

# PGX<sup>®</sup>

( PolyGlycopleX<sup>®</sup> )

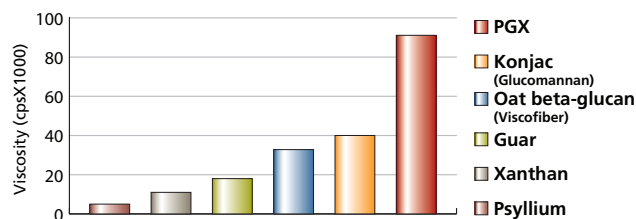
Regulates Glucose Levels · Lowers Cholesterol  
Controls Appetite · Increases Insulin Sensitivity

## History

Two of the polysaccharides used in the manufacture of PGX<sup>®</sup> were known to have a synergistic effect<sup>1</sup>. Work by researchers at InovoBiologic Inc. in Calgary, Alberta, built on this knowledge and made the remarkable discovery that the addition of a specific third polysaccharide led to a product with unexpected developing viscosity higher than any of its individual components. Since the early 2000's, work around the globe has been developing a body of scientific evidence in in vivo models on PGX<sup>®</sup>.

## Proprietary Composition

The method in which soluble fibres are made into PGX<sup>®</sup> (PolyGlycopleX<sup>®</sup>) is a proprietary process known as EnviroSimplex<sup>®</sup>. Each softgel, capsule, granule or powdered product contains the exact balanced ratio of components required to produce the desired characteristics of PGX. All manufacturing, processing and packaging steps meet or exceed government and industry standards and all Good Manufacturing Practices are adhered to. The PGX<sup>®</sup> composition is patent protected. It is a unique novel complex [( $\alpha$ -D-glucurono- $\alpha$ -D-manno- $\beta$ -D-manno- $\beta$ -D-gluco), ( $\alpha$ -L-gulurono- $\beta$ -D mannurono),  $\beta$ -D-gluco- $\beta$ -D-mannan] of natural polysaccharides that complement each other and have been shown to act synergistically<sup>2</sup> to form strong interactions resulting in an extremely high viscosity novel polysaccharide, 3-5 times higher than any currently known single polysaccharide (Figure 1). The physiological effects and overall benefits to human health of a soluble fibre are directly proportionate to its viscosity, as shown by Jenkins et al<sup>3</sup>. As PGX, gram for gram, produces a viscosity far higher than currently known soluble fibres, far less is needed to produce a physiological effect. The developing viscosity of PGX and the requirement for less material to be consumed for an efficacious dose, leads to ease of use, palatability and cost effectiveness.



**Figure 1:** Viscosity of PGX compared to other water soluble polysaccharides after hydrating for 3 hours. Measurements up to 90000 cps were taken with spindle 3. \*PGX viscosity not less than 90000 cps. (Cole Parmer Viscometer 98936 series, C=1.4%)

The discovery that the proprietary composition of the polysaccharides that make up PGX leads to a synergistic interaction and a developing viscosity are important characteristics of the product. This allows for far less material to be consumed and the developing viscosity over about 20-30 minutes allows for incorporation into foods and beverages without a thick mass resulting, which is unpalatable. Full viscosity develops over a 60 to 90 minute time frame. The creation of a stable gel “matrix” can suspend ingested liquid and nutrients for digestion using far less material than a conventional soluble fibre. When PGX is mixed with food in the gut, the matrix slows digestion and extends the area for nutrient absorption through the stomach and the small intestine. PGX's capacity to capture and suspend nutrients (such as sugars, fat and carbohydrates) is key to its physiological benefits, especially after meal glucose-lowering, as demonstrated in clinical trials.

