Research Paper

Complex Carbohydrates: Their Effect in Human Health

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Whole grain consumption is associated with diminished risk of serious, diet-related diseases, which are major problems in wealthy industrialised economies and are emerging in developing countries demographic and nutrition transition. These conditions include coronary heart disease, certain cancers (especially of the large bowel), inflammatory bowel disease and disordered laxation. Carbohydrates are important contributors to the health benefits of whole grains. Insoluble non-starch polysaccharides (NSP) are effective laxatives. Soluble NSP lower plasma cholesterol and so can reduce heart disease risk but the effect is inconsistent. Processing seems to be an important contributor to this variability and other grain components may be involved. However, starch not digested in the small intestine (resistant starch, RS) appears to be as important as NSP to large bowel function. Native Africans at low risk of diet-related disease through consumption of unrefined cereals may actually have relatively low fibre intakes. While NSP are effective faecal bulking agents, they are fermented to a very variable extent by the large bowel microflora. In contrast, RS seems to act largely through the short chain fatty acids (SCFA) produced by these bacteria. One SCFA (butyrate) appears to be particularly effective in promoting large bowel function and RS fermentation appears to favour butyrate production. Animal studies show that dietary RS lowers diet-induced colonocyte genetic damage and chemically-induced large bowel cancer which correlates with increased butyrate. These effects in long term could contribute to a lower risk of cancer and ulcerative colitis. Cereal grain oligosaccharide (OS) may also function as prebiotics and increase the levels of beneficial bacteria in the large bowel.

Key Words: Starch; Oligosaccharides; Non-Starch Polysaccharides; Cereals; Human Health; Resistant Starch

1. Introduction

Cereal based foods have been staples for humans race since agriculture evolved. Cereal grains contain the macronutrients (protein, fat and carbohydrate) required by humans for growth, development and maintenance. They also supply important minerals, vitamins and other phytonutrients essential for optimal health. However, it is becoming apparent that cereals in general have the potential for health enhancement beyond the simple provision of these nutrients and phytonutrients as their consumption can lower the risk of significant diet-related diseases. Morbidity and mortality from non-infectious diseases are significant problems in not only in affluent, but also in developed economies and include cardiovascular disease (CVD), Type 2 diabetes and certain type of cancers [10]. Most of the pericarp-seed coat, aleurone and germ containing (fibre, micronutrients, fat and protein) are retained in the whole grain while they have been removed by milling, polishing and processing in refined foods, leaving the starchy endosperm. Studies have shown that consumption of whole grain products is associated with lowered risk of CVD and diabetes [9]. Greater intake of whole grain foods is associated also with lesser obesity [13, 14]. Two hypotheses have been proposed to account for this conundrum [9, 23]. The first is that the whole grains contain a complete portfolio of bioactive components which provide comprehensive protection for the major diseases

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which have been identified in population studies [9]. This is the ‘‘whole grain package’’ model. The alternative is that whole grains possess a general characteristic which offers comprehensive protection and it has been suggested that a lower small intestinal digestibility of whole grain foods could be responsible [23]. This would translate to less metabolisable energy, lower glycaemic response (GR) and more resistant starch (RS). It must be remembered that some processing is essential for palatability, safety and adequate nutrient bioavailability. Wheat bran provides a ready example of this latter point. It contains both the pericarp-seed coat and the aleurone layer. Of these two, the latter is a rich source of nutrients including vitamins such as folate. However, most of this folate is not bioavailable in unprocessed bran and only when the aleurone layer is isolated and disrupted does it become so [7].

