedance); waist and hip measurements; glucose, triglyceride and cholesterol levels; and subjective assessment of hunger, energy, and appetite via the 10-point visual analog scale. Adherence to the study-recommended personalized diet was monitored with the help of a daily diet diary and weekly review with feedback from a registered dietician. All data were collected at baseline and at the end of weeks 1, 2, 3, and 4. A second blood test was obtained at the end of the study to confirm product safety. A closing interview was conducted to determine compliance on all components of protocol and to make a final determination of presence or absence of side effects. Compliance was additionally audited using pill counts and records of both exercise and diet support group attendance.

Bioassays

Standard metabolic spectro-photometric assays were run on a Cell Dyn 4000 machine (Abbott Laboratories, Abbott Park, Ill) for complete blood counts (including white blood cells, hemoglobin, hematocrit, and platelets), and comprehensive metabolic panels (including liver and kidney function tests) were run on an AU-5200 (Olympus Japan Co Ltd, Tokyo).

Apparati

The Tanita Body Composition Analyzer (Tanita Corporation of America, Inc, Arlington Heights, Ill) bioelectrical impedance machine was used to obtain body composition.

The Office Medic Electrocardiograph, version 4.23 (QRS Diagnostic, LLC, Plymouth, Minn), was used to obtain EKGs.

DESIGN AND PROCEDURES

A randomized, double-blind, placebo-controlled study was conducted for 4 weeks. Subjects participated in 5 visits over the course of 5 weeks; 1 baseline (week 0) and 4 clinical visits (weeks 1, 2, 3, and 4). Each subject provided written informed consent before entry into the trial.

Baseline Visit

The initial screening visit included a medical history, physical examination, body weight evaluation, and clinical chemistry and hematology laboratory tests.

Upon eligibility, subjects were randomized and given their medication instructions along with diet instruction from a registered dietician. The following clinical visit was scheduled 1 week from baseline.

Clinical Visits

End of Week 1 (Visit 2)

During the second visit, participants had their weight measured, and bioelectrical impedance was performed for body fat composition. Also, 10-point subjective scales for hunger, appetite control, and energy were completed.

End of Week 2 (Visit 3) to End of Week 4 (Visit 5)

From week 2 to week 4, participants had their weight measured, and bioelectrical impedance was performed for body fat composition. During each visit, 10-point subjective scales for hunger, appetite control, and energy were completed. On the last visit, an additional blood draw was executed to repeat clinical chemistry and hematology laboratory tests taken at baseline.

Statistical Analysis

Before conducting the statistical analysis, all appropriate tests were conducted and assumptions for parametric tests were met for all outcome measures. As such, for within-group analysis, 2-sided paired *t*-tests evaluating changes from baseline were conducted. For between-group analyses, independent *t*-test and analysis of variance was conducted.

Additional exploratory analysis was performed by stratifying subjects into tertiles (Low/Medium/High) based on body mass index, total carbohydrate intake, and net carbohydrate intake (total carbohydrate intake minus dietary fiber intake). All 7 efficacy parameters were analyzed separately for each stratum.

Sociodemographic Characteristics and Baseline Health Parameters

Table 1 describes the socio-demographic characteristics of the study sample: 54% of the active group was male vs 83% for the placebo group. The racial, marital, and educational distributions are also presented in Table 1. Due to sparse data, no statistical tests were used for the socio-demographic data. Table 1 also represents baseline data for glucose and total cholesterol levels and independent *t*-tests were conducted to examine group differences. The results indicate no statistically significant difference between the active and placebo groups for glucose and total cholesterol levels.

Of the 25 subjects who participated in the study, 13 participants were in the active group and 12 in the placebo group. The mean weight for the active group was 178.29 lbs and 178.35 lbs in the placebo group. Mean BMI was 26.93 kg/m² in the active group and 26.07 kg/m² in the placebo group (Table 2).

RESULTS

All blood work measurements were compared at baseline and end of study, and no significant differences were found between the 2 groups (Tables 3 and 4). For each week, average calories, carbohydrates, protein, fat, and fiber intake were computed and compared between the 2 groups. No significant differences were found except for fat intake in week 3. The active group had a higher fat intake—18.7 vs 17.1—than the placebo group (data not shown).

