Effect of Palatable Soluble Fibre-Containing Carbohydrate Foods on Postprandial Blood Glucose Response in Healthy Individuals

Master of Science Thesis by

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Effect of Palatable Soluble Fibre-Containing Carbohydrate Foods on Postprandial Blood Glucose Response in Healthy Individuals

Master of Science Thesis (60 ECTS)

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This thesis represents the final work of my Master degree in Molecular nutrition and food technology at Aarhus University, Denmark. The experiment work was done in Toronto, Canada between September 2015 – March 2016 at Risk Factor Modification Center at St. Michael Hospital, Toronto. The supervisor that guide me through my work and make it possible for me to expand my knowledge in Canada is Associate Professor, PhD, Per Bendix Jeppesen. In Toronto I was guided by co-supervisor Dr. MD Vladimr Vuksan.

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This thesis consists of two parts:

1) Review on diabetes and effect of viscous soluble dietary fibre on glycaemia.

2) Scientific paper regarding my study performed in Toronto, entitle:

Effect of Palatable Soluble fibre-Containing Carbohydrate Foods on Postprandial Blood Glucose Response in Healthy Individuals: A Randomized, Controlled, Double-blinded Study

By Vladimir Vuksan, Taja Karner, Amanda Ma, Elena Jovanovski, Fei Au Yeung
ADA: American Diabetic Association
AUC: Area under the curve
BMI: Body mass index
CHO: Carbohydrates
CVD: Cardiovascular disease
FFA: Free fatty acids
GI: Glycemic index
GLUT: Glucose transporter proteins
GM: Glucomannan
IRS: Insulin receptor substrate
ISF: Insoluble fibre
LADA: Latent Autoimmune Diabetes in Adults
MS: Metabolic syndrome
NEFA: Non-esterified fatty acid, equal to FFA: Free fatty acid
PGX: PolyGlycompleX
SCFA: Short-chain fatty acid
SF: Soluble fibre
T1D: Type 1 Diabetes
T2D: Type 2 Diabetes
VFB: Viscous fibre blend
VSF: Viscous soluble fibre
WG: Whole grain
WHO: World Health Organization
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ABSTRACT

Background: Increase of dietary fibre intake and improvement of postprandial glucose response could be achieved with fibre-enriched carbohydrate products. To evaluate PGX fibre’s incorporation, sensory assessment for palatability and effect on post-prandial glycemic response of enriched products was observed in healthy individuals.

Methods: The study consisted of two phases. Phase I: twenty-one healthy individuals (mean ± SEM, age: 25.2 ± 9 years, body mass index [BMI]: 22.5 ± 2.4 kg/m²) assessed palatability difference between control and treatment products using sensory evaluation questionnaires. Phase II: twenty healthy participants (mean ± SEM, age: 26.3 ± 10 years, BMI: 22.4 ± 3.6 kg/m²) were randomized to receive white bread, muffins, mashed potatoes and cream of wheat after overnight fasting on eight separate occasions. All products consisted of 50 g of available carbohydrates and were either implemented with 4 g of PGX or used as control. Blood glucose samples and satiety ratings were collected at fasting and over 2 hours postprandial.

Results: Incorporation of PGX results in no decrease in palatability for 3 out of 4 food products. There was no significant reduction in iAUC for any of the product separately, however a significant reduction was observed in pooled non-baked products, mashed potatoes and cream of wheat, compared to control attributes. Peak rises in glucose concentrations were significantly lower for treatment products compared with their refined counterparts.

Conclusions: Addition of VFB to different food matrices must be considered and evaluated on individual basis before any conclusions can be formed on its glycaemia reducing potential.
INTRODUCTION

At one hand the general quality of life in past decades is increasing with technology improvement, but on the other hand we are facing a very concern increase of chronic diseases globally. Lifestyle changes that include decrease of physical activity and increased consumption of highly processed food have been reflected in many metabolic dysfunctions known by the term metabolic syndrome (MS) (WHO 2003). MS is highly connected to the risk of developing type 2 diabetes (T2D) and cardiovascular disease (CVD) that are two dominantly chronic diseases nowadays (Singh et al. 2013). T2D is one of the diseases with the hugest increase in incidents in the past decades (Ezzati 2016). The prevalence for T2D was firstly connected to developed countries, however in the last decade much faster growth of incidents of T2D is observed in developing countries (World Health Organization 2016). Even though T2D used to be recognized as disease of elder population, it is now present also among children (Dabelea 2009).

Even though T2D is associated with genetic predisposition, environment factors and lifestyle play significant role and offer effective approaches to prevent from its development (Lam & LeRoith 2012). However, the approaches are very general and include taking care for overall health with regular exercise, healthy food, avoiding smoking and having blood pressure and lipid level in desirable range (World Health Organization 2016). The main recommendations of World Health Organization for preventing T2D and its complications include having sufficient dietary fibre (DF) intake with consumption of whole grains (WG), legumes, vegetables and fruits and limited intake of saturated fat and sugar to below 10 % of daily caloric intake, separately (Ahmad et al. 2001). However, despite the recommendations dietary fibre intake remain lower than desirable (Association 2008).