## Safety

PGX<sup>®</sup> has been evaluated by internationally recognized protocols to be remarkably safe. In an OECD 408 safety study (conducted in the USA<sup>4</sup>), PGX was evaluated at a 5% level in food and found to be safe according to these standards. A Human Tolerance Study (conducted in France<sup>5</sup>) also concluded that PGX was safe and two Genotoxicity study (Ames and MMA) also concluded PGX was safe (conducted in Germany<sup>6</sup>). A paper based on the Factors Group commitment to monitor its products will be available in the near future illustrating how safe PGX is. Since 2004, over 250 million softgels have been sold as well as many tens of millions of granular doses. Work with the Burdock Group in the USA led to PGX<sup>®</sup> achieving Self Affirmed GRAS (Generally Recognized As Safe) status as well as Self Affirmed Medical Food GRAS status. PGX has been submitted to the FDA for No Objection GRAS status.

## Slow Viscosity

The viscosity of PGX<sup>®</sup> develops slowly after mixing with water or other beverages, with maximum viscosity reached after 60 to 90 minutes. When using PGX granules, this means that it remains palatable when added to food or beverages and develops its full viscosity in the stomach and small intestine. Unlike many other fibres, PGX maintains its highly viscous properties in spite of the influence of stomach acid and digestive enzymes. Developing viscosity is very important, as if a product becomes viscous too quickly, hazards may result as well as the product being unpalatable.

## Optimum Volume

Studies have shown that the volume from food creates a sense of fullness in the stomach. This sense of fullness triggers the release of various signalling hormones that alert the brain to stop eating. When PGX® is taken before a meal or in a meal replacement, a sense of fullness and satiety develops, which lasts for hours. PGX studies have shown that the ingestion of PGX affects these signalling hormones. In the intestine, PGX remains highly volumetric and viscous, delaying the return of hunger pangs.

## Clinical Evidence

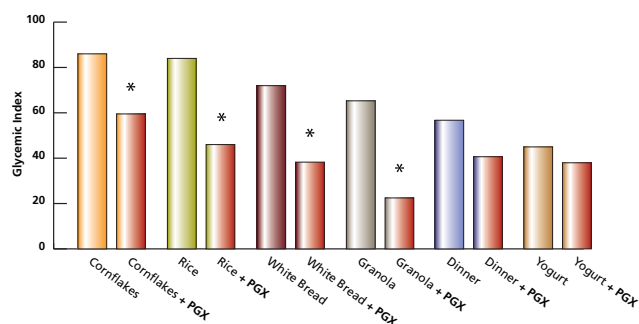
Evidence-based information of blood lipid reduction, diabetes control, improvement in colonic function and appetite and weight control comes from clinical trials conducted at Universities and Contract Research Organizations in Australia, Canada, England, France, Germany and the USA.

### 1 Glucose Control: Impact on the Glycemic Index

Two sets of experiments were undertaken at the Glycemic Index Laboratories in Toronto, to support the blood glucose lowering potential of PGX<sup>7,8</sup>. All experiments followed the methodology to determine glycemic index (GI). The first study investigated the impact of PGX on the glycemic index (GI) when added to liquid (glucose) and solid (white bread plus margarine) high carbohydrate food formulations. Three different doses, 2.5 g, 5 g and 7.5 g were administered with each food or beverage and the glycemic index calculated for each dose. The results for the glucose drink showed that 2.5 g, 5 g and 7.5 g of PGX reduced the GI by 16.3%, 22.3%, and 27.5%, respectively. The results for the white bread and margarine showed that 2.5, 5 and 7.5 grams of PGX reduced the GI by 28.9%, 44.2%, and 49.2%, respectively<sup>7</sup>.

In a second set of experiments, the effect of PGX on the GI was investigated when PGX is added into commonly consumed foods. The GI was determined for cornflakes with milk, rice, turkey dinner and yoghurt with or without 5 g of PGX sprinkled onto the foods. Addition of PGX to cornflakes, rice, turkey dinner and yoghurt resulted in a 26%, 45%, 24%, and 9% reduction in meal GI, respectively<sup>8</sup> (Figure 2).

Furthermore, PGX can be incorporated into foods and maintain its GI lowering potential. PGX® incorporated into a baked granola reduced the GI of all the granolas. Compared to the control granola, the 2.5 g and 5 g PGX granolas reduced the GI by 45% and 64%, respectively<sup>8</sup>.



