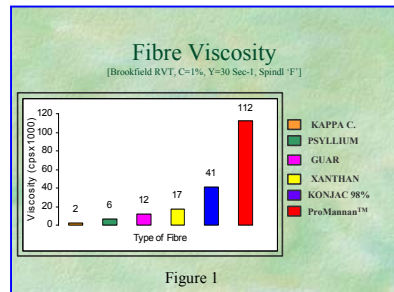
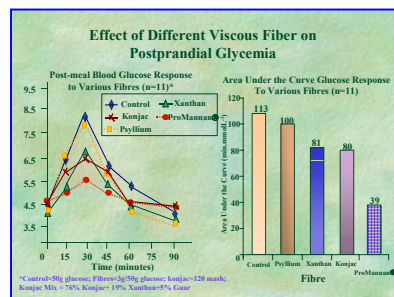


The Use of *Promannan*[®] to Regulate Human Health

Promannan[®] is a unique blend of carefully selected, highly viscous soluble fibers that act synergistically to develop a higher level of viscosity than any other viscous dietary fiber in the World, producing unparalleled physiological effects and health benefits. One of the main components (25-55%) of *Promannan*[®] is glucomannan, a glucose-mannose polysaccharide that is obtained from grinding the tuber root of *Amorphophalus Konjac C. Koch*, a plant that has been used as a food and remedy for thousands of years in the Far East. Highly refined and uniquely processed glucomannan possesses the greatest viscosity (gelling property) of all known dietary soluble fibers. It is 3-times more viscous than Guar, and approximately 7-times more viscous than Psyllium (Figure 1). The viscosity of *Promannan*[®] is amplified further with a viscosity 3-5 times higher than any glucomannan alone. This is paramount to its effects, as the viscosity of soluble fiber is directly related to its physiological effects and ultimately its overall health benefits in humans. Clinical studies support this relationship for *Promannan*[®]. We have repeatedly shown that



post-meal blood sugar levels, which are a major risk factor for heart disease, decrease as soluble fibre viscosity increases (Figure 2). This relationship has also been shown to hold true for improvements in insulin sensitivity, appetite, weight control, bowel movement, and serum cholesterol. The reductions in serum cholesterol are comparable to that shown with the best lipid lowering medications and 3-5 times that of any other viscous fiber. This impressive combination of effects led the American Dietetic Association to recognize *Promannan*[®] as one the first “evidence-based” dietary fibers (*J Am Dietetic Association*, July 2002). This strong support puts *Promannan*[®] in a unique position to meet the weight of scientific agreement required to qualify for a FDA “structure-function claim” by their revised (December 2002) labeling and health claim standards.



The secret to *Promannan*[®]'s superior viscosity and resultant physiological effects is in the blend. The best selected glucomannan is blended with common polysaccharides (soluble fibers) such as Xanthan, Carragenan, Acetan, Guar, and/or Xyloglucan to produce *Promannan*[®]. This process increases the viscosity of the original glucomannan material multiplicatively by 3 to 5 times. This highly viscous blend of glucomannan with other fibers is called *Promannan*[®]. We hold the patent (pending) for *Promannan*[®]'s structure (the fiber blend) and its health application (improvement of postprandial sugar, insulinemia, blood cholesterol, Syndrome-X and other heart disease risk factors [Figures 2 and 3]).

The additional benefits of using *Promannan*[®] as opposed to glucomannan alone are: (1) *Promannan*[®] can be given at much smaller quantities than other viscous dietary fibers to achieve comparable health benefits; (2) *Promannan*[®] results in less gastro-intestinal side effects than other viscous dietary fibers, and (3) *Promannan*[®] is technologically easier to incorporate into food products and/or supplements than other viscous dietary fibers. These added benefits make *Promannan*[®] one of the only viscous dietary fibers that can be taken in supplement dosages and yield powerful physiological effects.