Due to modern lifestyle people find recommendation hard to follow, therefore a lot of effort is put into seeking of new solutions to help people maintain overall health. Addition of fibre into different food products has been a practice for decades, however most of the products are enriched with insoluble fibre which do not offer desirable lowering of postprandial blood glucose that has been recognized as crucial parameter in diabetes control (Frontoni et al. 2011).
Moreover, most of fibre-enriched products are associated with decrease of palatability, therefore refined products, despite awareness of low nutritional value, remain general preference (Association 2008). Understanding of physicochemical properties of different fibre and their effects on glucose metabolism is a promising way to improve food products available on the market (Guillon & Champ 2000). Previous results have shown that the most significant reduction of postprandial glycaemia of carbohydrate foods can be achieved with viscous soluble fibre implementation (Jenkins et al. 1978). However, high viscosity does reflect in reduced palatability and therefore ways of implementing viscous soluble fibre in commonly consumed food without affecting their palatability are still sought. The aim of this master thesis is to evaluate previous studies on how viscous soluble fibre can improve post-prandial glycaemia and help to control blood glucose level and how their incorporation in food products can influence dietary fibre intake and improve diabetes rates.
1. DIABETES

1.1. Epidemiology of diabetes

Diabetes is consider to be the most represented endocrine chronic disease in the world (J. E. Shaw et al. 2010). In 1980 there were 108 million reported diabetic people in the world, whereas in 2014 this number has increase up to 422 million. The increase rate correspond to the rise from 5.7 % to 8.5 % adult population having diabetes (World Health Organization 2016). Type 2 diabetes is the most common type of diabetes and contribute to around 90 % of all diagnosed diabetes cases worldwide and to 80 % of all diabetic patients in Denmark (J.E. Shaw et al. 2010). It’s well established that the cause of the defect is a combination of genetic predisposition and environmental factors. In a contrast to type 1 diabetes (T1D) where a genetic predisposition plays a critical role, T2D is more related to many environmental factors and therefore easier to prevent (Scheen 2003). In case of T1D, autoimmune response of a body reflects in disruption of pancreatic beta-cells and it is being cured with insulin substitution. It occurs in childhood and progress through years (Drouin et al. 2009). It was assumed that only two forms of diabetes exist, however there are other less common forms. One of them is type 1 ½ diabetes or LADA (Latent Autoimmune Diabetes in Adults) that occurs in adult ages but have the same main characteristics as T1D (Fourlanos et al. 2005). It is an autoimmune disease and it needs an insulin supply which usually has to be increased over years. The fourth type is called gestational diabetes and can occur during pregnancy of overweight or obese women (Buchanan & Xiang 2005; Jensen et al. 1999). Abdominal fat cause decrease of insulin sensitivity which can be harmful for fetus if not controlled with healthier lifestyle or in some cases even insulin is needed (Langer et al. 2005). The main focus of this background is going to be T2D since it is the most common and preventable with dietary changes like increasing fibre consumption.
1.2. Type 2 diabetes

Type 2 diabetes is a complex chronic condition when insufficient insulin production as well as insulin sensitivity leads to increase of blood glucose levels (Kahn 2003). T2D is a disease that does not occur overnight and cannot be linked to one particular dysfunction in the body. At the point of diagnosis, most of the abnormalities are usually already present, therefore the primary cause is hard to establish. Its progression is slow and often pre-diabetic phase, an intermediate hyperglycemia stage, can last couple of decades before the full-blown diabetes occur (Saini 2010; The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus 2003). The diagnosis of T2D have to be done on two separate occasions and include fasting levels of plasma glucose at or above 7 mmol/L or if symptoms as weight loss and polyuria are present and casual plasma glucose concentration exceeded 11.1 mmol/L is consider as T2D marker (Fonseca 2009).

Due to its complexity the pathogenesis of T2D had been a debate for decades. Various disruptions of endocrine pancreas, liver, skeletal muscle, adipose tissue, central nervous system and guts may effect glucose metabolism and cause T2D if not treated preliminary (DEFRONZO 1988). Symptoms that may lead to T2D if not treated have been marked as metabolic syndrome and include obesity, hypertension, dyslipidemia, cardiovascular dysfunctions and coronary artery disease (Scheen 2003). Since most of the people with T2D suffer from obesity, visceral fat adipose tissues most possible play a crucial role in disruption of glucose homeostasis by elevating insulin resistance in both hepatic and muscular tissues (Kahn et al. 2006). Insufficient insulin sensitivity cause hyperglycemia and increase lipid formation, which leads in overproduction of insulin and potentially to failure of pancreas. Even though there are drugs that trigger insulin sensitivity, losing weight, increasing physical activity and avoiding glucose elevation with healthy diet have been more effective way to control and avoid preliminary consequences of T2D (World Health Organization 2016). For easier understanding of the mechanism behind T2D, glucose metabolism has to be discussed.
1.3. Overview of glucose metabolism

