



Open field, physician controlled evaluation of nutritional bar in management of non-insulin dependent diabetes mellitus (NIDDM)

INTRODUCTION

Nutrition plays an important role in the epidemiology, prevention and management of non-insulin dependent diabetes mellitus (NIDDM), also referred to as adult onset diabetes or diabetes type II. The health benefits of low glycemic index foods have been valued especially in NIDDM patients. The concept of "glycemic value" is based on findings that dietary carbohydrates differ in their potential to increase blood sugar levels. The glycemic index ranks carbohydrate-rich foods for their blood glucose raising potential. Pulses exemplify foods with low glycemic values, while white rice typifies carbohydrate rich foods with a high glycemic index, or value. The control of blood glucose homeostasis, or glycemic control, through proper nutrition translates into improved metabolic parameters, such as blood lipids, and prevention of cardiovascular disease in diabetic and healthy subjects. In addition, low-glycemic index foods increase satiety, reduce binging and may contribute to body weight management (1,2).

In two cross-sectional studies, low glycemic diets were associated with a healthy range of HDL cholesterol, especially in women. In patients with NIDDM, serum levels of total cholesterol, LDL cholesterol, apolipoprotein B and plasminogen activator inhibitor-1 improved significantly on a low glycemic diet as compared to the group receiving high glycemic diet (3).

Dietary fiber is another important consideration which shows promise in management of NIDDM (4). Sufficient dietary fiber (daily 20 to 35 g) in a meal tends to decrease the post-

prandial blood glucose levels, decrease insulin response and normalize blood lipid levels. Water-soluble fibers with greater viscosity appear to have a greater potential to have a positive effect on blood glucose, insulin, and serum lipid levels than insoluble fibers. Some of the beneficial mechanisms in NIDDM promoted with dietary fiber include delay of gastrointestinal glucose absorption, increase in hepatic extraction of insulin, increased insulin sensitivity at the cellular level, and binding of excreted bile acids, which prevents cholesterol synthesis (5).


Several botanical compounds and nutraceuticals, should also be considered in the management of NIDDM as a useful addition to nutritional and behavioral modification of life style (6). One of the promising, clinically tested anti-diabetic botanicals is an extract of heartwood and bark of *Pterocarpus marsupium* (fam. Leguminosae) standardized for 5% pterostilbene and 0.01% epicatechin. In clinical evaluation of *P. marsupium* extract (400 mg per day), normalization of blood glucose levels was attained in 67 (69%) of the 97 NIDDM patients. In addition, mean levels of glycosylated hemoglobin (HbA1c) decreased significantly ($p < 0.001$) in those patients from the initial value 9.8 to 9.4% after 12 weeks of treatment (7).

The present study aims were to evaluate a nutritional approach in the management of NIDDM with the daily consumption of a specially formulated nutritional bar. The bar was designed to function as a snack with healthy mineral and herbal ingredients which could be useful in curbing excess appetite, lowering post-prandial blood glucose levels and the insulin response, and alleviating obesity in patients with NIDDM.

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MATERIALS AND METHODS

The study was performed in the Marietta, GA, office of Dr. J.T. Cooper MD, MPH, a practicing specialist in bariatric medicine. NIDDM patients of both sexes, ranging in age from 34 to 68 years old were selected for the study. Patients with clinically evident kidney, liver, heart or neurological conditions were excluded from the study sample. In addition, pregnancy, lactation, a history of alcohol or other drug abuse, and allergies to spices or any of the ingredients of the nutritional bar were the exclusion criteria for the study.

The subjects who fulfilled the study's criteria were asked to sign an informed consent form. All participants were put on 1 diabetic bar, after a meal (breakfast, lunch, and dinner). The subjects were provided a 4-week supply of diabetic bars at the onset of the study and at each visit scheduled on weeks 4 and 8. All subjects participating in the study were given the same healthy diet and life style instructions and were told to continue their usual physical activity.

