Review

Bean Amylase Inhibitor and Other Carbohydrate Absorption Blockers: Effects on Diabesity and General Health

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Many believe that excessive intake of refined carbohydrates (CHO) plays a major role in the development of obesity/overweight, type 2 diabetes mellitus and insulin resistance, a collection of events commonly referred to as ''diabesity,'' and have sought natural means to overcome these linked perturbations. As a first approach, planned diets with low portions of refined CHO have become popular. However, these diets do not satisfy everyone; and many are concerned over replacing CHO with more fats. As a second option, addition of soluble fiber to the diet can slow absorption of refined CHO, i.e., lower the glycemic index of foods and overcome or at least ameliorate many of the adverse reactions resulting from increased refined CHO ingestion. Unfortunately, the general public does not favor diets high in fiber content, and various fibers can lead to gastrointestinal problems such as gas and diarrhea. A third choice to favorably influence CHO absorption is to use natural dietary supplements that block or slow CHO absorption in the gastrointestinal tract via inhibiting enzymes necessary for CHO absorption –amylase and alpha-glucosidases. Although a number of natural supplements with anti-amylase activity have been recognized, the most studied and favored one is white kidney bean extract. Animal and human studies clearly show that this agent works *in vivo* and has clinical utility. This paper reviews many aspects of diabesity and the use of ''carb blockers'' to prevent and ameliorate the situation. In many respects, carb blockers mimic the beneficial effects of fibers.

Key teaching points:

- Over the last few years, safe CHO blockers have been found that are effective in blocking gastrointestinal CHO transport.
- Current studies indicate that these products can prevent or ameliorate many of the deleterious happenings attributed to heavy CHO intake, particularly, overweight/obesity, insulin resistance, and diabetes mellitus.

The General Problem of Obesity and Diabetes

The incidence of both obesity and diabetes has risen alarmingly over the last few decades [1–5]. It was estimated in 2005 that the prevalence of obesity after age adjustment ranges from 13.1% to 30.0% and type 2 diabetes from 3.3% to 9.2% [3]. Therefore, as might be expected, increased prevalence of obesity occurs in type 2 diabetes and vice versa [1,6–9].

Obesity. The excess accumulation of body fat referred to as overweight or obesity, depending on its extent, results mainly from a chronic disequilibrium between food consumption and energy expenditure. Obesity is a complex condition with serious social and psychological dimensions affecting virtually all ages and socioeconomic groups. Regrettably, this excess accumulation of fat is becoming noticeably more prevalent in modern societies [4,5,10]. This is unfortunate for more reasons than just poor physical appearance, because the overweight/obesity state increases the risk of hypertension, type II diabetes, arthritis, elevated circulating cholesterol, cancer, serious hormonal imbalances in women that can lead to sterility, chronic renal disease, and even dementia and Alzheimer's disease [11–13].

This health problem is not limited to America, because globally there are over one billion overweight adults according to a multitude of sources including the World Health

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Organization (WHO) [14–17]. Although some countries such as China and Japan have ranges below 5% in adults, this percentage appears to be greater in children. Approximately, 22 million children under five are estimated to be overweight worldwide [16]. In the USA, the prevalence of obese children aged 6-to-11 years has more than doubled since the 1960s. In the early 21st century, overweight prevalence was 15.5% among 12–19 year olds, 15.3% among 6–11 year olds, and 10.4% among 2–5 year olds compared respectively with 10.5%, 11.3%, and 7.2% in the 1988–1994 (NHANES III) [18,19].

Diabetes. The American Diabetes Association recommends the following criteria for diagnosing diabetes mellitus: a glucose value after an 8 hour fast that is higher than 126 mg/ml, a 2 hour post load glucose level that is ≥200 mg/dl, or symptoms of diabetes mellitus and a random plasma glucose concentration ≥ 200 mg/dl. The relationship between obesity and type 2 diabetes is stressed above, but more than for general obesity, the risk of diabetes rises even more with abdominal (visceral) obesity [20–22]. Visceral fat tissue is often linked to the inflammatory state [23]. Obviously, it is not too surprising that avoidance of fat accumulation is a major tool in diabetes prevention and amelioration.