TABLE 1 Sociodemographic Characteristics, Baseline Glucose, and Total Cholesterol Levels by Study Group

Group	Male (%)	White (%)	Married (%)	Education			N	Glucose mean (SD)	Total cholesterol mean (SD)
				BA	MA	MA+			
Active	54%	46%	54%	34%	8%	46%	13	91 (14)	214 (86)
Placebo	83%	58%	33%	67%	8%	8%	12	90 (7)	178 (42)

TABLE 2 Body Mass Index

Tertile Ranges and Number of Subjects

	Range		Number of Subjects		
	Min	Max	White bean extract	Placebo	Total
Low	23.70	25.30	3	5	8
Medium	25.44	26.80	5	4	9
High	27.10	30.08	5	3	8

TABLE 3 Mean Dietary Carbohydrate Intake

Tertile Ranges and Number of Subjects

	Range (grams per day)		Number of Subjects		
	Min	Max	White bean extract	Placebo	Total
Low	57.13	58.43	3	5	8
Medium	58.61	59.55	5	4	9
High	60.19	61.63	5	3	8

TABLE 4 Net Dietary Carbohydrate Intake

Tertile Ranges and Number of Subjects

	Range (grams per day)		Number of Subjects		
	Min	Max	White bean extract	Placebo	Total
Low	18.84	24.16	4	4	8
Medium	24.38	27.18	3	6	9
High	27.89	33.84	6	2	8

Weight

The active group lost 6 lbs (3.4%) in 4 weeks, and the placebo group lost 4.7 lbs (2.6%) in the same time period (Table 5). The change from baseline was statistically significant in each group (active $P=.0002$, placebo $P=.0016$); however, the between-group analysis was not statistically significant ($P=.4235$).

When the groups were stratified by total carbohydrate intake, those in the highest tertile demonstrated a significant difference between groups. The active group lost 8.7 lbs, and the placebo group lost 1.7 lbs with a between-group difference of $P=.0412$. There were no significant differences seen in the low or medium tertiles for total carbohydrate intake nor were there any significant differences seen in the stratification of the BMI or net carbohydrate intake groups.

Waist Size

In 4 weeks, the active group lost 2.2 in from their waists

TABLE 5 Results: Weight Loss

Stratification	Active	Placebo	Between-Group Analysis
None	-6.0	-4.7	$P=.4235$
Low body mass index	-4.267	-4.96	$P=.7573$
Medium body mass index	-3.6	-1.9	$P=.5244$
High body mass index	-9.44	-8	$P=.5283$
Low total carbohydrate intake	-4.4	-3.9	$P=.8884$
Medium total carbohydrate intake	-5.8	-7.0	$P=.5905$
High total carbohydrate intake	-8.55	-1.65	$P=.0412$
Low net carbohydrate intake	-7.15	-7.0	$P=.9179$
Medium net carbohydrate intake	-7.733	-2.367	$P=.1448$
High net carbohydrate intake	-4.367	-7.1	$P=.4359$

($P=.050$ compared with baseline) and the placebo group lost 2.1 in from their waists ($P=.0001$ compared with baseline, Table 6). The between-group analysis was not statistically significant ($P=.8654$).

The stratum analysis revealed that the active group subset of subjects in the high total carbohydrate intake group had significantly greater reductions in their waist sizes compared with the placebo group. The active group lost 3.3 in from their waistlines, whereas the placebo group lost 1.3 in from their waistlines. The between-group analysis was significant, with a P value of .0100. Again, none of the other strata for the total carbohydrate intake subgroup and neither the BMI nor net carbohydrate intake groups demonstrated any significant differences between active and placebo regarding reduction in waist size.

Other Efficacy Parameters

Several other parameters were analyzed for changes from baseline including hip size; triglyceride, fasting glucose, and total cholesterol levels; appetite control; hunger; energy level; and body fat percentage. There were no significant differences seen between groups or from baseline in any of these parameters even when stratified by BMI, total carbohydrate intake, or net carbohydrate intake.