Glucose is the primary source of energy for all the cells in our body, therefore the mechanism of regulating the amount of glucose available in plasma is very well controlled. The main hormones that control glucose level are insulin and glucagon that are secreted from pancreas (Zierler 1999). Pancreas is crucial organ in glucose metabolism and has an important endocrine as well as digestive function. Human pancreas consists of approximately 1 million islets of Langerhans that are producing and secreting hormones to regulate the behavior of body cells and play a critical role in providing energy for all the cells in human body. Out of around 3000 cells that builds one islets, 48-59 % are beta-cells and 33-46 % alpha-cell that have the major endocrine function in glucose metabolism (Cabrera et al. 2006). After meal consumption the blood glucose level increase depending on the amount and type of carbohydrates consumed and the presence of fat and proteins in the meal (Jenkins et al. 1981). After insulin is secreted, the phosphorylation cascade occurs, with IRS phosphorylation and initiation of PI3K-AKT pathway that cause the glucose uptake in the cell. Furthermore, intracellular glucose transporter type 4 (GLUT-4) with its translocation to the outer cell membrane enables the muscle and adipose tissue to uptake the glucose and store it as glycogen (Saltiel & Kahn 2001). The absorption of glucose through gut wall is enabled with glucose transporter proteins (GLUT-2) that transport it into beta-cells. That reflects in series of reactions that increase ATP/ADP ratio and enclosed ATP-regulated K⁺ channels which leads to depolarization of plasma membrane and increase of cytosolic free Ca²⁺ (Henquin 2004). This stimulates insulin secretion from beta-cells that is further transported to liver and to the bloodstream where it is recognized by insulin receptors on the surface of the cells. Receptors has to be previously activated with insulin receptor substrate-1 (IRS-1), the key signaling molecule that induce glucose intake which reflect in lowering blood glucose concentration (Choi & Kim 2010). In muscle and liver cells the glucose is used for short-term energy storage as a form of glycogen, the adipose tissue take the glucose from plasma and transform it to fat as a long-term energy reserve, whereas other cells break down the glucose to ATP via glycolysis and Krebs cycle and use the energy for protein synthesis and other cells functions (Saltiel & Kahn 2001). Insulin secretion also influences the uptake of fatty acids (FA) and amino acids (AA) and suppress production of glucagon (Zierler 1999). Glucagon is a hormone with opposite function of insulin is called glucagon and is secreted when blood glucose level has
fallen and needs to be increased. In this situation, glucagon stimulates glycogen break down to glucose (gluconeogenesis) so that it is available for other cells to use it (Exton 1972).

1.4. Pathophysiology of T2D

1.4.1. Abdominal obesity

The main classification of obese people include their Body mass index (BMI) ≥ 30 kg/m² that is calculated as body weight divided by squared height in meters. However, this classification does not take into consideration where the extra fat is stored. It has been established that vascular fat accumulated at intra-abdominal cause major complications correlated with obesity, whereas subcutaneous fat is not so critical (Carr et al. 2004). To evaluate the risk for T2D diabetes the ratio between waist and height also needs to be consider (Ashwell et al. 2012). Abdominal obesity reflect in increase secretion of non-esterified fatty acids (also referred as free fatty acids - FFA) and various other pro-inflammatory molecules as leptin, tumor necrosis factor (TNF)-α, resistin, adiponectin etc. that influence glucose metabolism and potentially lead to insulin resistance as shown on Figure 1 (Montague & O’Rahilly 2000; Kahn et al. 2006). Even though abdominal fat was shown to lead to inflammation in the body, lipotoxification and overactive intravascular coagulation factors, clear correlations between obesity and developing of T2D have not been shown (Kahn et al. 2006).
1.4.2. Insulin resistance

Even though clear mechanism of how obesity contribute to insulin resistance is not totally clarified, it is well established that it is connected to abnormal secretion of free fatty acids from hypertrophied adipocyte tissue and that both are the major factor in developing T2D (Kahn et al. 2006). As mention before, production of FFA is increased in overweight people and it reflects in abnormalities in insulin-signaling pathway as shown on Figure 2. The recent hypothesis for insulin resistance as shown on Figure 2 include the act of intracellular FFA on activation of serine/threonine kinase cascade which leads to IRS-1 phosphorylation (Shulman 2004). These inactivate IRS-1 even though the insulin is present and consequently PI3K does not activate glucose transportation in the cell. Based on this hypothesis, any exceeded level of FFA in intracellular space can eventually lead to insulin resistance of muscle and liver cells and induce hyperglycemia (Shulman 2004). Moreover, many signaling and pro-inflammatory molecules like TNF-α and interleukin-6 (IL-6) were suggested to influence the same pathway but in different steps (Gao et al. 2002). To conclude, insulin resistance is complex state that is caused by excess rate of FFA in intracellular space and overproduction of pro-inflammatory cytokines by macrophages and contribute to decrease of fatty acid oxidation that leads to lipotoxicity.
Figure 2: Mechanism of impaired insulin sensitivity by exceeded intra-cellular FFA concentrations. Adopted from Shulman (Shulman 2004).

