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Daily Consumption of Reliv Glucaffect™ for 8 Weeks Significantly Lowered Blood Glucose and Body Weight in 50 Subjects

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A public change to healthier lifestyles with more physical activity and better nutrition, including caloric restriction, is required to address the obesity epidemic. Weight loss can be achieved by caloric restrictions; current research suggests that this may be achieved by consumption of slowly absorbed carbohydrates owing to the resulting prolonged satiety.

Our rationale was to prolong the satiety of overweight volunteers by supplementation with a proprietary formulation Glucaffect™ which delays absorption of carbohydrates. Glucaffect™ provides potent α-glucosidase inhibitors of herbal source such Pycnogenol®, Madeglucyl™ and various others which obstruct absorption of carbohydrates, such as starch.

Fifty overweight subjects received either Glucaffect™ or an inactive control product for eight weeks. Consumption of Glucaffect™ was found to statistically significantly lower blood-fasting glucose from baseline 145.3 mg/dL to 101.1 mg/dL (–30.4%) and Hba1c from 7.59% to 6.33% as compared to the control group where values decreased only marginally.

The weight and the body mass index (BMI) decreased significantly from an average of 88.5 kg (BMI 26.8 kg/m^2) to 81.3 kg (BMI 24.5 kg/m^2) as compared to the control group.

In conclusion, Glucaffect™ enabled subjects with metabolic syndrome to achieve healthy BMI and blood glucose levels. Glucaffect™ was well tolerated and no subject dropped out.

Keywords: BMI; metabolic syndrome; Pycnogenol™; Madeglucyl™; Weight loss.

INTRODUCTION

The prevalence of obesity has reached epidemic proportions worldwide and the incidence of overweight and obesity continues to rise. According to the World Health Organization (WHO) 65% of adult Americans are overweight with a body mass index (BMI) of ≥25 kg/m^2).

Weight loss can essentially only be achieved by a change to a healthier lifestyle with more physical activity and better diet, including energy restriction. The challenge is to achieve sustainable weight loss and prevent weight 'creep' without suffering and potential health risks. The modest success of low-fat diets has turned research toward alternative dietary strategies, including high-protein diets and low glycemic index (GI) diets (Brand-Miller *et al.*, 2008).

The GI depicts the blood glucose response after consumption of a specific carbohydrate meal relative to a rapidly absorbed reference carbohydrate, typically glucose or white bread. GI was originally designed for people with diabetes as a guide for selecting food with low GI which would help control postprandial hyperglycemia. The glycemic load (GL) takes into account the GI of a food item and the amount eaten (Venn and Green, 2007).

Currently, there is much interest in the potential of low-GI food in the management of obesity. Low-GI foods may benefit weight control in two ways: by promoting satiety and by extending fat oxidation at the expense of carbohydrate oxidation (Brand-Miller *et al.*, 2002). The theory of appetite developing in response to a transient fall in blood glucose was already introduced as the 'glucostatic theory' in 1953 (Mayer, 1953). Regulation of satiety in response to food consumption appears to be significantly complicated as a multitude of peptides are released in the small intestine, which interact with specific receptors of the peripheral nervous system. There is evidence from short-term studies that low-GI foods have higher satietogenic properties than high-GI foods (Bornet *et al.*, 2007). Only recently a clinical investigation with school children in the United Kingdom has pointed to a significantly decreased food intake when a low-GI breakfast was consumed (Warren *et al.*, 2003).

A group of substances known as α-glucosidase inhibitors affect the enzyme responsible for disassembling complex dietary carbohydrates, such as starch, into individual glucose molecules for absorption into the blood stream. From clinical experience with oral

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antidiabetic medications with α-glucosidase inhibitors for treatment of hyperglycemia, a favorable effect for decreasing body weight was found. This effect was attributed to the non-insulinotropic mechanism of action, and an effect on satiety (Purnell and Weyer, 2003).