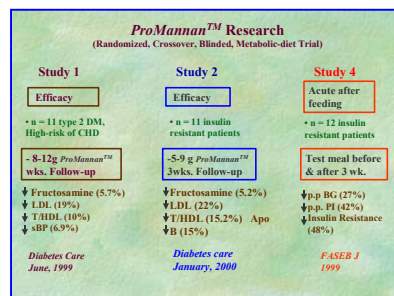


Figure 3

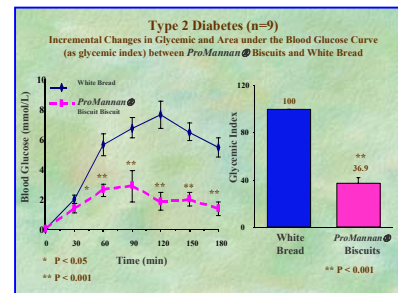
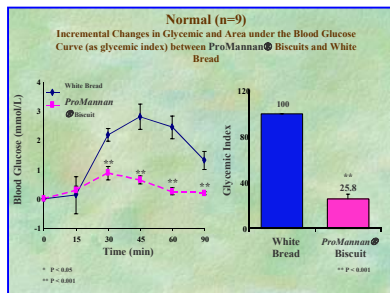
Promannan® is Clinically Proven

Over the last 10 years we at the Risk Factor Modification, St. Michael's Hospital, Faculty of Medicine, University of Toronto, have tested **Promannan®** in numerous acute and long-term clinical studies (**Figure 3**).

The Clinically Proven Effects of Promannan®:

- A. Reduces postprandial (after-meal) Glycemia (“Slow release” carbohydrate)
- B. Improves diabetes control (ADA: fiber supplement recommended for long-term diabetes control)
- C. Lowers blood cholesterol (“Drug-like” effect)
- D. Lowers blood pressure (Effects rarely seen with fiber)
- E. Suppresses appetite and reduces body weight (Multi-impact effect: 4-fold)
- F. Increases insulin sensitivity (Treatment and prevention of syndrome-X)
- G. Improves syndrome-X (Unique effect - presently no treatment available)

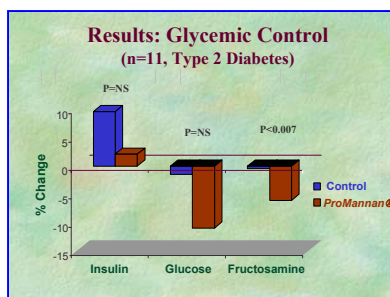
A. Reduction of Postprandial Glycemia (“Slow release” Carbohydrate)



In an acute study using **Promannan®**, we assessed the effect of 3g of **Promannan®** biscuits on glycemic response in a group of 9 healthy individuals (age=31±7, BMI=24±2), and 9 type 2 diabetic individuals (age of 59±7, BMI of 28±4, and HbA1C of 7.1±1%), comparing them to the same quantity of carbohydrate from white bread. The glycemic index of **Promannan®** biscuits equaled 25.8±7 and 36.9±8 in healthy and diabetic individuals, respectively. This exceptional reduction in postprandial glucose offers great potential for the long-term use of **Promannan®** in diabetes management.

Suggested use: Hyper- and hypoglycemia, Syndrome-X, sports & military nutrition, appetite control.

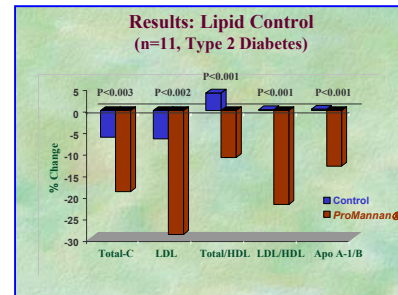
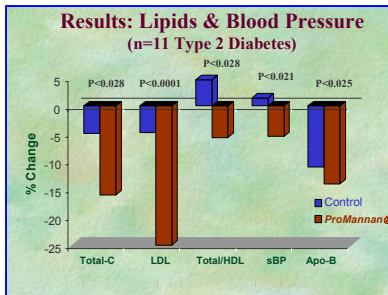
B. Diabetes control (Recommended by the American Dietetic Association)



Compared to placebo, **Promannan®** 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 **Promannan®** or placebo for 3 weeks (*Diabetes Care*, June 1999). Although **Promannan®** mildly improved glycemic control, the reduction was comparable to that found with the oral hypoglycemic agent such *Acarbose (Bayer, Germany)*.