Types of Carbohydrates

a. Simple carbohydrates

b. Complex carbohydrates

Carbohydrates can also be Classified on the Basis of Their Chemical Composition

a. Monosaccarides

b. Disaccharides

c. Oligosaccharides

d. Polysaccharides

2. Grain Carbohydrates and Human Health

Dietary carbohydrates can be divided very simply into two major groups solely on the basis of their susceptibility to digestion by human small intestinal enzymes. Humans possess a suite of small intestinal digestive enzymes but only α-amylase that can attack a complex carbohydrate. This enzyme can hydrolyze only one significant dietary polysaccharide starch. This specificity depends on the presence of α-1,4 glucosidic links in the target polysaccharide. All of the other major complex carbohydrates like oligosaccharides (OS) and non-starch polysaccharides (NSP)) seem to resist human small intestinal enzymic digestion completely. NSP are the principal components of dietary fibre and the lack of small intestinal digestibility explains their principal physiological properties. It must be emphasized that this solubility may be demonstrated under conditions which do not occur in the human small intestine [24]. Nevertheless, the terms ‘‘soluble fibre’’ and ‘‘insoluble fibre’’ have entered into common usage and also serve to segregate NSP on one of their best documented physiological effects of reducing plasma cholesterol, an established risk factor for CVD [5]. On the other carbohydrates found in physiologically significant quantities in some grains, OS are a relatively known quantity in terms of the health benefits of cereals. They contribute to the dietary fibre content of grains and have health benefits.

Starch is the most important polysaccharide in nearly all seeds grown and used as human foods. Slow digestion of starch leads to a low glycaemic response (GR) while reducing total small intestinal amylolysis increases RS. Amylose is slower to gelatinize and quicker to retrograde than amylopectin and so processed food products have higher RS.

3. Dietary Fibre and Health Outcomes

It is essential that any potential health benefits of foods or food components be substantiated to ensure their effectiveness and sustain consumer confidence. For dietary fibre there are two specific instances where the positive outcomes of greater consumption have been established namely laxation and plasma cholesterol reduction.

3.1. NSP and Laxation

Burkitt and Co-workers [3] in Africa noted that black Africans were at much lower risk of what have become known as the ‘‘diseases of affluence’’ than Europeans living in the same environment. The difference was ascribed to the greater consumption of unrefined foods by the natives. With time, research emphasis shifted to the apparently greater fibre content of these foods and the development of the so-called ‘roughage’’ model of dietary fibre [27]. This model hinges on the resistance of NSP to human small intestinal digestive enzymes which helps to explain the well recognized dose dependent effects of fibre rich foods in increasing faecal bulk. This bulking is taken as the mechanism of action of what is probably the best documented effect of dietary fibre promotion of regularity.

Diverticular disease is a herniation of the large bowel and is associated with chronic constipation. These bulking effects of fibre are greatest with cereal fibre, especially products high in insoluble NSP such as wheat bran [25]. Soluble NSP are generally less effective in increasing stool mass. The actual quantity of fibre required for the effect is not certain but would seem to be between 20 and 25 g/person/d. However, the very low fibre intakes in many countries (e.g. the US) provide an opportunity for the food industry to improve public health. However added fiber may not have the same effect as dietary fiber.

3.2. Soluble NSP and Plasma Cholesterol

Consumption of whole grains is associated with a lowered risk of coronary heart disease (CHD) [9]. CHD is a disease characterized by infiltration of cholesterol into the major arteries of the heart. Atherosclerosis leads to a progressive occlusion of the circulation resulting in impaired cardiac function and, if unchecked, tissue necrosis and death. CHD has a number of risk factors which cannot be altered. Modifiable risk factors include smoking, physical activity and raised plasma low-density lipoprotein (LDL) cholesterol. LDL is the major plasma vehicle for transporting cholesterol to the tissues. Preventive strategies for CHD include cessation of smoking, dietary modification, exercise and other lifestyle changes. Large scale intervention studies have shown that drugs which lower plasma total and LDL cholesterol are effective in reducing CHD events [5]. While drugs are effective, they are also expensive and dietary modification is a cheaper alternative. A portfolio diet (containing plant foods that lower cholesterol) approach has been tested whereby food intake is modified to accommodate a number of features known to lower CHD risk and has been shown to have positive impacts on biomarkers, including LDL cholesterol [11, 11a].