TABLE 6 Results: Waist Size

Stratification	Active	Placebo	Between-Group Analysis
None	-2.2	-2.1	<i>P</i> =.8654
Low body mass index	-3.667	-2.4	<i>P</i> =.2351
Medium body mass index	-0.7	-1.75	<i>P</i> =.5039
High body mass index	-3	-2	<i>P</i> =.2031
Low total carbohydrate intake	-2.25	-2	<i>P</i> =.8876
Medium total carbohydrate intake	0	-2.667	<i>P</i> =.1377
High total carbohydrate intake	-3.25	-1.25	<i>P</i> =.0100
Low net carbohydrate intake	-2.167	-2.125	<i>P</i> =.9712
Medium net carbohydrate intake	-1.667	-2.25	<i>P</i> =.7387
High net carbohydrate intake	-2.5	-1.5	<i>P</i> =.5060

Safety and Compliance

No side effects or adverse events were reported during the total trial period. Safety monitoring included kidney and liver function tests as well as blood and platelet counts. There were no significant differences between the 2 groups at baseline for blood screen data, nor were there any significant differences from baseline or between groups at the end of the intervention.

Compliance was determined through pill count and workout and therapy attendance. There were no significant differences between groups on compliance. Compliance rated at above 95% for both pill consumption and exercise. Therapy sessions had a compliance rate of 75%; attendance percentage was nearly identical for each group.

DISCUSSION

This short-term, multi-component study demonstrates that subjects who adhere to a program including dietary modification, exercise, and group behavioral support for dietary compliance can lose a significant amount of weight in a relatively short period of time. The inclusion of the white bean extract in addition to the multiple components of diet, exercise, and behavior did not make a significant group (active vs placebo) difference in this short time frame.

The results of the exploratory analysis showed that when the groups were stratified by the total number of carbohydrates that they ate, the tertile that ate the most carbohydrates did see significant differences in weight loss (8.7 lbs vs 1.7 lbs, *P*=.0412) and waist size (3.3 in vs 1.3 in, *P*=.0100) when using the white bean extract. If future subjects eat a larger percentage of carbohydrates and are able to diminish the effective caloric value of this

volume through the use of an alpha-amylase inhibitor such as the white bean extract, then those subjects may experience a decrease in weight and waist size greater than those who do not consume as many calories from carbohydrates.

Possible limitations of this study include the fact that the white bean extract or placebo was delivered with only 2 of the 3 meals per day. Carbohydrate intake was recorded on a daily basis and not merely for the meals at which the white bean extract or placebo was given. In addition, this was a very short study (4 weeks) and included only 25 subjects. The inclusion of the exercise program and group behavioral support components may have influenced groups differentially, though current data can not confirm this potential. The inclusion of the behavioral therapy component to address personal eating issues may have confounded results as well. Although subjects with overt eating disorders were excluded from the study, the psycho-social issues that accompany obesity are highly varied, and the effectiveness of a behavioral intervention is difficult to quantify.

The trends identified by this study in such a short time period need to be validated by further studies. A potential explanation is that the white bean extract's carbohydrate-blocking action prevents absorption of more calories in people whose dietary intake includes a larger proportion of carbohydrates than persons whose dietary intake includes fewer calories from carbohydrates. This finding certainly should be explored further, as the study included a very small range of appropriate carbohydrate intake, which was monitored by daily diary records reviewed by a registered dietician. Finding differences within such a small range of variation requires further probing. As some promising differentials for response to this therapy are reported here in this preliminary study, ideally it would be followed up with a sample in congruence with power calculation requirements to show efficacy between groups. In subsequent studies, the total carbohydrate intake should match that of the high total carbohydrate intake tertile from this study to determine whether the explanation for differences are based on even small dietary intake differentials. In addition, it might make physiological sense for the test medication to be given at all meals throughout the day rather than just 2 meals per day, as in this study.

Weight gain is truly a multi-factorial problem that encompasses the fields of endocrinology, psychology, nutrition, and exercise physiology. This study attempts to combine the approaches of these various disciplines and add a new variable in the form of alpha amylase inhibition to decrease carbohydrate digestion. These preliminary results from a subset of study subjects demonstrate that the white bean extract may have the potential to be a useful adjunct to traditional weight control methods; however, longer studies with a larger pool of subjects are minimally required before any definitive conclusions can be made. It was reported in 2005 that 60.5% of adult Americans were overweight, 23.9% obese, and 3% severely obese.¹⁵ Therefore, any additional knowledge about a potentially helpful product for weight reduction is warranted and should be investigated with more studies of greater sophistication as funding allows.

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