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Decreasing cardiovascular risk factors in obese individuals using a combination of PGX® meal replacements and PGX® granules in a 12-week clinical weight modification program

Abstract

In this open, clinically based, weight modification program, we determined in six sedentary obese adults (five women; one male; age range 30–62 years) that the combination of a modified calorie diet plus PGX® meal replacement and PGX® supplementation resulted in a significant reduction in several cardiovascular risk factors over a 12-week time period. This included a significant improvement in lipids (–0.98 mmol/l LDL-C), reduction in average weight (–9.2 kg), mean reduction in fat (–4.1%) and an increase in fat-free mass (2.8%).

Keywords: weight loss, soluble fibre, cardiovascular risk, cholesterol reduction, PGX

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Introduction

Obesity has been associated with cardiovascular disease and its individual risk factors [1]. It has also been strongly linked to other mechanical complications including osteoarthritis, gastroesophageal reflux (GERD) and obstructive sleep apnea [1]. In Canada, 57,000 deaths were associated with overweight and obesity over a 15-year period from 1985 to 2000 [2]. By comparison, obesity causes an excess of 300,000 deaths annually in the United States [3]. These findings do not bode well for the long-term health of those who are obese.

Dietary interventions through the use of meal replacement products have been shown to be effective in achieving clinically beneficial weight loss [4]. The use of meal replacement products reduces overall caloric intake from food potentially by simplifying food choices decisions, minimising food preparation efforts and preventing unintended dietary failures [5]. In the Look AHEAD trial, Wadden et al. [6] reported the use of meal replacement products as one of the predictors of successful weight loss. In a study conducted by Deibert et al. [7], meal replacements and a restricted caloric intake (1,000 kcal/day for the first six weeks and 1,500 kcal/day for the next 18 weeks) in 72 pre- and post-menopausal women (age 53 years; body mass index (BMI) 32.3 kg/m^2) resulted in a mean reduction in weight (–6.7 kg) and improvement in cardiometabolic risk factors. The pre-menopausal and post-menopausal groups had their average total and low-density lipid (LDL) cholesterol reduced by –22.9, –8.8 and –21.5, –6.6 mmol/L, respectively [7]. In addition, the post-menopausal group demonstrated a significant reduction in mean triglycerides (–0.34 mmol/L), fasting glucose (–0.14 mmol/L), systolic blood pressure (–1.3 mm Hg) and an increase in high-density lipid (HDL) cholesterol (+0.089 mmol/L). As a result, meal replacement products have been widely used as part of calorie-reduced diets.

While effective in promoting weight loss in the short-term, long-term compliance with calorie-reduced diets is often very low [8]. Calorie-reduced diets are not very satiating and people report high levels of hunger [8]. Soluble viscous fibre may enhance satiety and promote long-term adherence to calorie-reduced diets which, consequently, may lead to both enhanced weight loss [9, 10] and improved cardiovascular risk factors [11, 12].

A highly viscous fibre supplement, marketed under the trade name PGX®, has been studied in numerous randomised controlled trials [13, 14]. One such open-label clinical investigation by Lyon and Reichert [15], using 5 g of PGX® granules two to three times a day for 14 weeks, in combination with lifestyle modifications, demonstrated significant average reductions in weight (–5.79 kg), waist circumference (–12.07 cm) and percentage body fat (–2.43%) compared to baseline. Moreover, the use of PGX® in this investigation was associated with a clinically important reduction in mean total and LDL cholesterol levels by 19.26% and 25.51%, respectively, compared to baseline. The improvement in serum lipids by PGX® was confirmed in a randomised controlled study by Lyon et al. [16].

This single-arm pilot investigation was intended to provide preliminary proof of the effect of PGX®, in combination with a controlled calorie-restricted diet, on body weight, fat-free mass, resting metabolic rate, appetite scores and cardiometabolic risk factors, specifically the lipid profile, in a small group of volunteers from a clinical practice.