Various herbal extracts have been described to inhibit α-glucosidase, such as French maritime pine bark extract Pycnogenol® (Horphag Research, London, UK) (Schäfer and Hogger, 2007), *Syzygium cumini* Madeglucyl™ (Indena, Milan, Italy) (Teixeira *et al.*, 2004) and *Salacia oblonga* (Collene *et al.*, 2005), which all have been demonstrated to have hypoglycemic effects in humans. In this study we describe the effect of a complex meal replacement formulation, Glucaffect™ (Reliv Inc., Chesterfield, MO, USA), containing aforementioned α-glucosidase inhibitors plus additional natural hypoglycemic substances for controlling blood sugar and body weight in subjects diagnosed with metabolic syndrome.

MATERIAL AND METHODS

Subjects. Fifty subjects were recruited for this study after informed consent. They had a BMI ≥25 kg/m^2 and a fasting blood sugar above 126 mg/dL (7 mmol/L), both parameters meeting the criteria for metabolic syndrome according to the American Diabetes Association. The subjects were from central Italy (San Valentino) where a typical diet often includes an excess of refined sugars and starch (particularly bread and pasta).

Exclusion criteria for subjects were fasting blood glucose values exceeding 162 mg/dL (9 mmol/L) and any other metabolic or clinical conditions requiring medical treatment. Pregnant or breastfeeding females, individuals with any clinical condition, psychiatric disorders including depression, and subjects who participated in another study less than 30 days before the start of this study were excluded.

Subjects were randomly assigned either to the active compound or to the control group in a single blinded fashion. Subjects were free to leave the trial at any time.

Treatment. Following inclusion, subjects were supplied with canisters containing powdered material together with a scoop to roughly sample 12 g of product for preparation of one serving. They were advised to prepare a serving by stirring one scoop with 12 g into approximately 200 ml of water and stir thoroughly. Four such servings were to be consumed during a day, equivalent to 48 gr Glucaffect™ powder. After four weeks, patients were seen again to monitor tolerability and compliance by checking canisters. At this occasion they were supplied with another canister for the following four weeks until trial completion.

The Glucaffect™ formulation per 12-gr serving consists of a base of low-fat soy flour (8.78 g), soy lecithin (150 mg), both of non-genetically modified origin, together with natural and synthetic flavoring, ground cinnamon (44 mg), guar and xanthan gum (120 mg of each), inulin (400 mg), and acesulfame potassium (90 mg). It is further fortified with Omega-3 fish oils (750 mg), CoQ10 (20 mg), L-Glutathione (12.5 mg) and alpha lipoic acid (100 mg), respectively per serving. Active components per serving for lowering blood sugar and decreasing carbohydrate absorption were 15 mg French maritime pine bark extract Pycnogenol® (Horphag Research, London, UK), *Syzygium cumini* extract Madeglucyl™ 500 mg (Indena, Milan, Italy), *Salacia oblonga* extract 120 mg, *Pterocarpus marsupium* extract Silbinol® 250 mg (Sabinsa Corporation, Piscataway, NJ, USA), and *Lagerstroemia speciosa* extract Glucohelp™ 4 mg (Optipure, Los Angeles, CA, USA).

The control product did not contain any of the active components but consisted exclusively of low-fat soy flour, corn-based starch, sunflower oil, ground cinnamon and equivalent natural and synthetic flavorings and acesulfame sweetener to match taste, color and texture of the active product.

Subjects were advised to consume the product from Monday to Saturday as a means of meal replacement with the aim to substitute up to two meals a day during 8 am and 6 pm. They were advised to have dinner and were allowed to choose a meal of their choice. On Sundays they did not consume Glucaffect™ and were permitted to have food of their choice but were recommended to have low-calorie meals with limited amounts of carbohydrates. Subjects were briefed on limiting the use of refined sugar and advised to avoid sweetened beverages.

A personal exercise program was suggested to subjects before the diet period commenced. The exercise program included a total of at least 60 min exercise each day, divided into three separate episodes per day.

Only subjects willing to adhere to the diet and exercise program, with the expectation of good compliance and motivation, were considered for inclusion.

Study design. Subjects were examined at enrolment to meet inclusion criteria and briefed on procedures one week before trial start. Patients were seen again after four weeks to monitor tolerability as well as compliance. On this occasion another canister of study material was provided to them which would last until the total eight-week trial period was completed. Weekly contacts, either personal or by phone, were maintained during the study period.