**Figure 2:** Reductions of the glycemic index when PGX is added or incorporated into commonly consumed foods. \*Statistically different than food without PGX ( $p < 0.001$ )<sup>7,8</sup>.

The results showed that adding or incorporating PGX into a variety of different foods is highly effective in lowering the glycemic index irrespective of the type of meal it was added to. The extent of GI lowering may be greater when added to high GI foods. Therefore, if PGX is consumed regularly, it can reduce the glycemic impact of the overall diet.

PGX is a practical and effective means of lowering the postprandial glucose response of foods, which may also be highly beneficial for those with insulin resistance, metabolic syndrome and type 2 diabetes. This exceptional reduction in postprandial glucose offers great potential for the long-term use of PGX in diabetes management and control of appetite and body weight.

### 2 Diabetes Control

Compared to placebo, a viscous fibre blend (one of the precursors of PGX) reduced serum fructosamine, a marker of glycemic control, in a randomized, controlled clinical trial. This study was conducted in high-risk coronary heart disease (CHD) patients that also had Type 2 diabetes and were being treated with drugs for diabetes, high cholesterol, and elevated blood pressure. Eleven individuals consumed, in a cross-over design, a metabolically controlled NCEP Step 2 diet supplemented with VPB or placebo for three weeks<sup>9</sup>. Although this prototype of PGX mildly improved glycemic control, the reduction was comparable to that found with the oral hypoglycemic agent Acarbose (*Manufactured by Bayer, Germany*). In addition, the *American Dietetic Association*, in their position paper on the health implications of dietary fibre, state that considerable experimental evidence demonstrates that the addition of viscous dietary fibres slows gastric emptying rates, digestion, and the absorption of glucose to benefit immediate postprandial glucose metabolism and long-term glucose control in individuals with diabetes mellitus<sup>10</sup>.

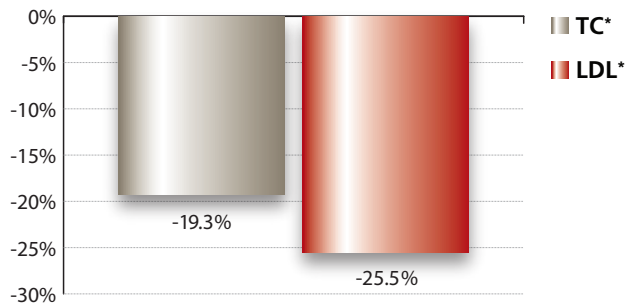
### 3 Metabolic Syndrome

According to data from the US (*JAMA, Jan 6, 2002*), approximately 47 million adult Americans (nearly one in three adults) are suffering from Metabolic Syndrome, and many of them will progress to full blown diabetes in the years to come. In Canada this number is about 1 in 4. Metabolic Syndrome is often developed in physically inactive individuals with high waist circumference and the presence of excessive abdominal fat, modestly high blood sugar and blood pressure, lower HDL-cholesterol and increased triglycerides, characterized by insulin resistance and compensatory hyperinsulinemia. PGX is an effective natural health ingredient that can help diminish the risk factors that characterize this syndrome. Studies conducted on PGX have illustrated reduce risk factors associated with metabolic syndrome by 1) reducing waist circumference and most likely reducing intra-abdominal fat<sup>11,12</sup> 2) lowering postprandial and fasting blood sugar levels<sup>7,11,14</sup>; 3) lowering cholesterol<sup>13,14</sup> and 4) improving insulin sensitivity<sup>12</sup>.

