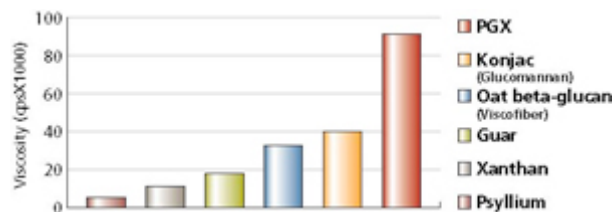


PGX[®] – What Is It?

PolyGlycoplex (PGX) is a proprietary mixture of highly purified, water soluble polysaccharides that acts by Induced Viscosity Technology[™] (IVT) and is produced using unique EnviroSimplex[™] technology. The mixture is associated with unparalleled physiological effects and health benefits that are patent protected and strongly supported by randomized clinical trials. This powerful blend is composed of three different polysaccharides that complement each other and act synergistically to form strong bonds for a level of viscosity more than 3-5 times higher than any known polysaccharide (*Figure 1*). The physiological effects and overall benefits to human health of a soluble polysaccharide are directly proportionate to its viscosity¹.



*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%)*

Novel Technology

EnviroSimplex is a process using precise and highly standardized steps developed by InovoBiologic and scientifically validated by *University of Toronto* researcher, Dr. Vladimir Vuksan. EnviroSimplex[®] technology is a conditioned chamber that allows a perfect micro-tabulation of the three polysaccharides to collide in exact and precise proportion, meaning that each granule consistently contains the proprietary ratio blend in equal proportion. Processing meets and exceeds the requirements of pharmaceutical industry standards and Good Manufacturing Practices. Every polysaccharide complex within PGX is an entity on its own and its perfect composition and particle sizes contribute to its maximum viscosity and health benefits.

Induced Viscosity Technology[™]

IVT is based on principles of rheology that have been studied and tested for more than 15 years by *University of Toronto* researcher, Dr. Vuksan. The main principles used to induce viscosity in PGX involve the synergistic effects of its individual polysaccharide components. A critical point is reached once the polysaccharides swell sufficiently to burst and release three individual polysaccharide coils. Two of the polysaccharides are complementary to each other and have the ability to hook together, while the third polysaccharide in PGX is used to fasten (*Figure 2*).

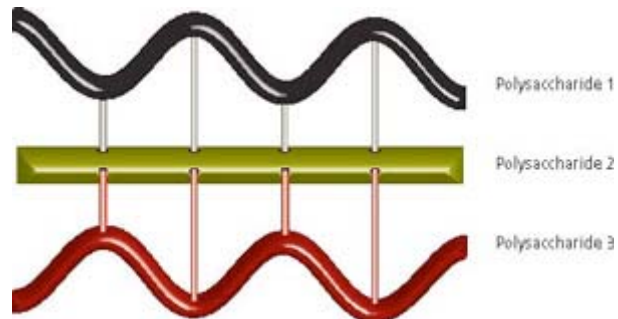


Figure 2: Three polysaccharides binding together at side bonds and forming an interlocking matrix.

This third polysaccharide joins the first two forming a strong interlocking matrix. In PGX, because the right soluble polysaccharides are blended, the side bond of the coils link with the side bonds of the other coils, acting synergistically, inducing a high viscosity and creating a stable gel matrix incorporating the ingested liquid and nutrients in solution.

When PGX is mixed with food and human digesta in the gut, a firm highly viscous polysaccharides/food matrix is induced causing the digestion process to be slowed and the area of absorption extended in the small intestine.

The strong capacity of PGX to capture and suspend nutrients (such as sugars, fat and carbohydrates) (Figure 3) is a key factor in the physiological benefits, especially postprandial (after meal) glucose lowering effects demonstrated in clinical trials.

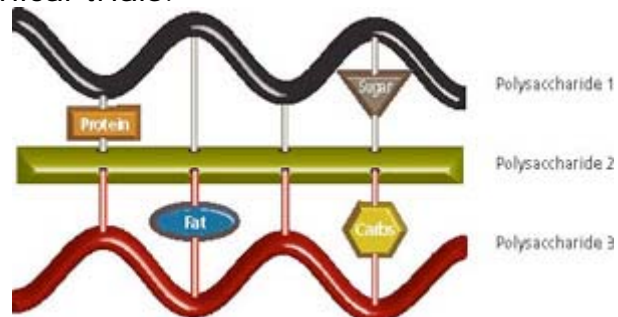


Figure 3: Trapping/strong holding capacity of macronutrients in the interlocking PGX matrix.