Materials and methods

Participants

Six sedentary obese adults (five females; one male) with BMI between 26–50 kg/m^2 and age ranged from 30 to 62 years were invited to participate in a 12-week cardiometabolic risk management program. Exclusion criteria included pregnancy or lactation for female participants; smoking; past history of gastrointestinal surgery; hypersensitivity to the study foods; taking medication, natural health products or other fibre supplements which may affect body weight; blood lipids and/or glycaemic control. Prior to their participation in this program, participants agreed to provide their written informed consent. The overall investigation was conducted in accordance with the ethical standards as set forth in the Helsinki Declaration of 1975.

Diet

Participants were instructed to follow a 1,200 kcal/day meal plan, regardless of sex, consisting of two meal replacement drinks at breakfast and lunch, a 500-kcal balanced dinner meal and 250 kcal snacks between meals spread throughout the day. Participants were advised by the registered dietitian to incorporate low-fat, low-to-moderate-glycaemic index (GI) foods. The meal replacement drinks were constituted by mixing the meal replacement powder mixes with 250 mL of water. Each serving of meal replacement drink contained 226 calories (945 kJ); 21 g whey protein concentrate; 6.6 g of fat; 21 g of carbohydrate including 5 g of soluble PGX® fibre. A three-day food diary was completed at baseline and the end of the program by all participants. Participants were encouraged to exercise but not given specific regimen through the 12-week period.

Supplementation

PGX® ((α-D-glucurono-α-D-manno-β-D-manno-β-D-gluco), (α-L-gulurono-β-D mannurono), β-D-gluco-β-D-mannan) is a novel patented (US Pat 8,062,686, CAN 2,604,253) complex, manufactured by a proprietary process from three fibres (konjac (glucomannan), sodium alginate and xanthan gum) to form a highly viscous polysaccharide with exceptional water holding and gel-forming properties, exhibiting a developing viscosity that is higher than its individual components [17–19]. The calorie-reduced diet was supplemented with PGX® through the use of PGX®-containing meal replacements (SlimStyles® Meal Replacement Drink Mix, Natural Factors, Coquitlam, Canada) at breakfast and lunch and PGX® granules or capsules (PGX® Daily, Natural Factors, Coquitlam, Canada) at snacks or dinner. Each serving of meal replacement and supplementation provided 5 g of PGX®. Instructions were provided to ensure a total daily dose of 15 g/day for the duration of the program. Participants were instructed to drink 500 mL of water per serving of PGX® product as needed for additional appetite control.

Anthropometric and other measurements

Program participants were evaluated at baseline and on a bi-weekly basis for weight (kg), height (cm), hip (cm) and waist (cm) measurements for the duration of the study. Waist and hip measurements were recorded using a standard medical-type tape measure at consistent anatomical locations: approximately mid-way between the lowest rib and the iliac crest for the waist, and around the hip at the greater trochanter. BMI scores were calculated from participant's height and weight using an online BMI calculator available through the US Department of Health and Human Services website. Participants' body composition

was determined using body impedance analysis (BIA; RJL Systems, Michigan, USA) at baseline and week 12. Using an algorithm available through RJL Systems, percentages of fat and lean body mass were calculated. Evaluation of participants' resting metabolic rate (RMR) was also determined using an indirect calorimeter (MedGem, Microlife Medical Home Solutions, New York, USA) at baseline and the three-month mark. In addition, a registered dietitian monitored and analysed participants' food intake at baseline, 6 and 12 weeks, using nutrition and fitness software (The Food Processor, ESHA Research, Oregon, USA). Moreover, participants were asked to complete and record their hunger and appetite ratings with a brief visual analogue scale (VAS) at baseline and 12 weeks in order to assess subjective appetite ratings.

Blood collection and laboratory biochemical analysis

Laboratory measurements were performed according to standard procedures by an independent and certified laboratory in British Columbia, Canada. At baseline and the conclusion of the clinical program, fasting venous blood samples were taken for measurement of total cholesterol (TC), triglycerides (TAG) and low-density lipoprotein cholesterol (LDL-C).

Statistical analysis

Descriptive statistics were calculated for the various variables at baseline, follow-up and for the change from baseline scores; all continuous variables were summarised using the mean, median, SD, minimum and maximum. The one-sample Student's t-test was used to test the null hypothesis that there was no change from baseline in a given variable; 95% confidence intervals were calculated for the mean change. Associations between various variables were examined using scatter plots, as well as with the Spearman rank correlation coefficient. The null hypothesis of no correlation between variables was tested using a z-test. All statistical tests used a significance level of 0.05.