Body weight and size, as well as fasting blood glucose and HbA1c levels were established using standard clinical equipment.

Statistical analysis. At least 12 subjects per group were needed to achieve statistical differences. As the distribution of values was unknown, non-parametric statistics were used.

Results are presented as the mean ± SD. Statistical analysis of fasting blood glucose, HbA1c, weight and BMI was performed with the Mann-Whitney U-test and analysis of the variance. Values of $p < 0.05$ were considered significant.

RESULTS

Twenty-four subjects were assigned to the active compound group receiving Glucaffect™, 14 men and 10 women, aged 30 to 60 years with a mean age of 42.3 years (±8.3). Twenty-six subjects were assigned to the control group, 15 men and 11 women, aged 30 to 58 years with a mean age of 43 years (±7.1). Groups were comparable for age, sex, and parameters for HbA1c, fasting blood glucose and BMI.

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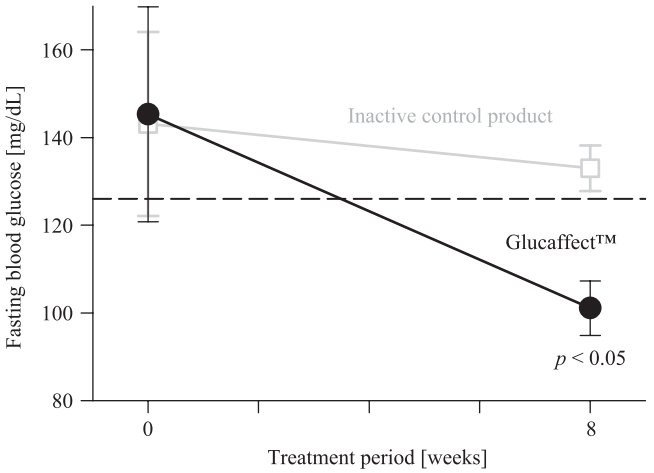

Figure 1. Development of the fasting blood glucose in the groups receiving either Glucaffect™ (black) or the inactive control product (grey). The subjects receiving Glucaffect™ show a significantly decreased fasting blood glucose as compared to both baseline as well as to the control group ($p < 0.05$). The dotted line depicts the 126 mg/dL (7 mmol/l) threshold which is the borderline fasting glucose above which individuals are considered prediabetic. Glucaffect™ lowers fasting glucose in subjects to values well below the prediabetes level.

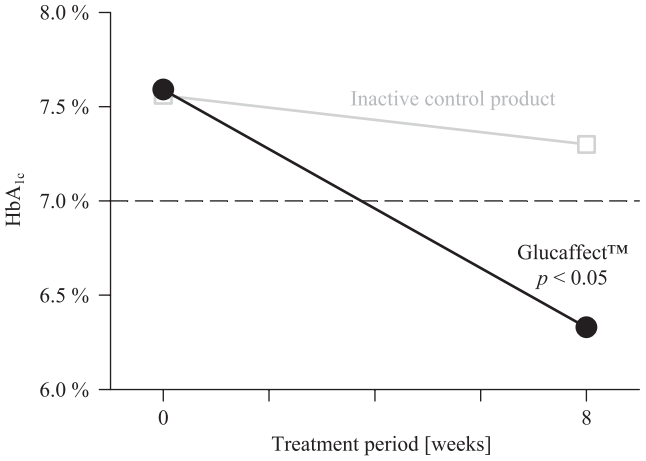

Figure 2. Development of the glycosylated hemoglobin (HbA1c) in the groups receiving either Glucaffect™ (black) or the inactive control product (gray). The subjects receiving Glucaffect™ show a significantly decreased HbA_{1c} level as compared to baseline ($p < 0.05$). The dotted line shows the 7% threshold value over which the HbA_{1c} level is considered prediabetic according to the American Diabetes Association. Glucaffect™ decreases HbA_{1c} values below the 7% mark suggesting good glucose control.

Control of returned canisters suggests good compliance with no more than two Glucaffect™ servings missed per week. No complications or side effects were observed during the study. No subjects dropped out.