PGX has a significant growing body of evidence that has repeatedly shown a diverse array of evidence-based health indications such as cholesterol reduction, appetite and weight control, and diabetes control.

Reaching Peak Viscosity

Importantly, the viscosity of PGX develops slowly after mixing with water, achieving its maximum viscosity after 60 - 90 minutes. This means that when PGX is used in a meal replacement drink or sprinkled on food, it remains palatable when first mixed for a sufficient period of time for ease of consumption. It then develops its full viscosity, utilizing principles of IVT later in the stomach and small intestine, where it is then able to reduce

appetite, control blood glucose and insulin levels, and reduce blood lipid concentrations. As well, unlike many other fibres, PGX was developed to maintain its highly viscous properties under the influence of stomach acid and digestive enzymes.

In addition, due to its high viscosity, PGX slowly absorbs several hundred times its weight in water, resulting in a high volume food material that provides a lasting sense of fullness when ingested. Studies have shown that the volume a food creates exerts a sense of fullness in the stomach. This volume results in the release of various signaling gut hormones, which alert the brain that the stomach is full and that the person should stop eating. When PGX is taken before a meal or in a meal replacement, a sense of fullness and satiety quickly develops. At the *University of Toronto*, studies have shown that the ingestion of PGX is accompanied rapidly by effecting gut hormones in people with Type 2 diabetes, including GLP-1 and GIP, a sign that PGX provides a strong signal to stop eating. Later, when PGX reaches and is in the intestine, it remains highly volumetric and viscous. It is these properties that lead to a prolonged delay in the return of hunger feelings. Therefore, both its volume and viscosity may lead to significant reductions in appetite, creating a sense of satiety and making it easier for overweight individuals to cut back on caloric intake.

Clinical Evidence

Evidence-based information of blood lipids reduction, diabetes control, reduction of systolic blood pressure, improvement in colonic function, and appetite and weight control comes from clinical trials at the Risk Factor Modification Centre, St. Michael's Hospital and the *University of Toronto*. The early research involved a preliminary viscous polysaccharide blend (VPB) which has now been further developed into PGX for ease of human application. Its mechanism of action, however, remains the same and its proven health benefits continue to be supported*.

1 Glucose control: Impact on the Glycemic Index

A series of experiments were undertaken at the Glycemic Index Laboratories in Toronto, to support the blood glucose lowering potential of PGX². All experiments followed the methodology to determine glycemic index (GI). 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 (*Figure 4*). 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.

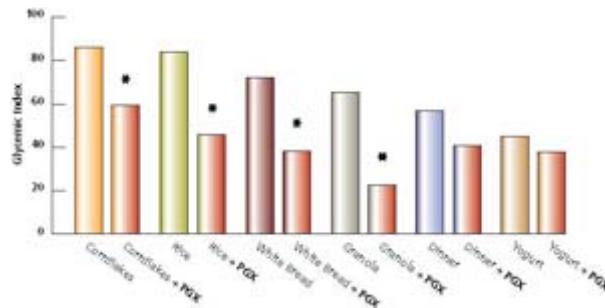


Figure 4: Reductions of the glycemic index when PGX is added or incorporated into commonly consumed foods². *Statistically different than food without PGX ($p < 0.001$)

2 Diabetes Control

Fructosamine Compared to placebo, VPB 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 weeks³. Although this early type 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 fibers 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 mellitus⁴.

3 Metabolic Syndrome

According to the most recent 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. 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 to help diminish the risk factors that characterize the syndrome. Studies done on PGX have been shown to reduce risk factors associated with the metabolic syndrome by 1) reducing waist circumference and most likely reducing intra-abdominal fat^{5, 6}; 2) lowering postprandial and fasting blood sugar levels^{2, 5, 7}; 3) lowering cholesterol^{7, 8}; and 4) improving insulin sensitivity⁶.