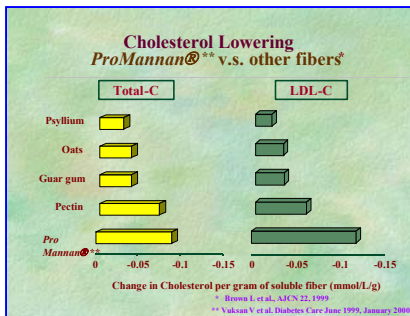
Suggested use: High-risk CHD individuals, effect beyond conventional treatment, adjunct to conventional therapies.

C. Exceptional lowering of Blood Cholesterol: (“Drug-like” effect)



In two studies (*Diabetes Care*, June 1999 and *Diabetes Care*, January 2000) we showed that **Promannan**[®] feeding significantly reduced total- and LDL-cholesterol by up to 19% and 29% in individuals with syndrome X or diabetes. This effect could be compared with the cholesterol lowering effect of a modest dose of the best cholesterol lowering medication (Statins drugs). It is reasonable to say that the results achieved are “*beyond effect of drugs*” since patients were kept on their regular cholesterol lowering medication throughout the entire length of the study.

Compared to the cholesterol lowering effects of major gel-forming fibers such as Psyllium, Oats, or Guar as reported by Brown et al. (1999), **Promannan**[®] has a 3 to 5 fold greater effect, expressed as a change in cholesterol per gram of consumed soluble fibre. It is important to mention that in the studies with **Promannan**[®], that we conducted subjects were at a very high risk for cardiovascular disease, and were being aggressively treated with cholesterol lowering medications. Also, we believe that the quantity of **Promannan**[®] given on our two studies was beyond the patient’s physiological threshold, and that comparable results could likely be achieved with considerably less **Promannan**[®]. Justification for this is derived from the results of our 3rd long-term study (unpublished) in which we compared Psyllium and **Promannan**[®] of an identical viscosity in mildly hypercholesterolemic subjects (typical North American population). We found that cholesterol was significantly



reduced using less than 3g of **Promannan**[®] compared to 17g of *Psyllium*. *Psyllium* did not show significant cholesterol lowering effects. One of the findings of the study was that **Promannan**[®] affected the microflora in the colon (*Probiotic effects*), increased short chain fatty acid (SCFA) generation (especially the cholesterol-lowering SCFA propionate), and resulted in significant excretion of bile acid through the stool (i.e. removing fat from the body).

It is important to mention 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 **Promannan**[®] intervention. These types of

effects are rarely seen in other fiber studies in which the background diet is simply low-fat and high-carbohydrate.

Suggested Use: Cholesterol-lowering in otherwise healthy, diabetic, and Syndrome-X individuals, on medication or drug-naïve individuals. It could also be used for control of appetite and reduction in body fat composition.

D. Improvement in Acute and Long-term Blood Pressure (Rarely seen effects)

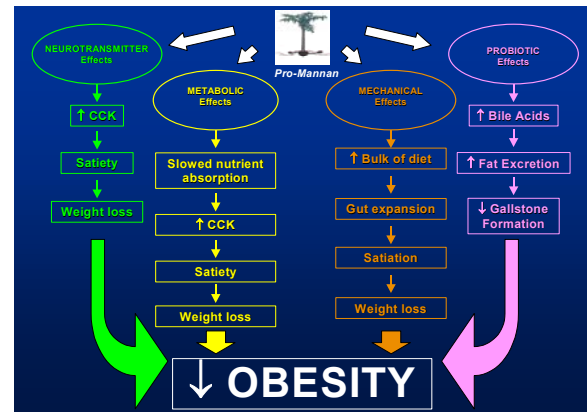
Systolic blood pressure was significantly reduced by 8 mm Hg. Please see Figure above from *Diabetes Care*, June 1999 study. Recently, an acute clinical study conducted in 13 Type 2 diabetic individuals showed that *Promannan*® significantly reduced blood pressure over a 6-hr period.