Dietary Approach to Obesity and Diabetes Mellitus

A primary practice that the general public used until recently to achieve weight loss was lessening intake of saturated fats – a dietary plan based on the well-recognized high caloric density of fat relative to the other macronutrients such as carbohydrates (CHO) and proteins [24,25]. Another reason for the popularity of this particular dietary regimen was that diets low in saturated fat should, by all accounts, lessen the risk for many chronic disorders, especially cardiovascular perturbations such as atherosclerosis. Interestingly, only a few voices mentioned the possibility that trans fats were more deleterious to health than saturated fats [26,27].

Suffice it to say, diets low in saturated fats did not prove to be as useful to overcome overweight/obesity as expected. Despite the fact that many health organizations and governmental agencies widely promoted the important influence of saturated fats on body fat accumulation and many cardiovascular disorders and many listeners adhered to these warnings, Americans continued to become noticeably fatter and fatter. As could be predicted from the rising prevalence of fatter people – diabetes, hypertension and numerous chronic disorders appeared more frequently with the passage of time. Finally, a marked change occurred in the dietary regimen for weight loss when the popularity of the Atkins diet raised serious doubts among dietitians concerning the elimination of saturated fats from the diet to ameliorate the overweight state [10,28,29]. The bottom line – many individuals lost significant body weight despite the high content of saturated fats in this diet [10,28,29]. Could there be another macronutrient in the Western diet contributing to the prevalence of overweight/obesity – even more than saturated fats? A number of experts now believe that CHO, particularly refined CHO rapidly absorbed in the gastrointestinal tract, may be a principal reason for the current epidemic of obesity and diabetes.

CHO, Characteristics and Absorption

CHO are formed in growing plants and, with few exceptions, are characteristically compounds containing carbon, hydrogen and oxygen in a molar ratio of 1:2:1 [30,31]. CHO are polyhydroxy aldehydes, ketones, alcohols and acids that can range in size from single monomeric units to polymers. Plants high in sugar content contain a single unit monosaccharides or disaccharides (two molecules bonded). Oligosaccharides (3–9 monosaccharide units) and polysaccharides (>10 monosaccharide units) complete the classification by size. In most diets, CHO makes up the greatest source of calories.

For absorption from the gastrointestinal tract into the blood stream, the various CHO moieties must be broken down into monosaccharides using two major enzymes, amylase located in saliva and secreted by the pancreas into the small intestines and alpha-glucosidase enzymes located in the brush border of the small intestines.

Starch digestion begins in the mouth via the action of amylase, a digestive enzyme present in saliva. Salivary amylase accounts for only about 5% of starch breakdown, because enzymatic activity is halted in the stomach due to the high acid content there. This acidity is overcome in the small intestines when the pancreas secretes bicarbonate to neutralize the acid. Mucous secretion from the tissue lining the small intestines is also alkaline. The pH change allows the amylase secreted by the pancreas to work effectively. CHO are thus broken down into smaller units such as monosaccarharides, disaccharides, and oligosaccharides. Worth repeating, all CHO must be broken down into monosaccharides before absorption can take place. The alpha-glucosidase enzymes located in the brush borders aid further in this final process. The alpha-glucosidase enzymes include sucrase, maltase and lactase.

Diets Low in Refined CHO

Over recent years, more knowledge has been gained about high dietary CHO intake and the potential harm to health, like augmented fat accumulation [32,33]. It is generally recognized that calories influence weight gain or loss, however, the types of calories consumed are important in determining whether weight change is directed toward fat or muscle [34]. CHO are a primary focus in this respect [33]. Of the various types of CHO, the major problem seems to be with rapidly absorbed, refined CHO. Based upon the rate of CHO absorption, those

with fast absorption are said to have a ''high glycemic index'' in contrast to those with slow absorption said to have a ''low glycemic index.'' It has long been known via animal and human studies that ingestion of CHO with a high glycemic indices correlates with insulin resistance and associated perturbations [34]. Therefore, it is not surprising; that slowing down absorption (lowering the glycemic index) and maintaining insulin sensitivity will prevent development of or, at least, ameliorate many metabolic disorders [35].

That a perturbed insulin system can play a major role in determining whether fat or muscle predominates in a weight loss regimen was demonstrated in a recent study examining niacin-bound chromium (NBC) [36]. Supplementation with oral NBC frequently ameliorates insulin resistance [37,38]. In a double-blind, placebo-controlled, crossover study on overweight African-American females, the addition of NBC to a regimen of caloric restriction and exercise increased fat loss and lessened muscle loss significantly compared to a control group receiving no additions [36].