The effectiveness of this approach has to be quantified relative to drugs. The potential of grain components to assist in risk reduction is fairly self-evident, given the relationship between whole grain consumption and lowered CHD risk. It was thought originally that dietary insoluble fibre was responsible, which reduced plasma cholesterol. The proposition was based on the observations that plant fibre concentrates and isolates bind bile acids *in vitro*. This binding is similar to that of a synthetic resin (cholestyramine) which has been used to lower plasma cholesterol in patients with high LDL levels [18]. The lowering of total and LDL cholesterol has been demonstrated particularly with oats and to a lesser extent, barley [28]. Both cereals contain soluble NSP b-linked glucans which are thought to be the active agents [6]. Glucans (and other soluble NSP such as psyllium) are thought to modulate digestion through their viscosity in solution [6]. This viscosity contributes to the effects of soluble NSP on the absorption of other nutrients e.g. glucose. Wheat fibre in general and wheat bran in particular does not seem to affect plasma cholesterol [28]. In some studies wheat bran has been used as a control fibre while some animal dietary studies suggest that wheat bran can actually raise plasma cholesterol relative to baseline [27]. It is possible that fibre alone does not account for the protection against CHD afforded by whole grains and cereal foods. The incomplete small intestinal digestion of starch is emerging as a potentially positive factor. This leads to reduced absorption of glucose in the small intestine and the passage of more starch into the large bowel. In the case of the large bowel, RS is fermented by the resident bacteria with the production of substantial quantities of end products (short chain fatty acids, SCFA) with specific health promoting attributes.

4. Starch and Human Health

The paradox between food consumption and relative risk can be reconciled by the facts that the African ate considerably more unrefined starch than the Europeans and that their cooking practices were rather different. In particular, the Africans ate maize porridge, which had been cooked in water and then cooled and stored for some time. While cooking increases the digestibility of starch and other nutrients, the cooling and storage leads to retrogradation of starch and the formation of RS. Human studies have confirmed that the stored cooked maize gruel was high in RS relative to the fresh product [1]. The importance of controlling the rate of small intestinal starch digestion to lower the GR is accepted. For optimal large bowel health, combinations of RS and NSP may be optimal [17].

RS as a health-related food component is probably quite simple. Starch has the potential to be hydrolyzed completely to glucose in the small intestine. In omnivores, this fermentation occurs principally in the large bowel. These data point to an important difference between RS and NSP. The human caecum and colon are home to a numerically large, taxonomically diverse and metabolically active, bacterial population. Most of the bacteria in adult humans are non-pathogenic and ferment unabsorbed dietary carbohydrates. These organisms resemble those found in the large bowel of obligate herbivores in metabolic capacity and end products, i.e. gases (H_2, CO_2 and CH_4) and short chain fatty acids (SCFA).

5. Short Chain Fatty Acids and Health Effects of Complex Carbohydrates

Health benefits of complex carbohydrates accrue from the short chain fatty acids (SCFA) produced in the large bowel [26]. SCFA have a number of general effects including the direct acidification of digesta. This lowering of pH leads to the ionisation of potentially cytotoxic compounds including biogenic amines and ammonia [30]. SCFA are absorbed on passage of the faecal stream and less than 10% of those produced appear in excreted faeces. The absorbed SCFA are metabolised by the viscera and contribute to their energy needs. Butyrate is the preferred metabolic substrate for colonocytes. Its metabolism is thought to drive the uptake of cations and water leading to water salvage. Incorporation of RS into the oral rehydration solution accelerates recovery and lowers net water loss in patients with watery diarrhoea [19]. Butyrate is also believed to promote a normal phenotype in colonocytes through the repair of damaged DNA and induction of programmed cell death in transformed cells. These actions are thought to lower the risk of colorectal cancer and have been shown in cultured transformed cells. SCFA have a number of other positive effects on large bowel health with butyrate being the most potent.