E. Control of Appetite and Obesity (Multi-impact Effect)

***Promannan*® & Obesity:** Obesity is a disease that arises through a multifaceted pathophysiology. Successful treatment of it thus requires a multi-strategic approach. Based on our clinical experience, *Promannan*® could serve as a potential agent in the long-term treatment of obesity. Support for this bold statement primarily extends from our finding that *Promannan*® is a powerful appetite suppressant. What makes *Promannan*® such an effective appetite suppressant is its unique inhibition of **FOUR PATHWAYS** that regulate food intake. These include:

- 1) the metabolic pathway,
- 2) the mechanical pathway,
- 3) the probiotic pathway, and
- 4) the neurotransmitter pathway

Each pathway is critically important for body weight regulation. Accordingly, inhibition of each will lead to profound appetite suppression. The ability of *Promannan*® to do so makes it the most powerful fibre-based material for weight loss. Additionally, *Promannan*® can exert this physiological effect when administered in very small quantities, such as in the form of a supplement. Just 2 to 3 grams of *Promannan*® per day is sufficient to significantly suppress appetite, and consequently food intake.

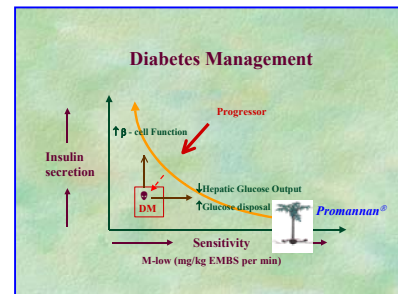
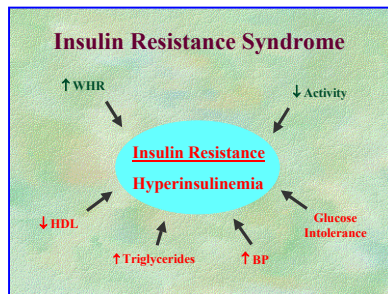


1. **METABOLIC EFFECTS** of *Promannan*® include unparalleled reductions in after-meal blood sugar and insulin, plasma counter-regulatory hormones (growth hormone and cortisol), as well as serum triglycerides and free fatty acids, all of which are highly correlated to appetite control. Also, due to its “*slow release properties*”, *Promannan*® significantly reduces the craving for food.
2. **MECHANICAL EFFECTS** of *Promannan*® include its acid-resistant, gel-forming property, which causes *Promannan*® to expand in the stomach and hold more than 600 times of water and digestive juices, including nutrients. This produces a strong feeling of fullness, which is prolonged due to the firmness and nonreversible expansion of the gel.
3. **NEUROTRANSMITTER EFFECTS** of *Promannan*® are mediated by its “*slow release properties*” which cause a prolonged and sustained secretion of CCK, the appetite suppression hormone. The consequent satiation is equivalent to that produced from the intake of large amounts of calorie-dense foods, such as high-fat foods.
4. **PROBIOTIC EFFECTS** include the secretion of short chain fatty acids such as propionate, which induce the production of bifidobacteria, lower the stool pH, and also increase the excretion of bile acids. By increasing bile acid production, *Promannan*® increases the excretion of fat (cholesterol & triglycerides) through the stool. It does so much more effectively than does chitosan. *Promannan*® also improves bowel movement, which tends to decrease in weight-loss programs due to the lower consumption of food.