1.4.3. Hyperglycemia

In normal conditions, increase of glucose in blood stream induces the production and secretion of insulin by pancreatic beta-cells that stimulate muscle, liver and adipose tissues in glucose uptake. In case of insulin resistance, the phosphorylation cascade stops at any of the previously mentioned steps and therefore excess glucose remain in the blood stream (hyperglycemia) (Saltiel & Kahn 2001). Many studies have demonstrated that defects in muscle glycogen synthesis play crucial role in lowering insulin sensitivity, since this shows up to be the major pathway for glucose metabolism in the condition of hyperglycemia and hyperinsulinemia (Shulman 2004). As shown on Figure 3, impaired muscle insulin sensitivity reflects in inactive GLUT-4 transporter and consequently reduction of muscles cells ability of glucose uptake (Samuel et al. 2010). Often hepatic gluconeogenesis is also not suppressed which lead to additional elevation of glucose concentration. In the developing stages of T2D, insulin sensitivity is reduced and for some period the body is still able to maintain normal glucose level, however over time insulin sensitivity drastically decrease if not treated and lead to hyperglycemia. Since the insulin is not efficient, the beta-cells keeps producing high amount of insulin which over time leads to beta-cells dysfunction. Both lipotoxicity and hyperglycemia are correlated with decrease of beta-cell mass and further complications of diabetes (Reaven 1988).
Figure 3: Comparison of muscle glucose mechanism in normal cells (left) and in the case of insulin resistance (right). Adopted from Samuel et al (Samuel et al. 2010).

Important mechanism for developing T2D is related also to dyslipidemia, which is defined as either overly increased level of triglycerides (TG) or decreased level of HDL-cholesterol but it is not going to be discussed in this master thesis (Scheen 2003).

All mentioned mechanism defects occur in variable proportions in patients with T2D and their degree of complication can improve over time if lifestyle changes are taking into account, otherwise the dysfunction of mechanism increase with disease progression (Scheen 2003). One of the lifestyle changes that is recommended by major health agencies and government bodies is the increase of dietary fibre consumption (Ahmad et al. 2001). Its correlation to T2D prevention and future opportunities for increasing their consumption are discussed in the next chapters.
2. CARBOHYDRATES

Carbohydrates (CHO) are the most consumed macronutrients globally and contribute to 40 – 80 % of daily caloric intake, where lower range are referred to developed and higher to developing countries (Burton et al. 2011). Since T2D is directly connection to carbohydrate metabolism, it was a debate for decades whether different type of carbohydrates play a role in preventing or causing defects in glucose metabolism. Studies had shown that type of dietary carbohydrates and their quantity are both critical in causing obesity and other contributed chronic disease as T2D and cardiovascular dysfunction (Mann et al. 2007). Increase of T2D over the years was correlated with increase consumption of refined carbohydrates depleted in fibre that brought out the hypothesis that dietary fibre may be an important parameter in blood glucose control (Mokdad et al. 2003). Those suggestions accelerated researchers to investigate carbohydrates metabolism and it was in 1981 that Jenkins et al introduced the use of glycemic index (GI) to classify different carbohydrate foods (Jenkins et al. 1981). GI represents the percentage of glucose that appear in bloodstream after meal consumption compared to the reference meal which is usually glucose solution or white bread. It’s calculated as a ratio between area under the curve (AUC) of a given meal divided by AUC of a reference with same amount of available CHO (Jenkins et al. 1981). The most significant factor that influence glucose availability is the content of dietary fibre which tend to impede the hydrolysis of carbohydrates in small intestinal and may decrease the diffusion rate of hydrolytic glucose throughout the gut lumen (D. J. A. Jenkins et al. 1987). Its effect depends on the type and quantity of fibre, however the overall effect of fibre on GI cannot be assumed only by fibre characteristic since it depends on many circumstances that are addressed in the next sections (Jenkins et al. 1981).
3. DIETARY FIBRE

3.1. Definition

Even though the term dietary fibre is in use for more than 50 years, its definition has been a discussion for decades. Most recent CODEX definition classifies dietary fibre as:

“Dietary fibre means carbohydrate polymers with ten or more monomeric units, which are not hydrolysed by the endogenous enzymes in the small intestine of humans and belong to the following categories’:

— edible carbohydrate polymers naturally occurring in the food as consumed,

— carbohydrate polymers, which have been obtained from food raw material by physical, enzymatic or chemical means and which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities,

— synthetic carbohydrate polymers which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities

Footnote 1: When derived from a plant origin, dietary fibre may include fractions of lignin and/or other compounds associated with polysaccharides in the plant cell walls. These compounds also may be measured by certain analytical method(s) for dietary fibre.”