A study using VPB was conducted in individuals who suffer from the metabolic syndrome. The results showed that consumption of VPB, improved overall metabolic control by reducing insulin resistance in this population. This was evidenced by the reductions in total-cholesterol 12.4%, LDL cholesterol 22.3%, total/HDL-cholesterol 15.2%, LDL/HDL cholesterol 15%, and ApoB:ApoA 13.1%⁷. A change in glucose tolerance was also seen following meal consumption. The results showed that the area under the curve (AUC) for glycemia and insulinemia were significantly reduced with VPB compared to control with reductions in after meal blood glucose by 23% and insulin over 35%⁹ (*Figure 5 and 6*). These decreases translated into a significant increase in insulin sensitivity of about 50% after consumption of VPB. In addition, subjects in this study also lost significant amounts of body fat compared to control wheat bran diet, even though the body weight remained unchanged and no specific dietary advice was given to encourage weight loss during the three week clinical trial. It is concluded that prolonged consumption of VPB reduces body fat and improves insulin sensitivity in people with the metabolic syndrome.

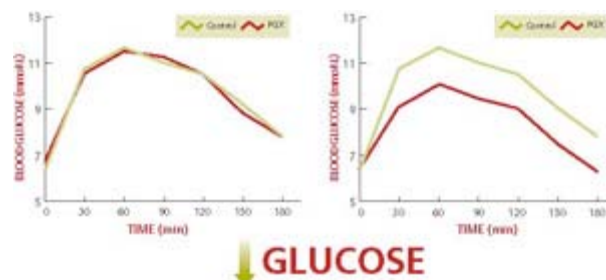


Figure 5: These graphs compare the changes in acute postprandial (after meal) glucose between those subjects who have been fed a standard dose of a non-viscous fibre (control group) and a similar group who were fed a standard dose of VPB for three weeks in a double blind, placebo controlled trial. After three weeks, the control group showed no improvement in glucose tolerance, whereas the VPB group had a significant improvement in postprandial (after meal) glucose tolerance⁹.

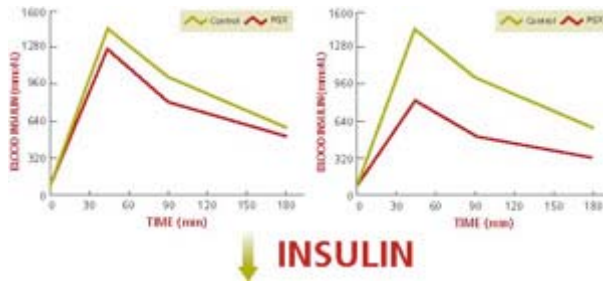


Figure 6: These graphs compare the changes in acute postprandial (after meal) insulin levels between those subjects who have been fed a standard dose of a non-viscous fibre (control group) and a similar group who were fed a standard dose of VPB for three weeks in a double blind, placebo controlled trial. After three weeks, the control group showed no improvement in after meal insulin levels (about double the normal values), whereas the VPB group had a significant reduction in postprandial (after meal) insulin levels⁹.

4 Cholesterol

Two studies showed that consumption of VPB significantly reduced total and LDL-cholesterol by up to 19% and 29% in individuals with Metabolic Syndrome or diabetes^{3, 7}. This effect could be compared with the cholesterol lowering effect of a modest dose of statin drugs. It is reasonable to say that the results achieved are “complementary to the effect of drugs”, since patients maintained their regular cholesterol medication dose throughout the study and VPB or wheat bran was added in addition to their dietary intake. Compared to the cholesterol lowering effects of major gel-forming fibres such as psyllium, oats, or guar¹⁰, VPB had a 3 to 5 fold greater effect, expressed as a change in cholesterol per gram of consumed soluble fibre⁶. It is believed that the quantity of VPB given in Vuksan’s 1999 and 2000 studies was beyond the patient’s physiological threshold, and that comparable results could likely be achieved with considerably less PGX^{®3, 7}. Justification for this is derived from a third long-term study (unpublished) in which low (wheat control), medium (psyllium) and high (viscous fibre blend, VPB) viscosity fibres were compared in regards to their lipid lowering effects in 22 healthy participants (12 male: 10 female, 34±11 yrs). It was found that total cholesterol was significantly reduced by 10.5% and LDL cholesterol by 15% with only 5 g of PGX[®] compared to 15 g of the control or psyllium¹¹. In addition, VPB increased the microflora in the colon (prebiotic effects), increased stool weight and transit time, and reduced methane excretion, with no significant gastrointestinal side effects. 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). It is important to note that the total cholesterol/HDL cholesterol ratio and the apolipoprotein A/B ratio on both studies (which are both associated with the insulin resistance syndrome) were also significantly reduced following the VPB intervention.