Suggested Use: Appetite control, weight reduction and weight maintenance in overweight healthy, diabetic, and Syndrome-X individuals, which are drug-naïve or on medication. We created a version of *Promannan*® called *PoundMan*®, which are an integral part and the main ingredient of a **Multi-Impact® Weight Loss Formula**.

F. Increase in Insulin Sensitivity (Treatment & prevention of Syndrome-X)

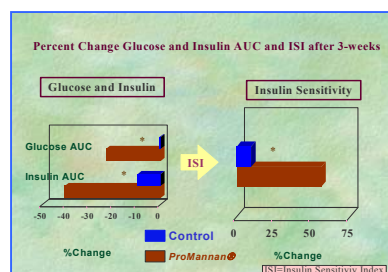
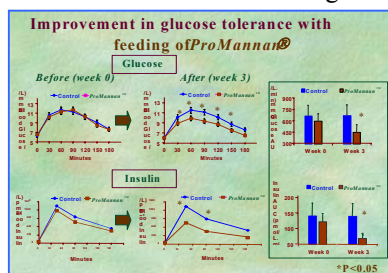
We conducted a study in individuals who suffered from Syndrome-X, a deranged metabolic condition that precedes the onset of type 2 diabetes (it is characterized by dyslipidemia, impaired sugar metabolism, high blood pressure and abdominal obesity). The results (published in *Diabetes Care*, January 2000) showed that Syndrome-X patients who consumed **Promannan**[®] considerably improved their overall metabolic control by reducing resistance of insulin. 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%). There was also an improvement in long term sugar metabolism (~5% decrease in serum Fructosamine).



Suggested Use: **Promannan**[®] is the only fibre to show improved metabolic control in individuals with Syndrome-X. According to the most recent data from the US, approximately 28 million adult Americans are suffering from Syndrome-X or pre-diabetes, and majority of them will progress to full-blown diabetes within the years to come.

G. Chronic Feeding of **Promannan**[®] Improves Insulin Sensitivity in Individuals with Syndrome-X: (Unique Effect - No Treatment Available)

The top figure below shows changes in glucose (sugar) tolerance to a test meal prior to and after 3 weeks of **Promannan**[®] enriched cookies (dark red) or wheat bran-cookie (blue) feeding. The upper panel on the left shows the incremental blood glucose results before **Promannan**[®] or wheat bran biscuits. On the far right is the area under the glucose curves (AUC) for **Promannan**[®] and control breakfasts. On the lower panel plasma insulin values are presented in the same manner as described above. From the graph presented, it is obvious that after 3 weeks of **Promannan**[®] feeding there were reductions in blood glucose (sugar) by 20% and blood insulin by 40%; as a result, the whole body insulin sensitivity index (ISI) was improved by approximately 50%.



The improvement in the whole body insulin sensitivity index (Matsuda & De Fronzo, 1999) confirms the sparing effects of **Promannan**[®] on insulin, indicating that insulin sensitivity was improved and insulin resistance was decreased (“*insulin economy*”- lower sugar concentration with less insulin secreted).

Suggested use: Individuals suffering from Syndrome-X who want to prevent the onset of diabetes. Also, individuals suffering from lack of insulin sensitivity such as obese persons can use it too. Use of **Promannan**[®] can assist them in control of their body weight.

SUMMARY: Overall Health Benefits of *ProMannan*®

When *ProMannan*® is added to the diet of individuals who have one or more of the following:

- (1) Elevated Serum Cholesterol
- (2) Normal or elevated body weight,
- (3) Type 2 diabetes, or
- (4) Syndrome-X (Insulin resistance)

and they are either drug naïve or are taking conventional medications, it results in clinically-proven, significant improvements in metabolic control. This means that *ProMannan*® feeding causes reductions in the levels of major risk factors associated with heart disease, diabetes, and obesity. As such, it could be offered as a novel therapeutic agent or a new preventive or therapeutic agent against any of these conditions or diseases in a population at increased health risk.