Insulin Resistance

Insulin resistance is a common finding both in obesity and diabetes and may explain, at least in part, the close linkage between the two disorders [39–41]. This is where the ''low carb'' diets fits into current weight loss regimens. Many believe that increased intake of rapidly absorbed, refined CHO, commonly present in the Western diet, is responsible for the prevalence of insulin resistance and many chronic disorders now being seen [42–46]. While calorie consumption has long been accepted as an important factor in the pathogenesis of diabesity, in more recent times the intake of refined CHO has also received extensive attention [47–51].

Insulin resistance, a common phenomenon during aging [52–54], contributes to many troublesome age-related perturbations including obesity, diabetes, various cardiovascular risk factors such as hypertension and dyslipidemias, and even premature aging itself [39,40,55–58]. Many nutritionists believe that diet plays a key role in the aging phenomenon; because, in addition to excess intake of calories, the recently increased dietary consumption of refined CHO is associated with the development of insulin resistance and its ensuing consequences [59–61].

Yudkin *et al*. were among the first to promote the concept that table sugar (sucrose) is responsible in many cases for the then recognized obesity epidemic [45]. His group was also at the forefront of connecting perturbations in insulin metabolism to the entities comprising the metabolic syndrome [42,45,46,62–65]. While aging is associated with insulin resistance, insulin resistance may hasten the aging process – a vicious circle [58–60]. For example, the most common experimental means to lengthen life span, caloric restriction, appears to work, at least in part, through its beneficial effects on the insulin system [66].

Accordingly, attacking obesity, insulin resistance, and/or aging, which we often refer to as the ''deadly triad,'' may result in an improvement of all individual age-related disturbances. While drugs have been used as therapy for obesity and diabetes, adverse reactions to them have lessened enthusiasm for their routine use, especially over long term. The associated, adverse side effects include cardiac valvular disease, seizures, hypertension, keto acidosis, sexual dysfunction and fecal incontinence [67–69].

Potential Natural Remedies

Low CHO Diets. Accepting that diets high in refined CHO are a major factor in the prevalence of diabesity, how can one lessen the deleterious influences of rapidly absorbed CHO? Seeking a remedy, many of the afflicted have turned to caloric-restricted diets proportionately low in CHO and have successfully lost weight on ''low carb diets'' [10,70–74]. Nevertheless, others are not yet prepared to accept this life style change. Issues ranging from the wisdom of replacing CHO with fats over a prolonged period of time to the palatability of a diet severely depleted in CHO have led to procrastination. Nevertheless, continued emergence of data strengthening a positive correlation between excess intake of rapidly absorbed CHO and obesity has challenged many investigators to seek more practical means to duplicate results found with the stringent depletion of refined CHO in the diet. Two possibilities exist. (1) Various fibers can slow CHO absorption and do have beneficial effects on weight loss [75–77]. (2) Inhibiting enzymes such as amylase and sucrase necessary for CHO absorption is another alternative to reduce the rapid gastrointestinal absorption of CHO [78].

Fiber Intake. Because solid evidence supporting a positive correlation between excess refined CHO intake and weight loss persists, many investigators continue to search for easier means to duplicate results found with low CHO diets. Therefore, if a significant portion of CHO must remain in the diet of many for the sake of palatability and reducing fat intake, an alternative would be to reduce or at least slow the gastrointestinal absorption of CHO. Viscous, soluble fibers provide a therapeutic benefit. It has long been known that soluble fibers can affect the rate of the absorption of refined CHO. Nutritionists have been imploring the public to consume more dietary fiber, especially soluble fiber, for years [79,80]. We have shown in animal studies, that the ability of soluble fiber to slow sugar absorption lowers elevated blood pressure and thus lessens a major cardiovascular risk factor [81,82]. Nevertheless, the general public has resisted increasing their fiber intake significantly, probably for reasons of taste and the known adverse effects of fiber ingestion on the gastrointestinal tract – gas, cramps, and frequent bowel movements.

Carb Blockers. Non-fiber products that slow CHO absorption through enzymatic inhibition, commonly referred

to as ''carb blockers,'' may become important therapeutic options in the general public's struggle with obesity [78,83–85]. The popularity of products that slow the absorption of CHO can be corroborated by examining the shelves of many stores where this class of natural products has gained a great deal of prominence, i.e., shelf space. To state the obvious, however, popularity over the short term does not necessarily mean they work. Therefore, what do we know about particular natural amylase inhibitors?