Results

Six participants (five females; one male) participated in the 12-week cardiometabolic risk management program. Since these six participants were highly committed, all of them completed the program over the 12-week period. The mean ± SD of weight and BMI at baseline were 112.94±26.37 kg and 38.3±9.8 kg/m^2, respectively.

The therapeutic use of PGX® meal replacement and PGX® granules or capsules, along with a calorie-restricted diet, is beneficial in improving body weight, BMI, waist and hip circumferences after 12 weeks of treatment (Table 1 and Figure 1). Significant reductions ($p<0.05$) in body weight (−9.2 kg), waist circumference (−9.9 cm) and hip circumference (−8.9 cm) were observed at 12 weeks compared to baseline. BMI also demonstrated a clinically important reduction of −2.4 kg/m^2 by week 12. This improvement however was not significant.

Significant differences in RMR and body composition measures over the 12-week time period of the calorie-restricted diet with PGX® supplementation were also observed (Table 1). Participants' RMR decreased from 2,250 kcal at baseline to 1,992 kcal at week 12. Meanwhile, reported as a percentage of overall body weight, participant's fat mass decreased by −4.1% compared to baseline and fat-free mass, as an indicator of lean body mass, increased by 2.8% over the 12-week time period ($p<0.05$).

TC and LDL-C significantly decreased from baseline (Figure 2). A significant reduction of −1.11 mmol/L was observed in serum TC level. Although LDL-C level decreased from 2.67 to 1.74 mmol/L ($p<0.05$) after 12

Table 1 Anthropometric, RMR and body composition measures at baseline and after 12 week of the calorie-restricted diet with PGX® supplementation.

Variable	Baseline	Week 12	Change from baseline	95% CI on change
Weight (kg)	112.9±26.4	103.7±30.8	−9.2*	[−16.0, −2.4]
Waist (cm)	115.1±22.9	105.2±27.2	−9.9*	[−17.0, −3.0]
Hip (cm)	130.3±20.8	121.4±24.9	−8.9*	[−13.7, −4.1]
BMI (kg/m^2)	38.3±9.8	36.0±13.0	−2.4	[−5.7, −1.0]
RMR (kcal)	2,250±362.5	1,992±291.7	−258*	[−462.8, −53.8]
Fat mass (%)	47.4±12.5	43.3±14.7	−4.1%*	[−7.0, −1.1]
Fat-free mass(%)	56.3±8.6	59.0±10.7	2.8*	[0.5, 5.1]

Data represent mean±SD with n=6 participants. *Asterisks represent significant difference from baseline ($p<0.05$).