As shown in Fig. 1, consumption of four portions Glucaffect™ per day for six days a week over a total period of eight weeks lowered fasting blood glucose from a baseline average of 145.3 ± 24.5 mg/dL (8.07 ± 1.36 mmol/L) to 101.1 ± 6.2 mg/dL (5.62 ± 0.34 mmol/L). A marginal reduction of fasting blood glucose was observed in the control group. Values decreased from baseline 143.1 ± 21 mg/dL (7.95 ± 1.17 mmol/L) to 133.0 ± 22 mg/dL (7.39 ± 1.2 mmol/L). Glucaffect™ lowered fasting blood glucose by 30.4% and this reduction was statistically significant as compared to baseline as well as to the control group.

The decreased blood glucose with Glucaffect™ is reflected by a significant reduction of glycosylated hemoglobin as shown in Fig. 2. During the eight weeks, HbA_{1c} values decreased statistically significantly as compared to baseline from 7.59% to 6.33%. In the control group, HbA1c decreased marginally from 7.56% to 7.3%.

It is an important finding that consumption of Glucaffect™ enabled subjects with pre-diabetic glucose levels to return to healthy blood-sugar levels.

The weight and BMI of subjects taking Glucaffect™ decreased significantly as compared to baseline as well as the control group (Fig. 3). At trial start, the average body weight was 88.5 ± 4.4 kg (BMI 26.8 ± 4.3 kg/m^2), which decreased to 81.3 ± 5 kg (BMI 24.5 ± 4.9 kg/m^2) after eight weeks' consumption of Glucaffect™. Thus, on average, subjects lost 7.2 kg weight within eight weeks and on average they slimmed to an extent that they achieved their optimal weight with a BMI <25 kg/m^2. No significant effect on body weight was found for the control group, in which average weight decreased merely from 87 ± 5.0 kg (BMI 26.5 ± 5.0 kg/m^2) to 85 ± 4.3 kg (BMI 25.99 ± 4.3 kg/m^2).

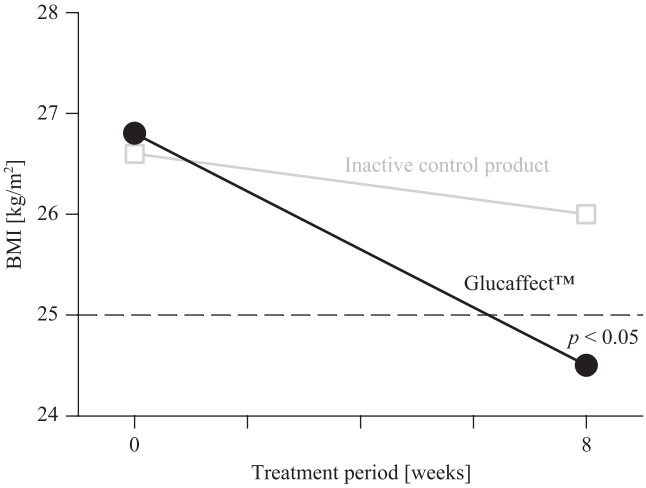

Figure 3. Development of the BMI in the groups receiving either Glucaffect™ (black) or the inactive control product (gray). Subjects receiving Glucaffect™ show a significantly decreased BMI as compared to baseline as well as to the control group ($p < 0.05$). The dotted line shows BMI of 25 kg/m^2, above which people are considered overweight. Consumption of Glucaffect™ for eight weeks brought the BMI below a value of 25 kg/m^2 which represents a successful slimming effort.

DISCUSSION

The development of an appetite is dependent upon interactions between physiology and the environment. The environment bears extremely influential factors overriding physiologic and metabolic processes operating to maintain body weight in many people, not only in children. During and immediately after eating, diverse physiological events are triggered which are referred to as 'satiety signals'. The satiation leads to the termination of food intake. When satiety signals subside, the feeling of hunger returns, leading to the

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consumption of the next meal. A delayed digestion and absorption of carbohydrates should stimulate nutrient receptors in the gastrointestinal tract for a longer period of time, resulting in a prolonged feedback via satiety signals.