Success of inhibitors to CHO-involved digestive enzymes would allow an individual to maintain a reasonable CHO proportion in the diet but lessen or at least slow the absorption of refined CHO with high glycemic indices. For example, it has been known for decades that certain bean extracts have the potential to inhibit the enzyme alpha amylase [78,83–85]. In addition to the potential to lower caloric intake and prevent insulin resistance secondary to rapid CHO absorption, the ability to convert starches into resistant starches is another advantage of carb blockers.

Resistant Starches

Those starches that escape enzymatic digestion are referred to as ''resistant starches'' and play a significant role in health. A good approximation is that 10% of all consumed starch passes through the gastrointestinal tract undigested [86]. In many cases, non digestion occurs because the starches located in the cell walls of plants are not available for enzymatic digestion. In addition raw starch granules due to crystalline structure and size are also unavailable. Many fibers such as cellulose, hemicellulose, pectins, gums and mucilages lack enzymes capable of digesting them. These resistant starches pass into the colon where they may be fermented into short chain fatty acids, organic acids, carbon dioxide, and hydrogen [87]. Of significant value, the fermented, undigested starches appear to have important health benefits that include weight loss, blood lipid improvement, glycemic control and antioxidant protection [84,88–90].

Carbohydrate Blockers

With the above brief background in mind, the remaining discussion will now concentrate on the labors to develop effective means to lessen and slow CHO absorption. Since the greatest effort has gone into characterizing and developing a bean extract to inhibit amylase and a 5-carbon sugar (*L-arabinose*) to inhibit sucrase, the major description will focus on these two preparations, but a brief review of others will be given.

White Kidney Bean Extract

Early Studies on a Bean Extract inhibitor of Alpha Amylase. Much of the early work carried on in the 70s and 80s on the bean extract inhibitor is discussed in the excellent reviews by Udani *et al* [83], Meiss [84] and Obiro *et al* [91]. Early *in vitro* studies showed great promise concerning amylase inhibition [92–95]. More recently, a report by Santimone *et al* [96] described a possible reaction scheme for the inhibitory mechanism of kidney bean alpha-amylase inhibitor against porcine pancreatic alpha-amylase – a much more complex mode then competitive inhibition. While the kinetics of the proposed model are beyond the scope of this discussion, understanding the mechanism of action is a necessary aspect to make a final conclusion concerning the potential of alpha-amylase inhibitors as clinically relevant compounds.

Using various trials combining the enzyme, substrate (amylose/maltopentose), and inhibitor at different time points, the following was found [96]. Inhibition of alpha-amylase does occur, but the forward reactions are very slow, suggesting that the inhibitory process is not favored to occur under normal conditions. As evidence, inhibition was observed only when the enzyme and the inhibitor were initially pre-incubated for at least 10 min before the addition of the substrate. In contrast, substrate showed a fast combination relative to the enzyme-inhibitor complex [96]. These results make it difficult to say decisively, one way or the other, if kidney bean extract does prevent starch digestion *in vivo* and clinically improves an obese patient's condition.

A range of crude bean amylase inhibitors were marketed as starch blockers in the early 1980's. The very earliest clinical trials to show efficacy were generally disappointing [97–100]. Thus, the Food and Drug Administration (FDA) suspended sales of the products in 1982. However, Layer *et al* pointed out that many preparations studied earlier showed insufficient anti amylase activity to explain the failure [101]. With the development of better preparations possessing greater capability to inhibit amylase, the subsequent clinical studies began to show more promised [101–107].

Later Studies on a Bean Extract inhibitor of Alpha Amylase. The bean extract used in the following studies is referred to as Phase 2^{TM1} starch neutralizer and has been shown to inhibit alpha amylase. Phase 2 was previously referred to as Phaseolamin 2250, because one gram of the product purportedly blocked 2,250 starch calories. Phase 2 is a water extract of the white kidney bean *Phaseolus vulgaris*. Whole white kidney beans are ground and then extracted for four hours. The liquid is filtered and concentrated under vacuum. The extract is filtered again, and then pasteurized before being spray dried. It has been shown to be relatively free of toxic metabolites, i.e., safe for human consumption [See below under Safety Studies].

Animal studies (rats and pigs) supported the possibility that bean extract would be useful to inhibit starch absorption *in vivo*

[1]Manufactured by Pharmachem Laboratories, Kearney, NJ.

