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AMERICAN BOTANICAL COUNCIL

HerbClip™

File: ■ White Bean (*Phaseolus vulgaris*)
■ Weight Loss
■ Glycemic Control

HC 121124-444

Date: March 15, 2012

RE: Comprehensive Review of Proprietary White Bean Extract Intake for Weight Loss and Glycemic Control by Preventing Carbohydrate Absorption

Barrett ML, Udani JK. A proprietary alpha-amylase inhibitor from white bean (*Phaseolus vulgaris*): A review of clinical studies on weight loss and glycemic control. *Nutr J.* 2011 Mar 17;10:24. doi:10.1186/1475-2891-10-24.

Obesity and its associated health risks are a medical problem worldwide. In addition to exercise and control of diet, foods that slow the absorption of carbohydrates can be an effective therapy. White bean (*Phaseolus vulgaris*) includes α-amylase and glucosidase inhibitors, which inhibit the enzymes that breakdown carbohydrates. The authors review the evidence that a branded, proprietary product can induce weight loss and reduce the spike in blood sugar that occurs with ingestion of carbohydrates.

Carbohydrates that consist of monosaccharides are absorbed quickly in the intestine and are called "high glycemic foods," while those that consist of polysaccharides are absorbed more slowly and are called "low glycemic foods." After eating high glycemic foods such as white bread, potatoes, and dates, there is a rapid spike in blood sugar and insulin levels. This can lead to the accumulation of lipids in the muscles and liver, and begins the progression to insulin insensitivity and type 2 diabetes. Spikes in blood sugar and increased insulin levels can also be key factors in the development of cardiovascular disease (CVD). Therefore, the type of carbohydrate ingested is very important. Carbohydrates that are naturally found in seeds, legumes, and unprocessed whole grains are "resistant" to digestion. Adding resistant starches to foods, such as bread, pasta, and nutrition bars, can be an effective way to lower the glycemic index (GI) of the food.

Another way to alleviate the spike in blood sugar and insulin that follows carbohydrate consumption is to prevent the breakdown of the carbohydrate in the intestine. Several pharmaceutical drugs such as Acarbose (Prandase®, Precose®) act in this way and have been shown to reduce the incidence of CVD and hypertension, as well as to improve insulin resistance in type 2 diabetes patients. Certain compounds in plants have shown similar effects, for example, raspberries (*Rubus idaeus* ssp. *idaeus*) and strawberries

(*Fragaria* spp.) contain anthocyanins which inhibit α-amylase activity and ellagitannins which inhibit α-glucosidase activity.

A-amylase inhibitors are also present in grains and beans. The most amount of research along these lines has been done on white beans, specifically the branded product Phase 2® Carb Controller (Pharmachem Laboratories; Kearny, New Jersey). It contains three isoforms of the α-amylase inhibitor (α-A1, α-A12, and α-AIL), which act by completely blocking access to the active site of the α-amylase enzyme. Early studies at the Mayo Clinic using a purified concentrate (6-8 times the protein content) showed it inactivated α-amylase in the saliva and intestine in a dose-dependent manner in humans. In one study using 5 g and 10 g of white bean extract (introduced via intubation), intestinal amylase was inhibited by 95% in 15 minutes, and the receipt of carbohydrates into the distal parts of the small bowel was increased by 22-24% (showing that the carbohydrates had not been absorbed in the upper intestine). The white bean preparation also reduced the spike in blood glucose by 85% and minimized the subsequent dip of blood glucose levels following metabolism. Levels of insulin, C-peptide, and gastric inhibitory polypeptide were also lower. Additional studies conducted with diabetics showed that as little as 2.9 g of whole white bean extract, taken as a powder or tablet, produced statistically significant differences in the same parameters. A longer term study (3 weeks) with higher doses (4-6 g) also confirmed these benefits. Gastrointestinal symptoms and diarrhea that occurred in some subjects on the first day resolved within a few days of continuing the supplement.