Footnote 2: “Decision on whether to include carbohydrates of 3 to 9 monomeric units should be left up to national authorities.” (Jones 2014)

In this definition are therefore included cell wall polysaccharides, lignin, resistant starch molecules and other minor components that have been shown to have beneficial physiological effects (Mongeau & Brooks 2016). The composition and their benefits on human health differ from its origin and physiological properties (Otles & Ozgoz 2014).

3.2. Dietary fibre classifications

To understand and predict how specific fibre influence consumers’ health many things have to be consider. Due to huge variety of fibre as part of human diet, it is not possible to link
them to specific physiological effect without specifying and classifying them into different groups (Lattimer & Haub 2010). Most standard classification of DF is based on their solubility, even though it’s mainly focused on fibre’ chemical properties and does not help with understanding of physiological responses (Flamm et al. 2001). Firstly, it’s should be acknowledged that the degree of solubility in water may be different than in gastrointestinal tract due to different physical conditions (Guillon & Champ 2000). Moreover, some of the DF might be soluble in saliva but not in acidic conditions present in stomach (e.g. pectins) (Wanders et al. 2014). It was long believed that soluble fibre (SF) were not common in consumed foods but they do contribute to one third of total daily fibre intake (Mongeau & Brooks 2016). SF are dissolved in water and are able to form gels which makes them slowly passing through small intestine and highly-fermented in large intestine. On the other hand, insoluble fibre (ISF) cannot be dissolved in human gastrointestinal track and they act like bulking agent, but can only be fermented by bacteria to limited extend (Wong & Jenkins 2007).

More important parameters that bring us closer to understanding of DF’s health effect are physicochemical properties of fibre like viscosity and fermentability. Viscous soluble fibre (VSF) are able to thicken and have gelling properties when mixed with fluids, which as suggested can slow down gastric emptying and absorption of nutrients in small intestine. The most researched VSF are gums, pectins, beta-glucans and Konjac Glucomannan. Degree of gelling capacity depend on their chemical composition as well as food preparation (Schneeman 1998; Dikeman & Fahey 2006).

The extent of fermentability depends on fibre properties, but it’s assumed that 70-80 % of total DF intake are fermented, including ISF that has long been assumed to not be fermented at all (Mongeau & Brooks 2016). Fibre that are easily fermented are increasing production of short chain fatty acids (SCFAs) that have been linked to many health benefits. Whereas, fibre that are fermented slowly or cannot be fermented completely act like bulking agent that are beneficial for laxation and increasing stool weight (Schneeman 1998).
3.3. Dietary fibre and food processing

After understanding classification of fibre that are based on their chemical composition and structural characteristic, one also have to take into consider food processing practices (Guillon & Champ 2000). As soon as the origin food is changed, the properties of DF content might be influenced. Heat treatment is a process that can break down glycoside bonds in polysaccharides which might reduce the DF content or change the ratio between ISF and SF. With heating in the presence of amino acids, Millard reaction of polysaccharides is started which produce new polymers that lose the fibre properties (Mongeau & Brooks 2016). One of the first things that was observed when testing how food processing influence glycemic response was that cooked food like wheat, corn and potatoes ingested significantly higher glucose response than their raw contributes (Bornet et al. 1989). Fibre are influenced also by cutting, milling, cooking and boiling. The greater is the transformation of grains, vegetables and fruits from their origin structure, the lower is integrity of a cell wall, less likely it is to have beneficial effects on health (Guillon & Champ 2000). However, changes that can be observed while food processing does not necessary correspond to what will be the change while digested. When food process increase solubility and viscosity of a meal, it does not necessary correspond to increase viscosity in small intestinal. Since there is no in vitro methods that would be able to show relationship between physicochemical properties of DF and their physiological effect, clinical studies have to be conducted to evaluate food processing influence on health benefits of fibre (Guillon & Champ 2000).

3.4. Dietary fibre recommendations

Dietary fibre are present in every unprocessed food like grains, vegetables, fruits, nuts and seeds. Even though they can be found in such broad area of food products, most of the people fail to reach daily recommendations. Average person fibre consumption has been decreased during last decades since the amount of processed DF-free food has dramatically increased (Mann et al. 2015).