6. Cereal Carbohydrates and Large Bowel Health

Cereal grains also promote large bowel health through their complex carbohydrates, especially RS. RS has lower metabolisable energy. The bacterial digestion of starch is intrinsically less efficient than that of the human small intestine. This means that the energy available to the host as SCFA and any other products is less than 50% of the glucose absorbed in the small intestine [16, 16a]. This has obvious implications for the control of obesity itself a risk factor for diet-related disease and it may be that the protection against CHD could be indirect via this mechanism.

6.1. Colorectal Cancer

Large bowel cancer is becoming an important cause of morbidity and mortality in emerging countries with greater affluence. The early human population studies indicated a protective role of complex carbohydrates, especially dietary fibre in this disease. The laboratory data are supportive of fibre and studies in rodents with experimentally induced large bowel cancer have shown a protective role for products high in insoluble NSP such as wheat bran [31]. Interventions in individuals with a predisposition to colorectal cancer such as adenomatous polyps have also failed to show any effect of dietary fibre supplements on polyp recurrence after surgical removal [20]. However, our increasing knowledge of plant carbohydrates and their effects on gut physiology suggests that a reappraisal may be timely. It is apparent that RS makes a significant contribution to large bowel fermentation. Given the role of the SCFA produced by this fermentation in large bowel health, it seems appropriate to factor these considerations into the relationship between dietary intakes and disease risk. Human and animal feeding trials have shown a substantial increase in large bowel and faecal SCFA, including butyrate, on consumption of RS in a variety of foods [26]. It is thought that RS fermentation by the large bowel microflora favours the production of butyrate above other SCFA. Studies in rodents with chemically induced large bowel cancer have shown significant protection with the feeding of RS as high amylose starch [14]. Starch and RS intakes were protective but NSP had no relationship to risk [4]. NSP are the main components of dietary fibre so that this absence of a protection is consistent with the prospective population data. However, there is inconsistency in the epidemiological data notably the demonstration of dose dependent, protection by dietary fibre in a large, multicentre European prospective study [2]. The total dietary fibre (TDF) method used to analyse foods to estimate intake includes not only NSP but also a fraction of RS. It follows that TDF may be an indirect measure of RS intake and this, rather than NSP alone may be a major part of the protective agency.

6.2. Gut Microbiology, Inflammatory Bowel Diseases and Health

The large bowel fermentation of RS and a variable fraction of NSP alter the landscape of the relationship between diet and health. Instead of considering carbohydrates solely in terms of small intestinal digestibility and physical faecal bulking, the relationship between the microflora and SCFA and their role in health becomes much more significant.

This may assist in examining the data in relation to other diseases as well as cancer. For example, inflammatory bowel diseases (IBD) are a significant socio-economic cost in developed countries [22]. There are two main variants of IBD-Crohn's disease (CD) and ulcerative colitis (UC). UC is generally located in the distal region of the large bowel whereas CD has a more diffuse distribution through the large bowel and may occur in the small intestine. In both cases there are similarities as well as differences. There is evidence of a breakdown of the mucosal barrier in both UC and IBD. This leads to translocation of bacteria which could provoke the inflammatory response [21]. A recent (relatively small) prospective study showed that greater dietary protein intakes were associated with loss of remission in patients with previously quiescent UC. The protection afforded by RS is also consistent with a proposed role of SCFA in protecting against UC. This amelioration was thought to come from the provision of butyrate to colonocytes which were otherwise starved of substrate. The hypothesis is possible for UC as it occurs predominantly in the distal colon, i.e. where the availability of SCFA is lower than in the proximal and median large bowel. It accords with reports that topical SCFA can lead to repair of UC and potentiate standard anti-inflammatory treatments [29]. A small study in UC patients has shown that consumption of a germinated barley resulted in a similar improvement [12].