[108–111]. Preuss *et al* performed both acute and sub chronic studies on rats to examine the ability *of Phaseolus vulgaris* and other CHO blockers to inhibit the absorption of rice starch and sucrose [110,111]. To estimate CHO absorption in rats in the acute studies, groups of nine SD rats were gavaged with water or water plus rice starch and/or sucrose; and circulating glucose was measured at timed intervals thereafter. In rats, glucose elevations above baseline over four hours following rice starch challenge as estimated by area-under-curve (AUC) were 40% of their internal control after ingesting bean extract at a given concentration in addition to the rice starch [110]. Giving the natural substances minus CHO challenge caused no significant changes in circulating glucose concentrations, indicating no major effects on overall metabolism.

When two Yorkshire pigs, weighing 150 and 200 lbs respectively, were studied, the pigs rapidly drank CHO and inhibitors in their drinking water (110). A formula including bean extract and other natural products such as L-arabinose, the sucrase inhibitor, significantly decreased both starch and sucrose absorption, even when the rice starch and sucrose were given simultaneously. These results support the hypothesis that the enzyme inhibitors at reasonable doses can safely lower the glycemic indices of starch and sucrose.

A sub chronic study was designed to determine whether selected inhibitors of gastrointestinal starch and sucrose absorption remain effective with continued use and to assess their metabolic influences after prolonged intake [111]. Sprague-Dawley rats were gavaged twice daily over nine weeks with either water or an equal volume of water containing a formula that included bean extract and L-arabinose. No toxic effects (hepatic, renal, hematologic) were evident. Blood chemistries revealed significantly lower circulating glucose levels and a trend toward decreased HbA1C in the nondiabetic rats receiving the natural formulation compared to control. Subchronic administration of enzyme inhibitors was also associated with many metabolic changes including lowered systolic blood pressure and altered fluid-electrolyte balance. It was suggested that proper intake of natural amylase and sucrase inhibitors may be useful in the prevention and treatment of many chronic disorders associated with perturbations in glucose-insulin homeostasis secondary to the rapid absorption of refined CHO.

Vinson Studies

In a series of studies between 2001 and 2004, Vinson *et al.* carried out two single dose human studies with the purpose of determining whether bean extract inhibited human CHO absorption [112]. Eleven fasting subjects were given sliced white bread and 42 grams of margarine with and without 1.5 grams of bean extract. Absorption was decreased by 66% via area under the curve estimation. A full meal study with seven subjects who received 0.75 grams of bean extract showed a trend, i.e., 28% to 41% reduction in CHO absorption.

Thom Study

One of the first studies on the use of a white kidney bean extract for weight loss was conducted in Norway and published in 2000 [113]. This randomized, double-blind, placebo-controlled trial utilized a test product containing white kidney bean extract, inulin, chicory root, and *Garcinia cambogia*. Forty healthy but overweight subjects with a BMI between 27.5 and 39 were randomized and instructed to take two tablets of the test product before all three meals for 12 weeks. Subjects were also instructed to follow a 1200 kcal low-fat diet.

A total of seven subjects dropped out of the study (six in placebo arm, one in active arm). An intent to treat analysis was performed on these subjects. No adverse events were reported. After 12 weeks, the active group lost an average of 3.5 kg (7.7 Ibs, $p=0.001$) and the placebo group lost 1.3 kg (2.86 Ibs, $p>0.05$). Between group statistical differences were not calculated. BMI decreased by 1.3 kg/m^2 ($p=0.01$) in the active group and by 0.5 kg/m^2 ($p>0.05$) in the placebo group. Percent body fat (as measured by bioelectrical impedance) decreased by 2.3% ($p=0.01$) in the active group and by 0.7% ($p>0.05$) in the placebo. Again, between group analysis was not provided for BMI or percent body fat.