The Phase 2 Carb Controller product is a water extract produced from non-genetically modified organism (non-GMO) whole white kidney beans, which are ground and then extracted for 4 hours. Phase 2 is odorless and tasteless and was designed to be more potent and stable than the earlier product tested by the Mayo Clinic. It can be used in powder, tablet, capsule, or chewable form, and is contained in approximately 200 products worldwide, including chewing gum, mashed potatoes, and yeast-raised dough. Typical dosing for the capsule form is 1 to 2 capsules (500 mg per capsule), taken before each of 3 daily meals, for a total of 1500 to 3000 mg per day.

Phase 2 has been tested in 10 clinical studies which demonstrated weight loss over time. Four studies compared Phase 2 to a placebo using doses ranging from 445 mg for 4 weeks to 3000 mg for 4 to 12 weeks. In a 12-week randomized, double-blind, placebo-controlled study in overweight individuals (n=60; body mass index [BMI] between 24 and 32 kg/m^2) consuming 3000 mg/day of Phase 2 in the form of a soft chew, subjects had an average loss of 6.9 lbs (3.1 kg), while the placebo group gained just under a pound. A randomized, double-blind, placebo-controlled study performed in China (n=101) used 3000 mg of Phase 2 split into 3 doses per day for 60 days, with an average weight loss of 4.9 lbs (1.9 kg) compared to 0.88 lbs (0.4 kg) in the placebo group ($P<0.0001$).

A third randomized, double-blind, placebo-controlled study in slightly overweight subjects (n=60) utilized a combination tablet of 445 mg Phase 2 and 0.5 mg of chromium picolinate per day taken before a high-carbohydrate meal. After 30 days, subjects had an average weight loss of 6.45 lbs (2.93 kg) compared with 0.77 lbs (0.35 kg) in the placebo group ($P<0.001$). There were also significant differences in BMI, fat mass, adipose tissue thickness, and waist/hip/thigh circumferences while maintaining lean body mass. A fourth study in overweight adults used 2000 mg of Phase 2 split into 2 doses per day for 4 weeks in addition to nutritional guidance, an exercise program, and psychological counseling. In this study, both the treatment and placebo groups lost

weight (6.0 lbs [2.7 kg] and 4.7 lbs [2.1 kg], respectively), and there was no statistically significant difference between them. When stratified by carbohydrate intake, they demonstrated that the more carbohydrate ingested, the greater the weight loss. No adverse effects were reported in any of the 4 studies.

Three studies demonstrated the efficacy of Phase 2 for weight loss over time, but did not provide significant comparisons to a placebo group. A randomized, double-blind, placebo-controlled trial (n=40) in overweight adults utilized a proprietary blend (Suco-Bloc®; Med-Eq AS; Norway) containing 200 mg of Phase 2 (Phaseolamin®; Leuven Bioproducts; Belgium), 200 mg of inulin (from chicory [*Cichorium intybus*] root), and 50 mg of garcinia (*Garcinia cambogia*) extract. There was a significant reduction in weight for the treatment group of 7.7 lbs (3.5 kg; P=0.001), while the placebo group lost 2.9 lbs (1.3 kg); body mass analysis showed this was mostly due to loss of fat.

In the second study, which was double-blind and placebo-controlled (n=60), subjects took 2 capsules of Thera-Slim™ (ProThera; Reno, Nevada) containing 500 mg Phase 2 plus 250 mg fennel (*Foeniculum vulgare*) seed powder, or placebo, for 12 weeks along with meals containing 100-200 g of carbohydrates. After the first 12 weeks, the treatment group lost 1.4 lbs (0.64 kg), while the placebo group gained an average of 0.6 lbs (0.27 kg). Also after the initial 12 weeks, all subjects took the Phase 2 product for an additional 12 weeks. Lastly, a randomized, double-blind, placebo-controlled study in obese subjects (n=39) taking 3000 mg of Phase 2 per day for 8 weeks following carbohydrate meals averaged a weight loss of 3.79 lbs (1.7 kg) compared with the placebo group, which lost an average of 1.65 lbs (0.75 kg); the between-group difference was not statistically significant. No adverse effects were noted in any of these three studies.