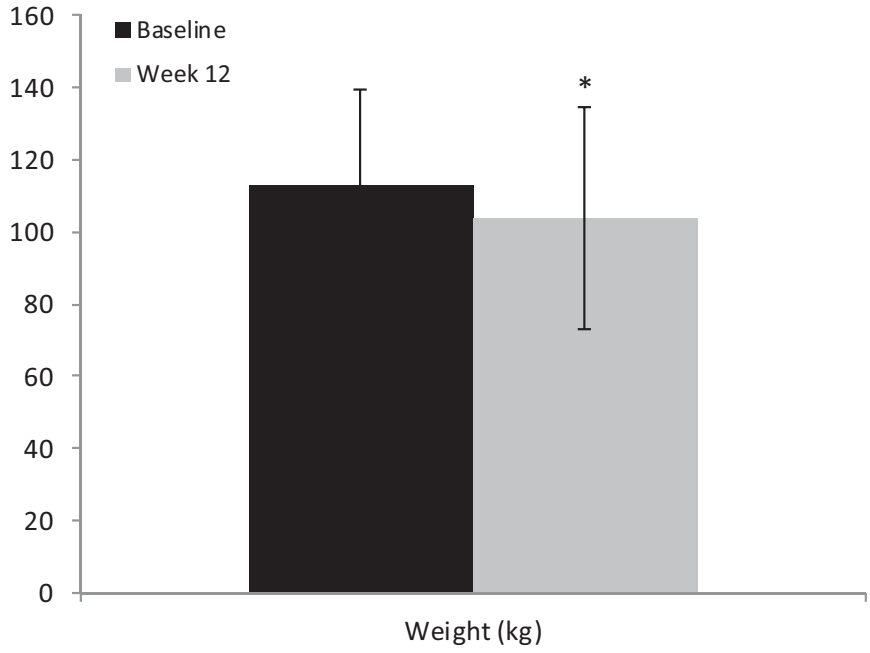

Figure 1 Body weight (kg) at baseline and week 12.
Notes: Data represent mean±SD with n=6 participants. *Asterisk indicates significant weight loss of −9.2 kg observed over 12-week time period of PGX® supplementation ($p<0.05$).

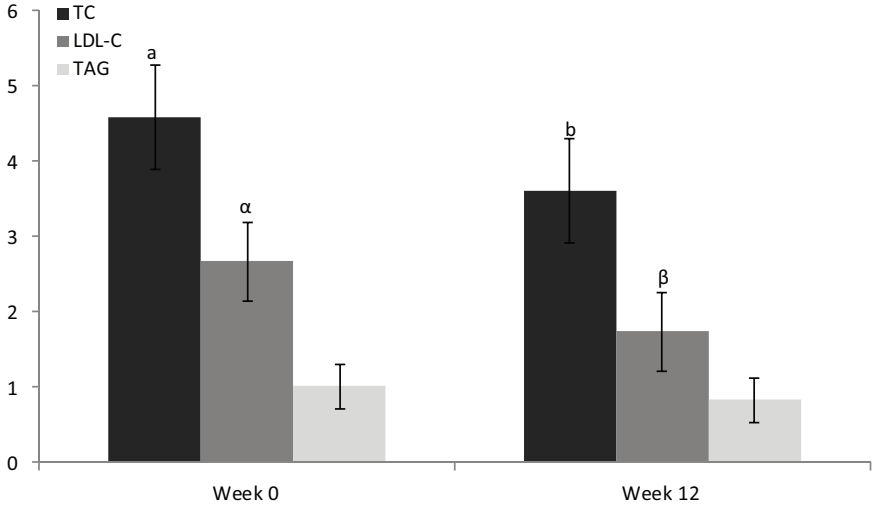

Figure 2 Biochemical measures at baseline and after 12 week of the calorie-restricted diet with PGX® supplementation.
Notes: Data represent mean±SD with n=5 participants. TC=total cholesterol; LDL-C=low density lipoprotein-cholesterol; TAG=triglycerides. ^{a,b}Different superscript letters represent significant reduction in TC over 12-week time period of PGX® supplementation ($p<0.05$). $^{\alpha,\beta}$Different superscripts represent significant reduction in LDL-C observed over 12-week time period of PGX® supplementation ($p<0.05$). TAG levels were not significantly reduced from baseline.

weeks of intervention, there was also a reduction in mean (95% CI) TAG level, but this did not quite reach significance [−0.22 (−0.08, −0.024) mmol/L].

Subjective appetite ratings (Table 2) and caloric intake of participants were analysed at weeks 10 and 12, respectively. Fullness scores, as assessed by VAS, generally increased over the 10-week period. This may indicate an improved feeling of fullness between meals with PGX® supplementation. Total VAS score and other VAS variables (i.e. hunger, desire to eat and prospective consumption) however did not significantly differ from baseline (data not shown). Although not significant, there was a trend three hours after dinner for both fullness ($p=0.07$) and total VAS score ($p=0.07$) (data not shown).

Table 2 Comparison of before breakfast, lunch and dinner fullness scores, as assessed by visual analogue scales (VAS), after 10 weeks of the calorie-reduced diet supplemented with PGX®.

Time of day	Baseline	Week 10	Change from baseline	95% CI on change
Before breakfast	15.2±16.6	51.2±31.1	36.0±32.0*	[2.4, 69.6]
Before lunch	39.5±22.3	37.3±36.6	−2.2±38.7	[−42.8, 38.5]
Before dinner	28.0±18.5	35.8±21.2	7.8±7.1*	[0.4, 15.3]

Data represent mean±SD with n=6 participants. *Asterisks represent significant difference from baseline ($p<0.05$).