Celleno Study

Another European study utilizing the bean extract for weight reduction was conducted in Italy in 2001 [114]. Sixty overweight subjects participated in a randomized, double-blinded, placebo-controlled clinical trial consisting of a 30 day run-in phase followed by a 30 day active phase. Subjects were between ages 20 and 45, were 5–15 kg overweight, and their weight had been stable during the preceding six months. During the run-in phase, subjects were educated on the test diet that included a 2000–2200 calorie diet with a complex CHO intake concentrated in one of the two main meals of the day. In addition, subjects were asked not to change the current activity/exercise. Subjects received either 450 mg of bean extract or placebo before the main CHO containing meal of the day. The active group lost an average of 2.93 kg (6.45 lbs) in 30 days compared with an average of 0.35 kg (0.77 lbs) in the placebo group ($p<0.001$). Body composition was measured with bioelectrical impedance and the active group demonstrated a 10.45% reduction in body fat compared with a 0.16% reduction in the placebo group ($p<0.001$). Waist and Hip circumferences were measured as well. The active group demonstrated 2.93 cm and 1.48 cm reductions respectively compared with 0.46 cm and O.11 cm reductions in the placebo group ($p<0.001$). No adverse events were reported.

Udani Studies

In a 2002 randomized, double-blind, placebo-controlled study, 39 obese subjects (BMI 30–43) were randomly allocated to receive either 1500 mg of bean extract or placebo [115]. Twenty-seven subjects completed the study (14 active and 13 placebo). They were instructed to take the test product with lunch and dinner each day 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 to 200 g of complex CHO intake per day. CHO intake was recommended for the subjects on the basis of estimated daily maintenance CHO requirement. Subjects were instructed to eat the majority of their CHO during lunch and dinner, since those were the meals at which the bean extract or placebo was taken. An intent-to-treat analysis was performed.

The study results at 8 weeks demonstrated that the treatment group lost an average of 3.79 lbs. (an average of 0.47 lbs. per week) compared with the placebo group that lost an average of 1.65 lbs. (an average of 0.21 lbs. per week)($p = 0.35$). Triglyceride levels in the treatment group were reduced by an average of 26.3 mg/dL compared to the 8.2 mg/dL decrease in the placebo group ($p=0.07$). Energy level (as measured by a 10 point Likert scale) demonstrated a 14% increase in the treatment group and a one per cent decrease in the placebo group. This difference did not approach statistical significance ($p>0.05$).

Several secondary outcomes were measured during the study including body fat percentage, waist and hip circumference, hunger, appetite, and circulating HbAlC, and total cholesterol. For each of these secondary measures, there were no clinically or statistically significant differences identified between the active and placebo group. No significant adverse events were associated with the active product. One placebo subject experienced abdominal pain, bloating and gas, and one treatment subject complained of an increased incidence of tension headaches. Safety data were obtained at time 0 and again at eight weeks. These data included creatinine as a marker of kidney function, electrolytes including sodium, chloride, carbon dioxide, calcium, and AST/ALT as markers of liver function. There were no clinically significant changes in any of these markers in either group.

In a second study approximately three years later, Udani and Singh carried out a 4-week, randomized, double-blind, placebo-controlled study of 25 healthy subjects consuming 1000 mg of proprietary fractionated white bean extract or an identical placebo twice a day before meals [116]. The active and control group both lost weight and waist inches – active group −6.0 lbs ($p=0.0002$) and −2.2 inches ($p=0.0050$) and the placebo group −4.7 lbs ($p= 0.0016$) and −2.1 inches ($p=0.0001$). However, there was no statistical difference in these parameters between the two groups. When the subjects were stratified by total dietary CHO intake, comparing the tertiles consuming the most CHO did show statistically significant differences between the active and placebo groups (Body weight −8.7 lbs vs. −1.7 lbs, $p=0.04$ and waist circumference −3.3 inches vs. −1.3 inches, $p=0.01$).

Combining these last findings with those of the Celleno *et al* study (114), one could surmise paradoxically that the use of *Phaseolus vulgaris* is more effective when complementing a relatively high CHO diet. The reason for this is not clear. Two possible explanations exist. First, the lessened small intestinal absorption of CHO with the subsequent fermentation in the large intestines converts the energy value of CHO from roughly 4.0 kcal/g to somewhere in the neighborhood of 2.0 kcal/g [31,117,118]. Accordingly, CHO might have a relatively low caloric density compared to the other macronutrients under these circumstances. Second, the increase in fermentable starch secondary to the greater CHO intake has a significant role in weight reduction [84,88–90].

Koike Study

In an 8 week, open label study performed in 10 subjects receiving white bean extract, a 2.4% reduction in weight, a 5.9% reduction in body fat, a 5.2% reduction in waist circumference, and a 2.9% reduction in hip circumference were noted [119]. All differences were statistically significant. No adverse events took place.