### 4 Cholesterol

In healthy subjects, 10 grams of PGX per day over 21 days has been shown to reduce total cholesterol levels by 14% and LDL levels by 17%<sup>5</sup>. In overweight and moderately obese individuals (BMI ranging from 27 to 40 kg/m<sup>2</sup>), 10 grams of PGX over a 14 weeks has been shown to reduce total cholesterol levels by 19% and LDL by 25%<sup>11</sup> (Figure 3). Two other studies using a precursor to PGX showed significant reductions of total and LDL-cholesterol by up to 19% and 29% in individuals with Metabolic Syndrome or diabetes<sup>9,14</sup>. This

effect could be compared with the cholesterol lowering effect of a modest dose of statin drugs. Compared to the cholesterol lowering effects of other gel-forming fibres such as psyllium, oats, or guar<sup>15</sup>, PGX has a greater effect expressed as a change in cholesterol per gram of soluble fibre consumed<sup>12</sup>. Therefore, comparable results with other soluble fibres may be achieved with considerably less PGX.<sup>2, 10</sup>



**Figure 3:** Percent change in plasma lipids from baseline after 14 weeks of PGX® (\*p < 0.05 from week 0)

Possible mechanism of action include: delay in nutrient absorption, increased generation of short chain fatty acid (SCFA) (especially the cholesterol-lowering SCFA propionate), and/or increased excretion of bile acid through the stool (i.e. removing fat from the body). A paper based on data obtained from a 54 person randomized, double blind study has been submitted for publication.

## 5 Weight Management

Obesity is a disease that arises through a multifaceted pathophysiology. Successful treatment of it requires a multi-strategic approach. It is hypothesized that consumption of PGX leads to multifaceted effects for weight management and satiety in the human body, which include mechanical actions (e.g. stomach distension and delayed gastric emptying), neural actions (e.g. gut derived appetite regulating peptides – PYY, ghrelin), prebiotic mechanisms (formation of short chain fatty acids e.g. acetate), and metabolic effects (e.g. carbohydrate and lipid metabolism). A paper based on a 54 person double blind placebo controlled study conducted in Europe evaluating PGX and satiety hormones has been accepted for publication in a peer reviewed journal.

Each pathway is critically important for appetite and body weight regulation. The ability of PGX to do so makes it the most powerful material as an aid for weight management.

### Appetite and Food Intake

When consumed, PGX develops its full viscosity in the stomach and small intestine. This added volumetric and viscosity bulk in the stomach produces a feeling of fullness and decreases appetite. A number of factors may contribute to this increased satiety associated with high viscosity including increased gastric distension and delayed gastric emptying, a blunting of the postprandial glucose and insulin surge and the release of various satiety hormones, which alert the brain that the stomach is full. Therefore, its volume and viscosity may make it easier for overweight individuals to cut back on caloric intake.

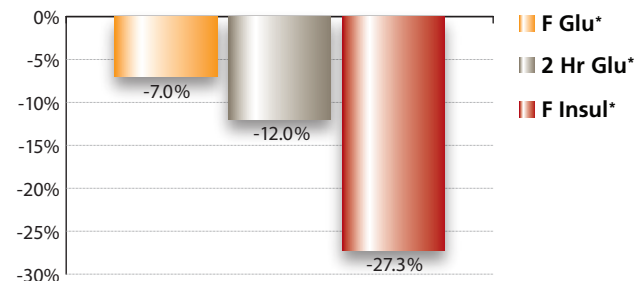
Viscosity of fibre has also been shown independently to affect food intake. In a double-blind randomized, controlled and crossover trial,

PGX® meal replacement preload significantly reduced ad libitum pizza intake in adolescents compared to two lower viscosity fibre meal replacements (glucomannan and cellulose)<sup>16</sup>. Even though the PGX group consumed less, they did not compensate for the calorie deficit at their next meal, indicating the possibility of a second meal effect.

### PGX® Weight Management Programs

The effects of PGX as a weight management aid has also been assessed in two open label weight loss programs conducted at the Canadian Centre for Functional Medicine in Coquitlam, British Columbia. In each of these programs, participants received basic instructions in caloric reduction and exercise, and were instructed to consume 5 grams of PGX two to three times per day.