Several open-label studies on weight loss have also been conducted. One study was conducted with Phaseolamin™ 1600 diet (Metabolic Company, Ltd; Japan; 750 mg Phase 2, 200 mg clove [*Syzygium aromaticum*], 20 mg lysine, 20 mg arginine, and 20 mg alanine) in overweight subjects (n=10). After 8 weeks, the subjects' body weight decreased significantly (2.4%; 74.5 ± 7.3 kg to 72.7 ± 7.8 kg; P=0.002), as did caloric intake (P=0.01), body fat (P<0.001), BMI (P=0.002), and blood lipids. A second study (n=37) used Precarb (Carb Intercept; Natrol; Chatsworth, California) at a dose of 2 capsules, 3 times daily with high-carbohydrate meals for 30 days. Body weight decreased by 5.15 lbs (2.34 kg; P<0.001), and there was also a significant reduction in mean waist-to-hip ratio of 2.77 ± 2.55 (P<0.001). Another study used Super Bows Diet Type B (Japan), which contains 500 mg Phase 2, forskohlii (*Plectranthus barbatus* syn. *Coleus forskohlii*) extract, and mushroom chitosan (Plus fort Barrious®; Barrious Laboratories; Tokyo, Japan), and was taken as a powder in water before lunch and dinner. There was no change in caloric intake, but total cholesterol did decrease significantly (P<0.05). Minor gastrointestinal symptoms with this product resolved after a few days of use.

Four crossover studies assessed the effect of Phase 2 on glycemic control and showed that the product could reduce spikes in blood sugar after a meal in a dose-dependent manner. A placebo-controlled, crossover study tested the blood sugar after consumption of 4 slices of bread with margarine in 11 subjects. In comparison to controls, glucose levels returned to normal 20 minutes sooner when subjects took 1500 mg of Phase 2. The area under the plasma glucose vs. time curve (AUC) was 66% smaller compared to the control (P<0.05). In the same study, 7 subjects were given a full meal (630 calories with 64 g carbohydrates) with or without 750 mg of Phase 2. The average plasma

glucose vs. time curve was reduced by 28% with the Phase 2. The authors conclude that there is a dose-related effect, with 1500 mg of Phase 2 being twice as effective as 750 mg. A 6-arm crossover study comparing a capsule and powder form of Phase 2 in 3 doses of 1500, 2000, and 3000 mg showed that only the 3000 mg powder dose caused significant reductions in the GI following a carbohydrate load. A study using Super Bows Diet Type B (n=13) showed that both blood sugar and plasma insulin levels decreased 30 minutes after consumption of carbohydrates (both $P<0.01$).

With respect to safety, there were no reports of serious adverse side effects in human studies with doses up to 3000 mg of Phase 2 for 24 weeks. There were no reported adverse reactions or signs of toxicity in an acute animal toxicity study (doses of 500-5000 mg/kg) or a 90-day subchronic study (doses of 200-1000 mg/kg). The no-observed-adverse-effect level (NOAEL) was established to be 2500 mg/kg/day, and an independent safety review by Cantox Health Sciences International concluded that it is safe for humans to consume up to 10 g of Phase 2. While raw beans contain phytohaemagglutinin, which can cause severe gastrointestinal disturbances in humans, this compound is found in low levels in white beans and is inactivated by processing.

The authors note that it is difficult to equate different carbohydrate blockers with one another, and therefore they focused on the Phase 2 product only. They conclude that the evidence presented in this paper indicates that Phase 2 reduces the rate of absorption of carbohydrates (thereby reducing the GI of foods) and also promotes weight loss when taken concurrently with meals containing carbohydrates.

—Risa Schulman, PhD

Referenced article can be found at http://www.nutritionj.com/content/pdf/1475-2891-10-24.pdf.