6.3. Resistant Starch, Oligosaccharides and Prebiosis

Live bacterial cultures is beneficial for health. These bacteria are referred to as probiotics and, for the most part, they belong to a group referred to as the lactic acid bacteria (LAB). Their principal substrates are oligosaccharides (OS). The latter include galacto oligosaccharides (GOS) but they also use others, including fructo-oligosaccharides (FOS) which are found in certain plants. LAB find industrial use in the manufacture of fermented milk products especially yoghurt but they occur normally in the human gastrointestinal tract. They are present in their highest concentration and relative numbers in infancy [8]. The fermentative product profile of breast milk-fed infants differs radically from that of adults. It includes ethanol and formate as well as lactate but little or no propionate or butyrate. This profile may be important for the early development of the human gut in terms of controlling the bacterial population. Oligosaccharides (OS) were the archetypal prebiotics given their importance as substrates for LAB.

7. Disorder of Carbohydrate Metabolism in Health

7.1. Glycogen Storage Diseases (see Table 1)

7.2. Galactosemia

Galactosemia defined as a high blood level of galactose is caused by lack of galactose-1-phosphate

Table 1: Glycogen Storage Diseases

Name	Affected Organ,Tissues or Cells	Symptoms
Type O	Liver or muscle	Episodes of low blood sugar levels (hypoglycemia) during fasting if the liver is affected
Von Gierke's disease (Type IA)	Liver and kidney	Enlarged liver and kidney, slowed growth, very low blood sugar levels, and abnormally high levels of acid, fats, and uric acid in blood
Type IB	Liver and white blood cells	1. Same as in von Gierke's disease but may be less severe 2. Low white blood cell count, recurring infections, and inflammatory bowel disease
Pompe's disease (Type II)	All organs	Enlarged liver and heart and muscle weakness
Forbes' disease (Type III)	Liver, muscle, and heart	Enlarged liver or cirrhosis, low blood sugar levels, muscle damage, heart damage, and weak bones in some people
Andersen's disease (Type IV)	Liver, muscle, and most tissues	Cirrhosis, muscle damage, and delayed growth and development
McArdle disease (Type V)	Muscle	Muscle cramps or weakness during physical activity
Hers' disease (Type VI)	Liver	Enlarged liver-Episodes of low blood sugar during fasting-Often no symptoms
Tarui's disease (Type VII)	Skeletal muscle and red blood cells	Muscle cramps during physical activity and red blood cell destruction (hemolysis)

uridyl transferase enzymes necessary for metabolizing galactose

7.3. Hereditary Fructose Intolerance

Hereditary fructose intolerance is caused by lack of fructose-1-phosphate aldolase enzyme needed to metabolize fructose.

7.4. Mucopolysaccharidoses

Mucopolysaccharidoses are a group of hereditary disorders caused by the absence or malfunctioning of lysosomal enzymes like N-acetylglucosaminidase, Galactose-6-sulfate sulfatase, Beta-galactosidase needed to break down molecules called glycosamino glycans.

7.5. Disorders of Pyruvate Metabolism

Pyruvate metabolism disorders are caused by lack of the enzymes pyruvate carboxylase and dehydrogenase which are involved in pyruvate metabolism.

8. Conclusions

There is strong evidence that cereal polysaccharides have benefits in the control and prevention of human diseases. Their capacity to improve health status is established reasonably well in some areas, for example, soluble NSP and plasma cholesterol control. In other areas, their benefits are only just beginning to emerge. This is especially the case for starch and its digestibility. Controlling starch digestion was considered substantially in terms of the rate of hydrolysis in the small intestine, i.e GR. However, manipulating digestibility has much broader implications, especially as current starchy foods seem to be very low in RS. One of the most radical recent developments in the relationship between dietary carbohydrates and health is the emergence of the importance of the large bowel microflora in human health. It is becoming clear that many of the large bowel actions ascribed to complex carbohydrates are actually due to the products of their fermentation by the large bowel microflora. Understanding the relationships between the metagenome, carbohydrates, SCFA and health will offer great opportunities to improve health. This should include obtaining an understanding of the interactions between cereal OS and the microflora. The new cereal cultivars are aimed at improving public health in important areas, including diabetes. These new technologies will also help to unravel the relationships between gut microflora, food polysaccharides and health.

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