One program looked at the effect of PGX on weight loss over a 14 week period in people who were sedentary and overweight or obese. There was a significant reduction (p < 0.05) from week 0 or baseline in group weight (-5.8±3.6 kg), waist circumference (-12.1±5.6 cm), percent body fat (-2.4±2.4%), and BMI (-2.26±1.2 kg/m<sup>2</sup>). Moreover, these latter changes were paralleled by a significant decrease in total cholesterol (-19.3%), LDL (-25.5%), fasting glucose (-7.0%) and insulin (-27.3%) levels over a relatively short time span of 14 weeks<sup>11</sup> (Figure 4). Body composition was measured (Bioelectrical Impedance Body Composition Analyzer; RJL Systems Inc.) and most subjects lost body fat and increased their lean muscle mass with little change in body water.

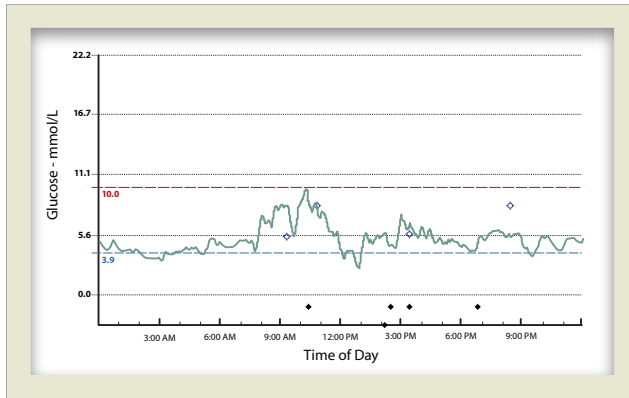


**Figure 4:** Percent change in fasting glucose, 2 hour postprandial glucose, and insulin from baseline after 14 weeks of PGX® (\* p < 0.05 from week 0)

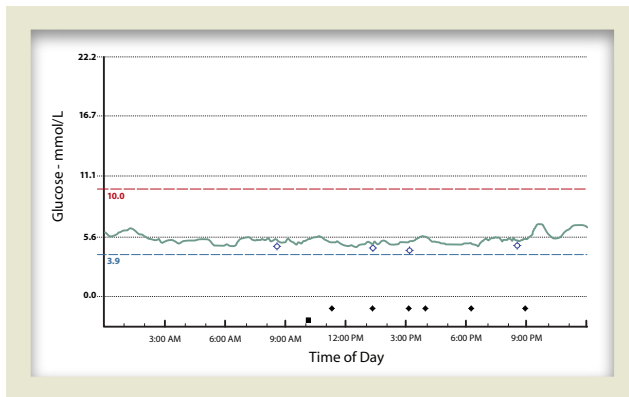
The second program utilized a meal replacement containing PGX and PGX granules on weight loss in people who were overweight or obese over a 10 week period. From the subjects that participated, there was an average reduction in group weight of 5 kg and waist circumference of 6.4 cm. Most subjects reported that the meal replacement drink created a sense of satiety and completely controlled their hunger for 2 – 4 hours.

In addition, subjects in the weight management group were connected to a continuous blood glucose monitoring system (CGMS) by Metronics Inc. Results show that individuals with weight challenges have very volatile blood glucose levels with wide and frequent swings between hypoglycemia and hyperglycemia. From the program, most overweight and obese subjects were found to have increased glycemic volatility at baseline and then exhibited markedly diminished glycemic volatility after administration of PGX (Figure 5 and 6).

The weight loss consistently experienced on the PGX Weight Management Programs translates into a healthy weight loss of about 0.5-0.8 kg (1-1.5 lbs) per week.



**Figure 5:** Uncontrolled and erratic blood sugar levels of an obese woman over 24 hours with a poor diet and no physical activity (Continuous Glucose Monitoring System, Medtronic).



**Figure 6:** Controlled and balanced blood sugar levels of the same woman after consuming PGX for 6 weeks and experiencing a healthy weight loss of 2 pounds per week.

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PGX PATENT PENDING

For more information, please contact:

InovoBiologic Inc. 104 - 1240 Kensington Road NW, Suite 409, Calgary, Alberta T2N 4X7  
tel 1.800.916.1650 fax 1.800.574.9607 · email info@inovobiologic.com