Table 3 Daily energy and nutrient intake at baseline and week 12 of participants consuming the calorie-reduced diet with PGX® supplementation.

Variable	Baseline	Week 12	Change from baseline	95% CI on change
Energy (kcal/day)	2,039±818.6	1,188±317.5	−851*	[−1,487.6, −214.3]
Protein (%)	18.6±5.1	29.6±5.8	10.9*	[6.6, 15.2]
Carbohydrate (%)	41.7±7.3	42.2±5.8	0.5	[−4.7, 5.8]
Fat (%)	35.4±5.5	26.2±3.1	−9.1*	[−16.2, −2.1]
Soluble Fibre (g)	2.0±0.5	9.4±2.6	7.4*	[4.4, 10.4]

The improvement observed in fullness scores was parallel to the overall reduction in mean caloric intake after 12 weeks of intervention (Table 3). Participants' caloric intake reduced by −851 kcal/day from baseline ($p<0.05$). While the overall intake of carbohydrates remained similar to baseline, participant's dietary protein intake increased by 10.9% over the 12-week period ($p<0.05$). Higher intake of soluble fibre was observed at week 12 ($p<0.05$), which was likely due to the supplementation of PGX® to the calorie-restricted diet.

Discussion

A calorie-restricted diet supplemented with PGX® was shown to be well tolerated and result in significant, clinically meaningful weight loss over a 12-week period. The weight reduction seen in the present investigation is consistent with the finding of another study showing the effectiveness of meal replacement in obesity care. Winick et al. [20] reported that 286 overweight and obese participants (BMI: 27.40–32.90 kg/m^2) achieved significant weight loss after being prescribed with a calorie-reduced diet (providing approximately 1,160 kcal/day), consisting of two meal replacements along with snacks and a reduced-calorie dinner meal, for three months. The significant weight loss of −9.2 kg observed in our participants was comparable to the reduction in body weight of the male participants in Winick et al. [20] at −8.47 kg for participants belonged to the occupational group (i.e. firefighter) and −8.45 kg for participants belonged to the clinical group (i.e. health care). There was no significant reduction of BMI, when compared to baseline, which may be due to the small sample size. However, the direction of the difference generally showed a strong reduction at −3.5%. The current investigation showed a significant decrease in waist and hip circumferences ($p<0.05$). The reduction in waist circumference is an important factor for cardiovascular risk reduction. It has been suggested that for every 1-cm increase in the waist circumference, there is a relative increase of 2% in cardiovascular events [21].

Significant reductions in several important cardiovascular risk factors including TC and LDL-C were observed in the study. The decrease of LDL-C observed in our participants is comparable to the effects seen in those employing statin medications [22]. A meta-analysis evaluating the effects of statins on LDL-C and cardiovascular events noted that a 1 mmol/L (39 mg/dL) reduction of LDL-C lowered overall mortality and coronary mortality by 15% and 24%, respectively [22]. Moreover, the program's calorie-reduced diet that consisted of liquid meal replacements may also play a role in reducing LDL-C. This is consistent with the study findings reported by Deibert et al. [7] that the use of a meal replacement and fat-reduced diet lowered LDL-C in pre-menopausal women.

RMR is estimated to be approximately 60–70% of daily energy expenditure [23]. It is well established that weight loss secondary to a restriction in caloric intake is linked to a decrease in the RMR [24]. In the present investigation, our participants also had a significant reduction in RMR from 2,250 to 1,992 kcal (−258 kcal on average) from baseline. While not universally accepted,

indirect calorimetry has been shown to be a valid and clinically acceptable measurement of RMR [25]. McDoniel [26] indicated that the mean difference between three adult studies using a Douglas bag or indirect calorimeter to be less than 1% (1,568 versus 1,559 kcal). McDoniel et al. [27] further indicated that the use of indirect calorimetry as an adjunctive weight-loss tracking tool positively influenced the therapeutic outcomes of a 90-day weight control program.