USA recommendations of dietary fibre to reach adequate intake are 14 g/1000 kcal which correspond to approximately 28 g/day for women and 36 g/day for men (Usda & Dhhs 2010). In 1994 USA reported that 76 % of people who eat below 20 g of fibre per day have self-
reported that they are eating sufficient amount of fibre daily (Alaimo et al. 1994). Even though the awareness of importance of dietary fibre has increased, the food consumed is reduced in fibre content and it reflects in the average intake of fibre only 15 g/day in USA (Association 2008). It’s surprising that most of the fibre consumed by Americans comes from white flour and potatoes despite low DF values, since their consumption are the highest (Association 2008). In Denmark and other Scandinavian countries the recommendation of DF intake are 25-35 g/day which correspond to US guidelines (Nordic Nutrition Recommendation 2012). In 2008 there were only 6 % of Danes that meet the DF recommendations every day, therefore the country started the campaign to raise the awareness of health benefits from eating enough WG products and fibre. In 5 years after the campaign started, 27 % of adult Danes and 43 % of children met the recommended amounts of whole grain food per day. The average consumption of whole grains have risen from 36 g/day to 63 g/day (75g/day recommended), respectively (Danish Whole Grain Partnership 2014).
Main recommendations are usually approaching increase of WG consumption even though there are controversial results between epidemiologic and clinical studies whether WG have an effect on diabetes parameters (Schulze et al. 2007; Jenkins et al. 1978). On one hand many epidemiologic studies show that WG and cereals that mainly consist of insoluble fibre have the most prospect effect on risk of cardiovascular disease, incident of T2D and mortality (Schulze et al. 2007). Beneficial effects observed in cohort studies are most possible a result of many beneficial ingredients in WG and cannot be directly correlated only to higher DF intake (Babio et al. 2010). In addition to ISF, whole grains also contain polyphenols, vitamin E and magnesium that possibly influence overall health being (Council n.d.). Cohort studies are due to many correlations that might influence the results, not able to provide reliable facts to establish definitive conclusions (Concato et al. 2000). However, their results are stimulating research groups to construct randomize control trials to test predicted correlations.

Cohort studies included in review by Babio et al, have simultaneously shown decrease in risk for developing T2D associated with higher WG intake (Babio et al. 2010). However, there was no specification of grain and fibre types that could give us clear information of what has caused those results. One of the shown correlations from cohort studies was that cardiovascular incidents are more connected to elevated postprandial glycaemia than fasting glucose, therefore more clinical studies were conducted to test the effect of carbohydrate products on glucose response and evaluate their GI (Jenkins et al. 1987; The DECODE study 1999; Brand-Miller et al. 2003). Clinical studies were not able to show beneficial effect of WG on glycemic response, therefore American Diabetes Association (ADA) in 1995 concluded that dietary fibre probably have insignificant effect on glycemic control (Complications 2002). The inconsistency of results is a reflection of different dietary fibre properties that was firstly not taken into account. Studies of dietary fibre were in the beginning mainly focused on the question how much fibre is needed to have beneficial effect and secondly they have investigate what type of fibre offer better physiological effects (Guillon & Champ 2000). In clinical studies, ISF that are the main type of fibre in WG products, did not perform desirable effect on glycemic respond and other risk factors of developing T2D (D. J. Jenkins et al. 2002).
In 1978 Jenkins et al. first compared different DF and their analogs to test the effect on glucose tolerance and to investigate correlations between fibre properties and their effect (Jenkins et al. 1978). Out of six different fibre added to the products, only guar gum showed significant reduction in peak rise of glucose concentration. They showed positive correlation between increase viscosity of fibre added and greater reduction in peak rise and AUC. Increased viscosity reflects in slower glucose absorption and transit time and therefore offers effective way to decrease postprandial glycaemia. That was even further confirmed when they compare the effect of the same fibre with no viscous properties and showed that hydrolyzed guar gum did not perform any reduction of glucose response. The suggested mechanism is twofold, firstly viscous fibre delay gastric emptying and transit time and secondly slow down glucose absorption in intestinal (Jenkins et al. 1978).

Even when comes to viscous fibre, not all of them perform the same physiological effect. In vitro studies showed that glycemic response of solid foods with incorporated VSF corresponds to molecular weight of fibre and their concentration that influenced viscosity (Lan-Pidhainy et al. 2007; Tosh et al. 2008). However, the situation in digestive system might be different due to different physiological properties and environmental factors, therefore each fibre effects have to be tested individually (Guillon & Champ 2000).

1. Viscous soluble fibre supplementation

Eating sufficient amount of SF is a challenge, since they are only present in beans, lentils, chick peas, okra, barley, and oats. Moreover, it was shown that some of the natural occurring soluble fibre, like agar and pectin, do not have an effect on postprandial glycaemia even though they might delay food digestion (Sanaka et al. 2007). For guar gum it was shown that it may lose its activity due to hydrolysis in stomach acid that reflects in reduction of viscosity (Regand et al. 2009). Moreover, even oats that are rich in viscous beta-glucans, show no differences in GI compared to other high GI products (Granfeldt et al. 1995). Therefore, many supplements are available on the market that could help in glycemic control (Chutkan et al. 2012). One of the supplements that just recently have got the approved health claim from
Health Canada is a Polysaccharide Complex (PGX – PolyGlycompleX), containing glucomannan, xanthan gum and sodium alginate, that was used in the study conducted for this master thesis (US Patent No: 8,062,686) (Anon n.d.).

1.1. Konjac Glucomannan

The main component of PGX is a glucomannan that is derivated from Konjac root (*Amorphophallus Konjac*) and it is a soluble, fermentable and highly visous dietary fibre that have ability to absorb up to 50 times its weight when diluted (Keithley & Swanson 2005; Davé & McCarthy 1997).