Other researchers have previously demonstrated a decrease of fat mass in healthy, moderately overweight subjects using low-GI foods, by using diets rich in wholegrain (Bouché *et al.*, 2002). There are various short-term studies supporting this notion as reviewed by Bornet *et al.* (2007); however, the authors conclude that longer-term health benefits of 'satietogenic food or diet' are lacking.

The rationale for the intervention with Glucaffect™ was different as we attempted to slow down absorption of dietary carbohydrates of standard meals by diminishing the activity of the enzyme α-glucosidase. In turn, the decreased degradation of complex carbohydrates, predominantly starch, leads to a much slower absorption, decreased insulin secretion and prolonged satiety (Heacock *et al.*, 2005). A typical substance with this pharmacologic profile is acarbose, widely used for treating hyperglycemia (Laube, 2002). In clinical trials on treatment of hyperglycemia it was noticed that acarbose has a favorable effect on body weight (Purnell and Weyer, 2003). Acarbose has been successfully tested for controlling body weight in hyperinsulinaemic women with polycystic ovarian syndrome, which showed a significant reduction of BMI after six months of treatment (Penna *et al.*, 2005).

Substances like French maritime pine bark extract Pycnogenol® have recently been shown to exceed the potency for inhibition of α-glucosidase of acarbose by two orders of magnitude (Schäfer and Hogger, 2007). In a clinical trial, a daily total dosage of 50 mg Pycnogenol® affected carbohydrate absorption for significantly decreasing postprandial blood glucose after three weeks by 10.5% (Liu *et al.*, 2004). There are several herbal extracts which have been described to inhibit the activity of α-glucosidase, and these, together with Pycnogenol®, have therefore been chosen for creation of the Glucaffect™ formulation. *Salacia oblonga* extract was recently demonstrated to lower postprandial glucose peaks after a carbohydrate-rich meal because of α-glucosidase inhibition (Williams *et al.*, 2007). Inulin was further added because this indigestible sweet-tasting polysaccharide supports the perception of satiety.

For our study we chose prediabetic, overweight subjects for whom we suspected a particularly high impact for lowering blood glucose. The decrease of fasting blood glucose as well as HbA1c in our subjects after two months' consumption of Glucaffect™ exceeds values described for acarbose in diabetic patients. This cannot exclusively be attributed to α-glucosidase inhibition, as the formulation bears further ingredients which lower blood sugar by other modes of action (Dhanabal *et al.*, 2006). Glucohelp, the extract of banana leaves (*Lagerstroemia speciosa*), contains corosolic acid which was suggested to up-regulate glucose transporters for facilitating better glucose supply to tissues (Fukushima *et al.*, 2006). In clinical trials, corosolic acid was described to significantly lower blood glucose. Alpha-lipoic was demonstrated in various clinical trials to have a hypoglycemic effect in humans. This effect was described to result from the improved insulin sensitivity with alpha-lipoic acid in Type 2 diabetes patients (Kamenova, 2006).

It has been argued that unlike high-protein, low-carbohydrate (Atkins-style) or very high carbohydrate diets with their potential for adverse effects, there would be no safety concerns surrounding low-GI diets (Brand-Miller *et al.*, 2008). As shown for low-GI diets, the consumption of Glucaffect™ improved glycosylated hemoglobin levels without increasing LDL-cholesterol or the risk of hypoglycemia.

A major factor in our study was that subjects managed to skip two meals a day over weeks with the exception of Sundays. The latter was a concession to Italian lifestyle, which, on the other hand, ensured that subjects otherwise strictly followed the protocol. The massively decreased caloric intake surely did not only further contribute to the lowering of blood glucose but explains the surprising loss of weight of subjects. The average lowering of BMI by more than 2 kg/m^2 and 7.2 kg body weight within two months was more than we anticipated.

CONCLUSION

This study provides evidence that consumption of Glucaffect™ has a positive effect for keeping blood sugar in a healthy range and allows for reducing caloric intake with a resulting loss of weight when applied in conjunction with a healthier lifestyle involving better nutrition and regular moderate exercise.

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