The primary evaluation time-points on week 0, 4 and 8 included the following clinical and laboratory parameters of safety and efficacy evaluation of the nutritional intervention: body weight, vital signs, and self-assessment of appetite levels. These were collected during each patient's visit. Appetite levels were evaluated based on the following scale: 0 not hungry; 1 somewhat hungry; 2 hungry, 3 very hungry; 4 extremely hungry. The clinical biochemistry of the participants was evaluated at the onset of the trial and at the completion of the trial and included fasting blood glucose levels and levels of glycosylated hemoglobin (HbA1c).

Statistical evaluations were performed with Wilcoxon matched-pairs signed-rank test – a non-parametric test of the significance of difference for dependent samples. Matching was used to control potentially confounding variables, and to increase power and precision.

The composition of the diabetic bar included: Maltitol, Coating (contains: Maltitol, Salatrim, Cocoa (may be processed with alkali), Sodium Caseinate, Soy Lecithin (an emulsifier), Artificial Flavors, and Acesulfame Potassium), Inulin, Fiber Herbal Blend (Contains: *Trigonella foenum-graecum*, *Pterocarpus marsupium* and *Camellia sinensis*), Peanuts, Peanut butter, Soy Protein Isolates, Soy Crisp Nuggets (Contains: Isolated Soy Protein, Rice Flour, Malt, and Salt), Gelatin Hydrolysate, Water, Peanut flour,

Natural Flavors, Peanut Paste (Contains: Fructose, Maltodextrin, Peanuts, Water, Modified Food Starch, Salt, Carrageenan, Soy Lecithin, and Natural Flavors), Soy Fiber, Canola Oil, Vitamin and Mineral Blend (Contains: Vitamin A Palmitate, Ascorbic acid, dl-Alpha Tocopheryl acetate, Niacinamide, Zinc oxide, d-Calcium Pantothenate, Pyridoxine-Hydrochloride, Copper Gluconate, Riboflavin, Thiamine mononitrate, Folic acid, Biotin, Potassium iodide and Cyanocobalamin), and Soy Lecithin Oil (8).

RESULTS

Fourteen individuals with clinically diagnosed NIDDM, 7 men and 7 women, entered the study. Of this group 6 women and 4 men completed the 8-week clinical protocol (Figures 1-4). Those who dropped-out were with gastrointestinal complaints in the form of flatulence and increased frequency of loose stools. None of the subjects who failed to complete the program reported any serious side effects during the trial, but rather inconvenience and/or incompatibility of undesired symptoms with their daily occupational schedule.

The data for individual patients who completed the study are listed below and indicate that consumption of the specific nutritional bar resulted in a decreased craving for food, usually after the first four weeks of therapy, accompanied by gradual body weight loss. The laboratory data indicate reduction in blood glucose and glycosylated hemoglobin levels which became more significant with the increased duration of the therapy.

Patient 1

Male age 51, initial weight 214.6 lb, hunger level 4, blood glucose levels 189 mg/dL (limits 65-115) and HbA1c 7.4% (limits 4.1-6.1%). On the second visit (week 4) weight was 209.2, hunger level 1, blood glucose levels 135 and HbA1c 6.8. Patient reported that he cut out alcohol, but had troubles keeping away from fast foods. During the third visit (week 8) weight was 197.8, hunger level 1, no problem with food craving, blood glucose levels 123 and HbA1c 5.9.