Wu Study

In China, a randomized, double-blinded, placebo-controlled study was conducted on 101 volunteers with a BMI between 25–40 [120]. The volunteers were divided into two groups that received either placebo or the active substance. Two capsules containing *Phaseolus vulgaris* extract (1,000 mg) or placebo were taken 15 minutes before each meal for 60 consecutive days. Body weights, waist and hip measurements and blood for chemical analysis were obtained. After 60 days, 51 subjects receiving *Phaseolus vulgaris* extract compared to a placebo group of 50 subjects had clinical and statistically significantly greater average reduction of body weight [−1.9 Kg vs. −0.4 Kg, ($p<0.001$)] and waist circumference [−1.9 cm vs. −0.4 cm, ($p<0.001$)], but no difference in the changes of average hip circumference [−0.3 cm vs. −0.3 cm, ($p=0.84$)]. The results indicate that *Phaseolus vulgaris* extract taken under the conditions of study produces clinically and statistically significant decrements in body weight and waist circumference.

Safety Studies

Brudnak raises interesting points concerning the safety of bean extracts [85]. Kidney bean lectins can present serious problems. Fortunately, the extraction process for the bean extract used in the above-described studies is freed of lectins

and thorough laboratory studies on rats, acute and sub chronic, have shown no toxicity [121,122]. Ingesting up to 2.5 g/kg body weight produced no changes in hematological, biochemical, and histopathological parameters after seven days of administration [121]. When the *Phaseolus vulgaris* was given at 3.0 g/kg of body weight for 90 days, again no adverse changes were noted. Adverse reactions were not seen in the clinical studies described above. In some early studies, ingesting CHO blockers led to gas and bloating. However, Boivin reported that this could be ameliorated with proper dosing [105].

Other Potential Carb Blocker

This paper concentrates on an extract of white kidney bean *Phaseolus vulgaris* that has been well examined. Using laboratory studies (*in vitro* and *in vivo*) white bean extract carefully handled can be a safe, effective amylase inhibitor. However, other choices exist that influence gastrointestinal absorption of CHO via inhibition of various digestive enzymes. In previous rat studies, hibiscus extract proved as effective and safe as white bean extract [110,111]. Although further studies are indicated, hibiscus alone or combined with other ingredients could prove quite effective [123–125]. In 1998, Lankisch *et al* reported on the use of an amylase inhibitor extracted from wheat [126]. They found that the inhibitor delayed CHO absorption and reduced peak postprandial plasma glucose concentrations.

In the realm of alpha-glucosidase inhibitors, a good deal of work has been performed on L-arabinose. Studies in rats show that it could be quite effective *in vivo* [110,111]. L-arabinose is a naturally occurring compound that has been shown to have specific inhibitory activity on the digestive enzyme sucrase [127]. After a sucrose challenge to rats, the effects of sucrase inhibition have been shown to be wide –ranging from suppressing increases in blood glucose to preventing the initiation of lipogenic enzyme activity [128]. A human study [129] reported that consumption of L-arabinose led to a significant suppression of serum glucose levels after a sucrose challenge and attenuated sucrose-induced hyperglycemia in diabetic and non-diabetic subjects when the L-arabinose was consumed in conjunction with 30 grams of sucrose. A word of caution – L-arabinose will not work on high fructose corn syrup which is rapidly replacing sucrose in the market place. High fructose corn syrup, a mixture of free glucose and fructose, does not require sucrase for absorption.

It may be possible in the near fuure to develop formulas from a wide array of natural CHO blockers after further research has been performed on them. Gymnema sylvestre [130,131] and apple extract (phloridzin) [132] may inhibit glucose transport. Glucose tranport may also be inhibited by flavonoids via effects on the Glut2 sugar transporter [133], and fructose transport is influenced by eucalyptus leaf [134].

Possibilities

Many years ago, Burkitt lauded the benefits of dietary fiber on overall health [135,136]. It is widely recognized that despite all the information on the subject, the public in general does not ingest an adequate amount of fiber. With more research and understanding, ‘‘carb blockers’’ may be an adequate substitute, at least to some extent, for fiber in the diet. Fiber can lower appetite through a feeling of fullness, can lower the glycemic indices of many CHO, and can provide starch to the large intestines for fermentation and all the health benefits that emanate from that circumstance. Similarly, CHO blockers can theoretically slow bulk absorption and thus decrease appetite, can lower the caloric density of the CHO, can lower the glycemic indices and can provide CHO for fermentation distally.

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