In this clinical investigation, participants' dietary protein intake increased by 10.9% ($p<0.05$) at the end of intervention. This was likely a result of the inclusion of whey protein in the PGX® meal replacement. A higher protein intake during caloric restriction has been found to maintain fat-free mass relative to weight loss [28]. A statistically significant positive correlation between the changes in dietary protein intake and fat-free mass was noted in our analyses (data not shown), suggestive that the 2.8% increase in participants' fat-free mass ($p<0.05$) was due to the increase in dietary protein intake. The positive association between dietary protein intake and lean mass may also play a role in preventing the reduction of energy expenditure during times of energy restriction [29]. Although our participants had a significant reduction in RMR, this reduction may have been less have they undergone the same hypocaloric diet with other sources of dietary protein. Acheson et al. [30] reported that whey protein improved meal thermogenesis by 14.4% in comparison to either casein (12%) or soy (11.6%).

However, the impact of higher protein intake on energy expenditure may not be as important as the effect of protein on satiety [31]. Satiety is strongly influenced by the source of protein in a meal, with whey protein having a statistically greater impact on satiety than other types of protein sources including tuna, turkey and egg [32]. Moreover, the use of a whey protein may provide some cardiovascular advantages over other types of protein in a meal replacement product. A randomised study has noted that daily consumption of 27 g whey protein isolate in 89 overweight and obese individuals (BMI: 25–40 kg/m^2) for 12 weeks significantly improved mean fasting lipids (–7% cholesterol; –7% LDL) compared to a casein group and a control group [33]. The same study further reported that whey significantly lowered mean insulin levels by 11% at the end of intervention.

The use of fibre has also been shown to influence satiety and reduce food intake [34], suggesting that high-protein and high-fibre content in a diet may have synergistic effects on satiety and weight loss. A high-fibre high-protein diet (30% protein; 50% carbohydrate; 30% fat; 35 g/day dietary fibre) was reported to significantly improve body weight, body composition (e.g. total fat and truncal fat) and metabolic risk factors (e.g. TC and LDL-C), compared to a standard diet low in fat and high in carbohydrates (20% protein; 50% carbohydrate; 30% fat; 25 g/day dietary fibre), in overweight or obese women with either a positive family history of diabetes or of Asian ethnicity after 10 weeks of intervention [35].

Human clinical trials on PGX® suggested its role in satiety [36, 37], glucose control [13, 14], insulin sensitivity [15] and lipid modification [15, 16]. Several potential mechanisms exist by which PGX® may exert favourable effects on satiety, body weight and cholesterol levels. Viscous soluble fibres like PGX®, in addition to displacing energy from the diet, also encourage gel formation, increase the volume of gastric contents, reduce gastric emptying while decreasing the small-intestine transit time and absorption of macronutrients [38], as well as influence the secretion of gut satiety hormones such as peptide YY and glucagon-like peptide-1 [37]. The hypocholesterolemic effect of viscous soluble fibre has been proposed to be attributed to the prevention of bile acid re-absorption from the small intestine leading to an increased bile acid excretion in the stool and decreased hepatic cholesterol synthesis modulated by reduced insulin stimulation and/or increased generation of short-chain fatty acid, particularly propionate [11].

In conclusion, the supplementation of highly viscous PGX® to a calorie-restricted meal replacement plan improved cardiometabolic risk factors in obese and overweight individuals. This indicates the potential of PGX®, through the use of PGX® meal replacements and PGX® granules or capsules, as a simple, well-tolerated and practical weight management aid for calorie-restricted diets.

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Conflict of interest

RGR and MRL are consultants to Factors Group of Nutritional Companies. SW is a consultant to InovoBiologic Inc. RJG is the owner of the Factors Group of Nutritional Companies and retains an interest in PGX® VK is an employee of the Canadian Centre for

Functional Medicine. MP was an employee of the Canadian Centre for Functional Medicine. PM has no conflict of interest. PGX®, PolyGlycopleX® are trademarks of InovoBiologic Inc. Slim Styles® and PGX® Daily are trademarks of Natural Factors. All other marks are the property of their respective owners.

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