Patient 2

Male age 67, initial weight 198.4, hunger level 4, blood glucose levels 146 and HbA1c 7.8. On the second visit, (week 4) weight was 195.2, hunger level 1, blood glucose levels

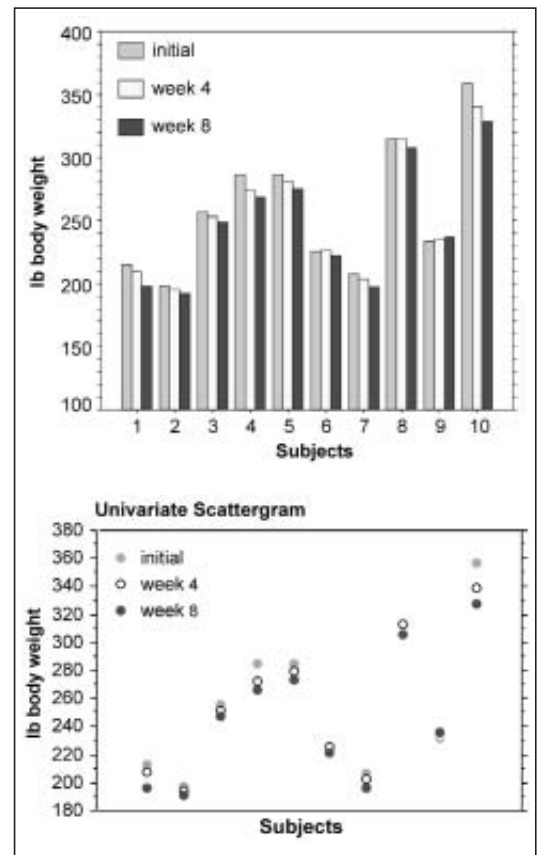


Figure 1 – Change in total body weight in subjects receiving nutritional bar tid for 8 weeks

131 and HbA1c 7.4. During the third visit (week 8) weight was 192, hunger level 1, blood glucose levels 123 and HbA1c 6.0. Occasional loose stool complaint.

Patient 3

Male age 68, initial weight 257.2 lb, hunger level 4, blood glucose levels 134 and HbA1c 8.4. On the second visit (week 4) weight was 253.4, hunger level 1, blood glucose levels 137 and HbA1c 7.6. Patient reported diarrhea which was alleviated by cutting down on daily bars and then gradual increase to the dose of 3 bars per day. During the third visit (week 8) weight was 249.8, hunger level 1, no problem with food craving, blood glucose levels 126 and HbA1c 6.1

Patient 4

Male age 57, initial weight 286.4, hunger level 4, blood glucose levels 219 and HbA1c 7.5. On the second visit, (week 4) weight was 273.6, hunger level 2, blood glucose levels 163 and HbA1c 6.7. During the third visit (week 8) weight was 268, hunger level 1, no problem with food craving, blood glucose levels 142 and HbA1c 5.5. Feels that he benefited greatly and asked for commercial availability of the bars.

Patient 5

Female age 50, initial weight 286.6, hunger level 3, blood

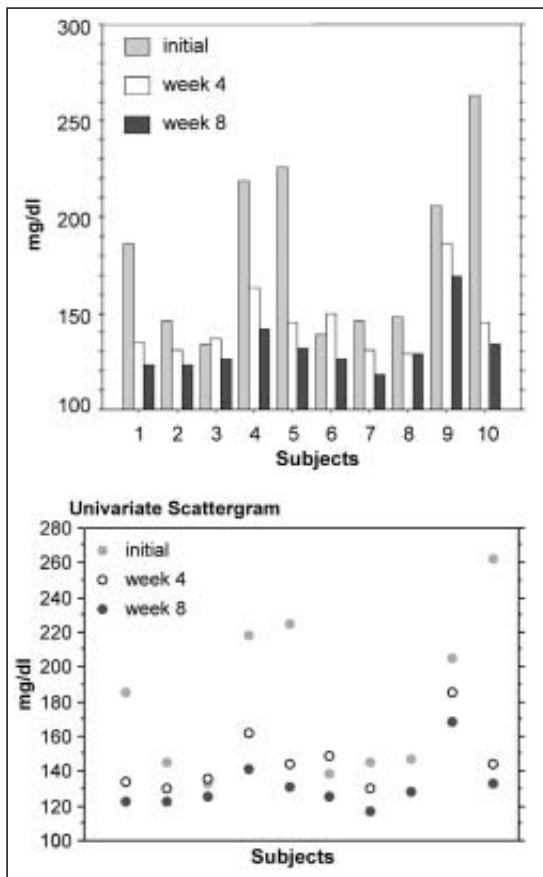


Figure 2 – Blood glucose levels in subjects receiving nutritional bar tid for 8 weeks