*Picture 1: Amorphophallus Konjac illustration of fibre isolation steps. Source webpage wrapfataway.com – link at Picture reference (1).*
Konjac glucomannan (GM) has 5 times higher viscosity than guar gum and beta-glucans and it was shown to be one of the fibre with the highest viscosity (Davé & McCarthy 1997). In Japanise culture it has been used as food and remedy for a very long time and they were also the first one that started to investigate their positive outcomes as a dietary fibre (M. et al. 1980).

Konjac glucomannan was shown to be beneficial for many health parameters. Vuksan et al. were the first to show its beneficial effect on high-risk diabetic patients when using it implemented into biscuits. High-risk individuals with T2D gained improvement in metabolic control when GM-enriched biscuits were added to conventional treatment (drug therapy and low-saturated fat diet)(Vuksan et al. 1999). Glucomannan has shown beneficial effect on glycemic control when used as a longer as well as shorter (acute) treatment. Its use also reflects in decrease of short-term marker of degree of diabetic control – fructosamine, however they show no effect on fasting or insulin secretion. It was suggested that GM may
potentiate the effect of drugs used for diabetes treatment. Furthermore, the same group continues with the study and test GM-enriched biscuits with wheat bran fibre biscuits to see the difference in effect of VSF compared to insoluble. Results were very similar to previous research and supported better glycemic control for GM-group, significant reduction was observed in hyperglycemia and hyperlipidemia (Vuksan et al. 2000). Great reduction properties for lowering LDL cholesterol have been shown and if compared to other fibre, GM offers triple lipid-reduction compared to psyllium, oat product and guar gum as well as twice the capacity of pectins (Brown et al. 1999; Vuksan et al. 2000).

1.1.1. Polysaccharide Complex (PGX)

PGX is a formulation of three viscous fibre that act synergistically and induce several times higher viscosity when used together. This offer a great potential to achieve the same health results using smaller quantities. Since implementing viscous fibre in food remains a challenge due to their high viscosity, implementing PGX might be the solution to obtain palatability of products. Compared to other VSF like guar gum that reaches extreme viscosity immediately when mixed with water, PGX gels slower and reaches the highest viscosity with delay which is very beneficial in food production (Brand-Miller et al. 2010). A. L. Jenkins et al showed that adding 10 g of VFB to biscuits results in 74 % of GI reduction in healthy participants and in 63 % GI reduction in diabetic patients compared to white bread control, respectively (Jenkins et al. 2008). To compare this with other fibre, Glycemic Reduction Index Potencial (GRIP) that tells the degree of reduction per gram of added fibre, was calculated. GRIP values are therefore 7.4 when used in healthy patients and 6.3 for diabetic patients, which is stronger reduction than was reported of any of other soluble fibre, even GM alone (A. L. Jenkins et al. 2002; Chearskul et al. 2007; Sanaka et al. 2007; Dahl et al. 2005).

PGX is very potential fibre blend also because of its effect on weight loss (Onakpoya & Heneghan 2015). As mention before, T2D is very correlated to vascular fat and the first recommendation every diabetic patient receive is to lose weight. Fibre-enriched meals have lower energy dense since the volume of the volume of the meal increase and reflect in higher satiety. Moreover, they are digested slower and are able to prolong the feeling of fullness also due to the effect on hormonal hunger signalization (Kristensen & Jensen 2011). The effect is most possible threefold, firstly viscosity of a meal increase transit time and reflects in slower
gastric emptying (Dikeman & Fahey 2006). Secondly, the metabolic effect is observed in slower absorption of glucose and other macronutrients that reflects in lower postprandial glucose elevation, and thirdly, endocrine effect was observed in lower production of hunger-related hormones like peptide YY, glucagon-like peptide-1 (GLP-1) and cholecystokinin (Wren & Bloom 2007; Jenkins et al. 1978). These characteristics are all the effective approaches to help in weight control (Howarth et al. 2009). Study conducted by Vuksan et al compared viscous fibre blend preload (same properties as PGX) effects on food intake and conclude that significantly lower intake was observed in VFB group compared to insoluble cellulose fibre, as well as GM itself (Vuksan et al. 2009).

1.1.1.1. PGX health claims

In May 2016, Health Canada approved health claims for the use of PGX in food industry referring to reducing of postprandial glycaemia and cholesterol. In postprandial glycaemia, they conclusion was based on six randomized control trial with cross-over design, that showed significant reduction in postprandial glucose iAUC in 80 % of treatment arms. The effect is achieved when a minimum of 5 g of PGX is added to consume meal directly prior consumption. This health claim is not allowed if PGX is added to products that require any kind of food processing prior consumption, since there is no evidence to support the effect when enriched meals are baked, frozen or boiled (Anon n.d.). In cholesterol lowering effect, four studies showed significant reduction in total cholesterol for 75 % of treatment arms and in LDL cholesterol levels for all arms. These results require a minimum of 10 g of PGX daily for at least 2 weeks when fibre are added directly prior consumption (Anon n.d.).