These types of effects are rarely seen in other polysaccharide studies in which the diet is simply low-fat and high-carbohydrate.

5 Weight Management

Obesity is a disease that arises through a multifaceted pathophysiology. Successful treatment of it thus requires a multi-strategic approach. It is hypothesized that consumption of PGX leads to multifaceted effects on weight loss and satiety in the human body including mechanical actions (e.g. stomach distention, delay gastric emptying), neural actions (e.g. gut derived satiety hormones), prebiotic mechanisms (formation of short chain fatty acids), and metabolic effects (e.g. carbohydrate and lipid metabolism).

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

Appetite and Food intake

When consumed, PGX utilizes the principles of IVT and 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 full⁴. Therefore, its volume and viscosity may make it easier for overweight individuals to cut back on caloric intake.

A clinical trial conducted at the *University of Toronto* supports the beneficial effects of polysaccharide viscosity as it relates to controlling food intake. *Breitman et al.* (2004) performed a randomized, double-blind, crossover placebo controlled trial to investigate the effects of 5 grams of cellulose (low-viscosity, 3000cps), glucomannans (medium-viscosity, 42000cps) and PGX (high viscosity, 70000cps) dietary fibres added to meal replacement drinks on appetite and food intake in 31 healthy weight adolescents. Ninety minutes after the preload drinks, subjects were provided pizza to consume ad-libitum. The amount eaten was used as an objective measure of appetite suppression. Those who drank the PGX-based meal replacement consumed the least amount of pizza ($p < 0.05$) compared to the low and medium viscosity drinks. Even though the PGX group consumed less, they did not compensate for the calorie deficit at their next meal¹².

PGX Weight Loss Programs

The effects of PGX as a weight loss aid has also been assessed in two open label weight loss programs conducted at the *Canadian Center 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 sedentary and overweight or obese adults. There was a significant reduction ($p < 0.05$) from week 0 or baseline in group weight (-13.0 pounds), waist circumference (-5.0 inches), and percent body fat (-2.5%). Moreover, these latter changes were paralleled by a significant decrease in total cholesterol (-18.0%), LDL (-25.0 %), fasting glucose (-7.0%) and insulin (-26.0%) levels over a relatively short time span of 14 weeks³. 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. The second program utilized a meal replacement with PGX and PGX granules on weight loss in overweight and obese adults over a 10 week period. From the patients that participated, there was an average reduction in group weight of 11 pounds and waist circumference of 2.5 inches. Most subjects reported that the meal replacement drink created a sense of satiety and completely controlled their hunger for 3 - 4 hours.

In addition, patients 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 figures below, 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.

The weight loss consistently experienced on the PGX Weight Loss Programs translates into a healthy weight loss of about 1-1.5 pounds per week.



Figure 7: 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 8: 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.

* (NOTE: The development of PGX[®] and its effects have been studied for over 15 years by head researchers Dr. Vuksan (Risk Factor Modification Centre, St. Michael's Hospital and University of Toronto, Toronto, ON) and Dr. Lyon (Canadian Center for Functional Medicine, Coquitlam, BC). The early research involved a preliminary viscous polysaccharide blend (VPB) which has now been further developed into PGX for ease of human application. Its mechanism of action, however, remains the same and its proven health benefits continue to be supported. Previous names of these prototypes in Dr. Vuksan's publications include: konjac-mannan, konjac-mannan polysaccharide mix, viscous fibre blend or viscous polysaccharide blend.)

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