glucose levels 226 and HbA1c 7.7. On the second visit (week 4) weight was 281.3, hunger level 2, blood glucose levels 145 and HbA1c 6.8. Patient reported initial gas and occasional diarrhea which symptoms cleared after 2 weeks on the bar. During the third visit (week 8) weight was 275.2, hunger level 1, no problem with food craving, blood glucose levels 132 and HbA1c 5.4. Patient is busy executive who travels frequently and likes the convenience of bars.

Patient 6

Female age 37, initial weight 225.8, hunger level 3, blood glucose levels 139 and HbA1c 7.2. On the second visit (week 4) weight was 226.8, hunger level 2, blood glucose levels 150 and HbA1c 6.8. Patient reported not much hunger feeling, but she has a stressful life and admits to eating out of frustration. During the third visit (week 8) weight was 222.6, hunger level 1, no problem with food craving, blood glucose levels 126 and HbA1c 5.6. Most of her causes of stress are no longer present. Not as much desire to eat. Bars occasionally give her gas, but not bad. She likes the bars because of their help with constipation for her. Energy levels are higher. Sleeping well now.

Patient 7

Female age 60, initial weight 207.8,

hunger level 3, blood glucose levels 146 and HbA1c 7.9. On the second visit (week 4) weight was 203.6, hunger level 1, blood glucose levels 131 and HbA1c 7.2. Registered nurse working several shifts, tends to wake up at night and nibble. During the third visit (week 8) weight was 197.4, hunger level 1, no problem with food craving, blood glucose levels 118 and HbA1c 5.9. Good compliance.

Patient 8

Female age 52, initial weight 314.6, hunger level 4, blood glucose levels 148 and HbA1c 7.3. On the second visit (week 4) weight was 314.6, hunger level 3, blood glucose levels 129 and HbA1c 7.1. Patient reported she feels a lot of stress at work, eats a lot and is a compulsive eater and eats not because of hunger. During the third visit (week 8) weight was 307.6, hunger level 1, no problem with food craving, blood glucose levels 129 and HbA1c 6.8. Feeling much less hungry.

Patient 9

Female age 34, initial weight 233.4, hunger level 4, blood glucose levels 206 and HbA1c 11.9. On the second visit (week 4) weight was 235.2, hunger level 3, blood glucose levels 186 and HbA1c 10.8. Lots of personal problems. Isn't really hungry, but is eating compulsively. During the third visit (week 8) weight was 236.8, hunger level 1, no problem with food craving, blood glucose levels 169 and HbA1c 8.4. Problems: Still having personal problems. Feels the bars have "saved her" or she would have eaten more. Size has diminished and clothing is looser as compared to 2 months ago when she started the program. Is optimistic she can control her weight and her diabetes.

Patient 10

Female age 46, initial weight 358.4, hunger level 4, blood glucose levels 263 and HbA1c 8.6. Patient has sleep apnea assisted by CPAP. On the second visit (week 4) weight was 340.2, hunger level 2, blood glucose levels 145 and HbA1c 7.3. During the third visit (week 8) weight was 328.6, hunger level 1 no problem with food craving,

blood glucose levels 134 and HbA1c 6.2. Problems: hectic work routine sometimes results in skipping lunch and overeating at dinner. Bars have helped, but occasionally give her gas. She is satisfied with them. Patient still has sleep apnea, but rests better. There is a lot less hunger than before. Is continuing her program.

Patient 11

Male age 59, initial weight 233.0, hunger level 3-4, blood glucose levels 140 (fasting) and HbA1c 7.4. Patient is a retired School Superintendent. He is on no medications, diet only. On the second visit (week 4), hunger level 1 when on bars, but had diarrhea, even when bars were cut into halves or thirds. Was satisfied with satiety effect, but had hemorrhoid flare-up because of frequent stools. Declined to use bars for more than 2 weeks. Left the study with last HbA1c reading of 6.7 on this date.

Patient 12

Male age 43, initial weight 239, hunger level 3, blood glucose levels 146 and HbA1c 6.9. On the second visit (week 4) weight was 230, hunger level 2, and HbA1c 6.5. Patient reported too much gas, plus some very loose stools that interfered with his work. Wants to use bars, but side-effects are too much for him.

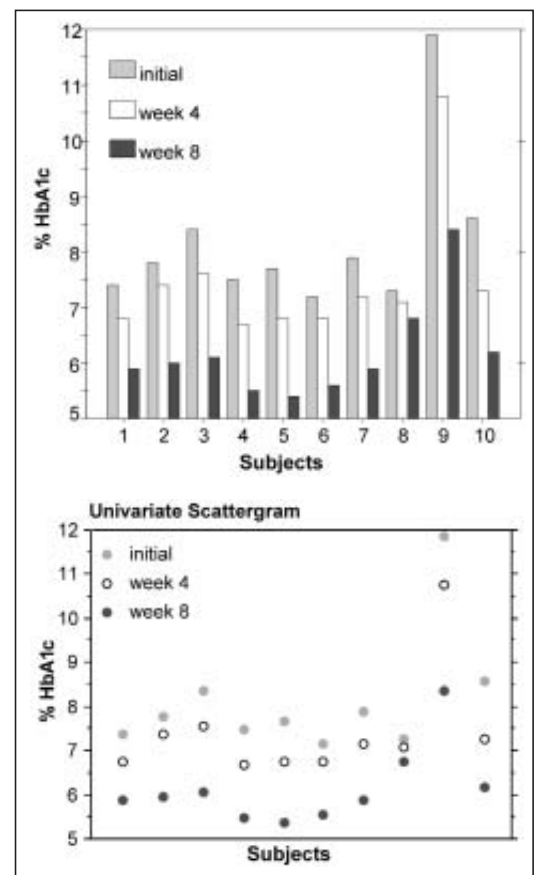


Figure 3 – HbA1c levels in subjects receiving nutritional bar tid for 8 weeks

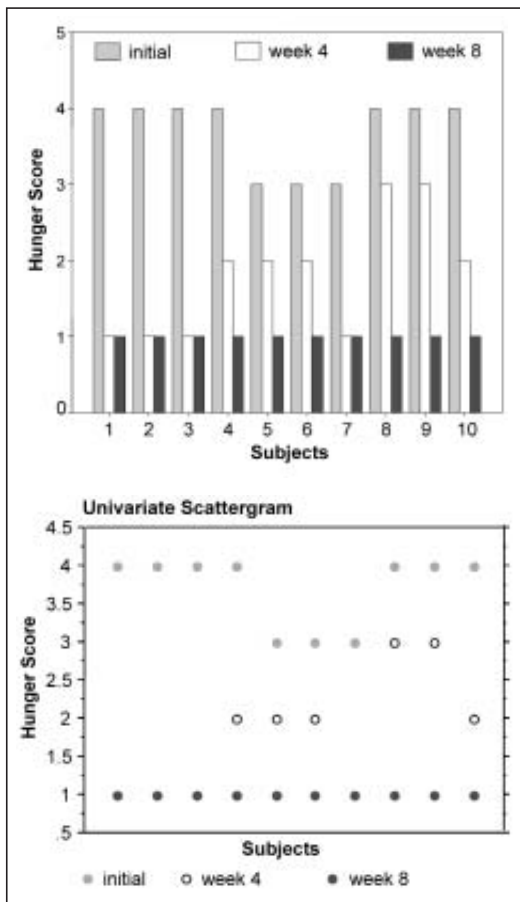


Figure 4 – Perception of hunger score in subjects on nutritional bar tid in course of 8 weeks administration

Patient 13

Female age 69, initial weight 166.6, hunger level 4, blood glucose levels 128 and HbA1c 5.8. Patient uses Wellbutrin for depression – is under a lot of family stress. Patient did not return for monthly visit, but returned 4 months later and commented that she could not tolerate the bars because they “upset her stomach” and preferred not to continue. She said the bars tasted good and were satisfying, but the fiber or something else gave her gas and diarrhea. Hunger level for the six days she was on the bar was 1. She declined to get HbA1c done, but it was not relevant this long after she tried the bars.

Patient 14

Male age 65, initial weight 234.4, blood glucose levels 139 and HbA1c 7.1. Patient never came back for follow up. His wife reported that he had too much gas and only used the bars for two days.

Daily supplementation with the dietary bar decreased total body weight significantly from an average initial value of 258.32 ± 52.18 lb to 253.31 ± 48.67 lb ($p < 0.05$) after 4 weeks and 247.5 ± 47.34 lb ($p < 0.01$) after 8 weeks respectively. The blood

glucose and HbA1c levels were decreased significantly from the initial average values of 181.3 ± 45.15 mg/dL and $8.17 \pm 1.38\%$ to an average of 145.2 ± 17.76 mg/dL and $7.45 \pm 1.21\%$ after 4 weeks ($p < 0.05$) and 132.2 ± 14.57 mg/dL and $6.18 \pm 0.87\%$ after 8 weeks ($p < 0.01$). The majority of participants reported a significant decrease in self-assessed hunger levels from an average score 3.7 ± 0.48 at the onset of the study to scores 1.8 ± 0.78 ($p < 0.05$) and 1 ± 0.0 ($p < 0.01$) after 4 and 8 weeks of bar supplementation respectively.

DISCUSSION

The weight loss results with the nutritional bar treatment could be explained, to some degree, by the fact that most of the patients ate less due to decreased cravings for food. The appetite lowering effect of the treatment had a tendency to hold after the initial four weeks and throughout 8 week regimen.

The blood chemistry data indicate that regular consumption of three bars per day resulted in a gradual and significant decline in fasting blood glucose levels and levels of glycosylated hemoglobin. Some patients who completed the 8 week regimen reported occasional excessive flatulence and loose stool. However, these symptoms were alleviated by temporary altering of the prescribed study regimen, e.g. skipping the bar or eating it at a different time of the day. The consensus among participants of the study has been that the bar is convenient and effective nutritional intervention, which improves the quality of life for a patient suffering from NIDDM. Several of the participants inquired about commercial availability of the bar.

In conclusion, the studied diabetic bar could possibly address the following mechanisms and clinical symptoms which cause and aggravate diabetes:

- Elevated blood glucose levels that fuel the citric acid (Krebs) cycle which provide building blocks for fatty acids synthesis. This process directly contributes to elevated blood cholesterol (especially an increase in blood triglycerides, nicknamed “ugly” cholesterol) and obesity which often accompanies diabetes of the NIDDM type.

- Abnormal processing of protein glycosylation, i.e. how the carbonyl group of glucose reacts with amino groups in target proteins. These glycation reaction products accumulate in tissues not only in conditions of diabetes, but also with advancing age and renal failure. There is emerging evidence that these compounds may play a role in vascular pathology (accelerated atherosclerosis), neural (diabetic neuropathy), ocular (cataract formation) and renal complications (diabetic renal failure) associated with diabetes and aging.
- Clinical symptoms, excessive thirst, hunger and excessive urination. The excess glucose in the blood acts as a diuretic; excessive diuresis contributes to thirst; and tissue(s) starving for glucose may trigger an excessive appetite for food.
- Premature aging due to wasting of body nutrients; extensive damage to skin, tissues and internal organs (Glycation reaction); rapid deterioration of cardiovascular system (so called “small vessel” disease); and damage to the autonomous and peripheral nervous systems (neuropathy).

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