1.1.1.2. Incorporating PGX into different food matrices

All the beneficent effects of PGX were shown when dry powder was sprinkled on the top of food meals right before consumption. However, asking people to sprinkle something on the top of the food is not the most efficient way to make general population eat more soluble fibre. Therefore, Risk Factor Modification Center in St. Michael Hospital in Toronto, where I did the practical work for this master thesis, have got the vision of implementing PGX into commonly consumed refined carbohydrate products during processing. Refined products are despite awareness of their low nutritional value, still the most consumed carbohydrates in
Canada and USA (Association 2008). Whole grains are recommended by general health institutions, but due to lower palatability, no improvement in amount of their consumption have been achieved in last decades (Association 2008). A potential way to improve this could be to implement PGX into different refined carbohydrate products with retaining their palatability. Since PGX is highly effective in lowering postprandial glycemia, lower amount can be added to final products, which might be a potential way to not influence palatability.
My work in Toronto started with baking and preparing testing samples to ensure I was able to prepare the same products that have been done before. Before my arrival they already conducted the phase I of the study, so they already knew that the implementation of PGX in product did not influence palatability in most of the cases.

After all the products were baked, prepared and sampled we recruit healthy individuals to participate in the study. Recruitment room is shown on Picture 2.
On the picture 3 is the lab we used for analysis blood samples. After we finish with participants and sample analysis, I focused on analysis of results and compared them to what has previously been established. I learned a lot about the protocol of the clinical trails, which
things have to be taken in account, what can go wrong and how to prevent it. Most of all it was an excellent experience that will help me to understand other clinical trials more since I was once a part of one.

The results of our study showed beneficial effects in lowering postprandial peak values in glucose rise, however no effect was observed in glucose iAUC. Interesting observation from the individual meal responses is that both cream of wheat and mashed potato (non-baked) treatments displayed a slightly more prominent glucose lowering response compared to white bread and muffin treatments (baked products). It is very likely that un-sufficient ability to reach fibre’s highest viscosity masked its positive effect on postprandial glycaemia. Even though there were significant results in many aspects in overall treatment products compared to overall control, products individually lack significance and did not perform as desirable. For detailed results refer to the paper: “Vladimir Vuksan, Taja Karner, Amanda Ma, Elena Jovanovski, Fei Au Yeung: Effect of Palatable Soluble Fibre-Containing Carbohydrate Foods on Postprandial Blood Glucose Response in Healthy Individuals: A Randomized, Controlled, Double-blinded Study” (not published yet).
CONCLUSION

Consumption of highly viscous fibre was shown to successfully lower postprandial blood glucose and offer potential way to address high glycemic responses related to increase risk of developing T2D. Incorporation of VSF into commonly consumed CHO products has a potential to reduce GI of highly processed food. Since VSF incorporation reflect in lower products’ palatability, fibre blends like PGX with fibre combination that acts synergistically and can perform the same health effects when used in smaller dosage, might offer a solution to develop palatable fibre-enriched products.

In the performed study we were able to obtain palatability of 3 out of 4 products. However, no significant effect was shown in glucose iAUC between fibre-enriched and control samples. Since healthy claim regarded PGX refer to the use of fibre blend sprinkled on the food right before consumption, cooking and baking process in our study might influenced overall potential. Moreover, it was concluded that 5 g of PGX are necessary to perform desirable physiological effect. However, in the study performed, only 4 g was implemented into food products. Even though the success of implementing is not proven efficiently yet, we should not take this opportunity for granted and more facilities and companies should work together and find the best solution how to incorporate this or similar highly viscous blends into variety of products. Eating higher amount of fibre and still enjoying hedonic appearance of refined product could be a potential way to improve overall health, decrease diabetes rates and improve people’s diets. However, the propose of this improvement is not to support people to eat more refined products, therefore clear statement should be made to clarify that this is still not a healthy meal due to low nutritional value. Clear and non-misleading marketing should be a priority when put on a market.
PERSPECTIVE

Further development of products where PGX could reach its maximum viscosity properties should be considered. PGX could be added to various different products, based on the most consumed refined product in specific country. Adding PGX to cereals and white bread, which are most traditional breakfast foods, is a potential way to help consumers not to rise glucose level too high first thing in the morning. That might lower the risk of developing T2D, since insulin sensitivity is at its lowest point after overnight fasting, possibly due to elevation of FFA during the night (D. J. Jenkins et al. 1987). It would also be interesting to look into second meal effect, since it was shown that metabolic response of a meal may influence next meals in a day. If we provide breakfast products with increase level of viscous soluble fibre, it may flatter the response of the next meal, even if refined and do not contain any fiber (Jenkins et al. 1982; Brand-Miller et al. 2010)

Long-term study to evaluate the effect of everyday consumption of developed products in diabetic patients could be considered and evaluation of its effect on hyperglycemia and hyperlipidemia can be an interested aspect to see how it can benefit patients with diabetes.


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John, L. & Jeffery, A., 2000. Beneficial effects of viscous dietary fiber from Konjac-mannan in ...


Picture 4 and 5 reference:
