

## Dietary fibre, lente carbohydrates and the insulin-resistant diseases

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Several epidemiological studies link consumption of fibre-rich foods to a reduced risk of type 2 diabetes and CHD. The 'fibre hypothesis' suggested that this was a direct effect of fibre. However, fibre-rich foods contain different types of fibre as well as other potentially beneficial compounds, and many foods naturally high in fibre have low glycaemic and insulinaemic indices, possibly due to food form. The question therefore emerges as to the effect of isolated fibre *per se* on insulin sensitivity, lipids and other risk factors associated with the metabolic syndrome. Many beneficial effects are seen with pharmacological doses of isolated viscous soluble fibre, including improved insulin sensitivity, decreased LDL-cholesterol levels and decreased clotting factors. Similar effects are seen with low glycaemic-index foods. In contrast, insoluble non-viscous cereal fibre is not seen to act directly on risk factors when taken in refined foods such as in milled flour. Since cereal fibre, the major type of fibre in western diets, does not directly act on the risk factors for the metabolic syndrome, the question remains as to possible mechanisms. Until now, fibre and the nature and processing of the starch and particle size have been seen as the main determinants of the metabolic response to starchy foods. However, fibre-rich foods also have an increased protein-to-carbohydrate ratio. Hence we suggest that the protective effect of fibre may also be due to increased vegetable protein content, which may act directly to reduce clotting factors and oxidized LDL-cholesterol levels.

### Insulin resistance: Dietary fibre: Low glycaemic index: Diabetes mellitus type 2: Cardiovascular diseases

#### Introduction

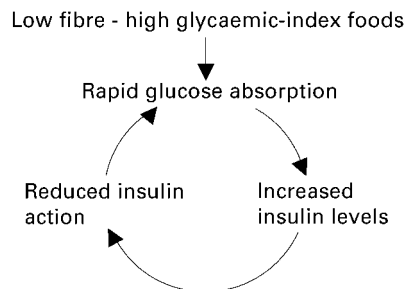
Affluent western lifestyles are associated with a number of chronic diseases including diabetes, CHD and cancer. Links have been established between sloth (Dorn *et al.* 1999; Manson *et al.* 1999) and gluttony (Higgins *et al.* 1993; Hu *et al.* 1997) and a number of chronic diseases. On the other hand the dietary fibre hypothesis proposed that these same diseases were the result of a lack of fibre in the diet (Burkitt *et al.* 1972; Trowell 1978). Several observational studies have provided strong support for a beneficial role of what is termed whole-grain intake in reducing the risk of CHD (Jacobs Jr *et al.* 1998; Liu *et al.* 1999). In addition, high intakes of whole-grain foods have been suggested to reduce the risk of developing diabetes (Salmeron *et al.* 1997a, b), hypertension, and some types of cancer (Levi *et al.* 1999). Since diabetes, cardiovascular disease and probably cancer are associated with insulin

resistance, there is considerable interest in whether fibre might reduce insulin resistance.

#### Hypothesis: fibre and insulin resistance

The working hypothesis is that fibre-depleted foods will lead to higher glucose levels and stimulate excessive insulin secretion. Hyperinsulinaemia, in turn, may result in down-regulation of the insulin receptors, lower levels of relevant signalling molecules (Virkamäki *et al.* 1999), and thus an elevation of the fasting blood glucose. Once insulin resistance is established there may be an even greater sensitivity to the deleterious effect of low-fibre, high glycaemic-index foods, thus maintaining a vicious cycle (Fig. 1). Viscous fibre may act to break this cycle by reducing the rate of absorption and lowering the postprandial glycaemic and insulinaemic responses. To achieve these effects, viscous

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**Fig. 1.** Potential mechanisms for the relationship between dietary fibre and insulin resistance.

fibres convert the small intestine into a storage organ for the slow release of glucose to the portal circulation. In this way fibre may impact on western chronic diseases. Alternatively, fibre and low glycaemic foods may operate by mechanisms separate from insulin resistance by acting directly on risk factors for chronic disease.

### Lente carbohydrate

A number of mechanisms may operate to reduce the rate of carbohydrate absorption. Enzyme access to starch may be retarded. Viscous fibre may impede bulk diffusion of the products of luminal digestion to the mucosal surface. Other factors, possibly more important in everyday life, are taking foods resistant to rapid digestion (low glycaemic-index foods) (Jenkins *et al.* 1981), taking more frequent, smaller meals (nibbling) (Jenkins *et al.* 1989; Powell *et al.* 1999), or directly inhibiting amylolytic digestion and disaccharide absorption ( $\alpha$ -glucosidase inhibitors). The glycaemic index of the food, in turn, is dependent on the nature (Granfeldt *et al.* 1995; Liljeberg *et al.* 1996) and processing (Ross *et al.* 1987; Collings *et al.* 1981; Granfeldt *et al.* 1994) of the starch; food particle size such as whole grains (Jenkins *et al.* 1988; Liljeberg *et al.* 1992; Järvi *et al.* 1995); the presence of viscous fibres (Torsdottir *et al.* 1989), and the interaction of other nutrients with the starch. The factors resulting in the production of lente carbohydrate foods are thus interconnected, and in many studies it is not easy to separate the different effects of viscous fibre and low glycaemic-index foods. Their effects will therefore be addressed together and separated from the effects of insoluble fibre on insulin resistance and other risk factors for chronic disease.

### Viscous fibre, lente carbohydrate and insoluble fibre

Whole-grain foods often have a low glycaemic index and also provide dietary fibre, resistant starch, minerals, vitamins, phytochemicals, vegetable protein and other substances. The specific role of the fibre in modifying insulin sensitivity and risk factors for CHD has challenged investigators and clinicians for around two decades. Some studies in diabetic subjects have reported improved insulin sensitivity or decreased insulin needs by the use of foods rich in cereal fibre (Karlström *et al.* 1984; Harold *et al.* 1985). However, isolated cereal fibre does not appear to reduce the rate of carbohydrate absorption when the integrity of the whole grain is destroyed, as in the making of flour. Only in

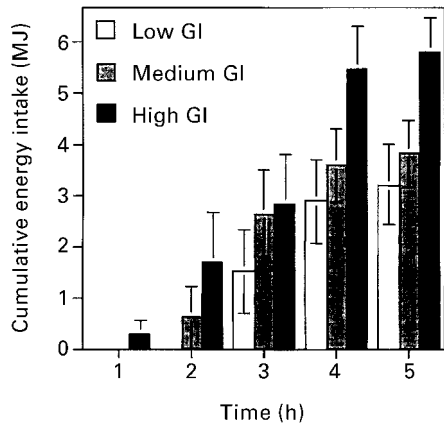
one study did chronic bran feeding improve postprandial glucose and insulin levels in persons with impaired glucose tolerance (Bosello *et al.* 1980). Hence the role of cereal fibre *per se* in the metabolic syndrome remains unclear.

In contrast, isolated soluble fibre is seen to decrease serum total cholesterol and LDL-cholesterol concentrations (Jenkins *et al.* 1979; Bosello *et al.* 1984). Moreover, when the viscous fibre guar was given as a supplement to 25 healthy men, 10 g three times a day for 6 weeks, insulin sensitivity, triglyceride levels, clotting factors and blood pressure were improved (Landin *et al.* 1992). Similar results have been seen in type 2 diabetics receiving 4 g of guar twice a day (Tagliaferro *et al.* 1985). In another study of healthy men, a high-carbohydrate, high-fibre (soluble and insoluble fibre) diet also improved insulin sensitivity and cholesterol levels (Fukagawa *et al.* 1990). In contrast, the addition of 15 g guar gum to a standard diet was of no benefit to type 1 diabetic patients either in metabolic control or insulin sensitivity; only cholesterol levels were decreased (Bruttomesso *et al.* 1991). A recent meta-analysis of studies using isolated fibre sources (pectin or guar gum) or fibre-enriched ingredients (oat bran or psyllium) confirmed that viscous fibres significantly reduce LDL-cholesterol levels whereas no effect of soluble fibre is seen on HDL-cholesterol or triglycerides (Brown *et al.* 1999). Thus, despite the effect of viscous fibre in decreasing the rate of glucose absorption when taken in pharmacological doses, its use in the prevention of the metabolic syndrome needs further clarification.

When intact foods are considered as the source of fibre, reductions are seen in LDL and the apolipoprotein B:A1 ratio in hyperlipidaemic subjects (Jenkins *et al.* 1993), and the overall effect on insulin sensitivity and risk factors for CHD appears to be greater. Similar effects are seen with low glycaemic-index foods. Insulin sensitivity measured using the short insulin-tolerance test was greatly improved following a 3-week low glycaemic-index diet in healthy women with or without a family history of CHD (Frost *et al.* 1998). A recent study by Järvi *et al.* (1999) using a low compared to high glycaemic-index diet in 20 type 2 diabetics failed to find improved insulin sensitivity, but demonstrated reduced mean day-long blood glucose and insulin levels, and reduced serum fructosamine and plasminogen activator inhibitor-1. Previous studies have demonstrated beneficial effects with low glycaemic-index diet on glycaemic control, but none has noted effects on clotting factors. The finding of low plasminogen activator inhibitor-1 with lente carbohydrate foods is therefore of potential interest for CHD risk reduction.

Increased body weight contributes to insulin resistance and risk of diabetes and CHD. In this respect the study by Ludwig *et al.* (1999) is of particular importance in demonstrating that food form and glycaemic load (glycaemic index  $\times$  total carbohydrate) of the preceding meal predicts food intake of a subsequent meal in obese boys (Fig. 2). Such studies raise questions concerning the role of nutrient release on glycaemic and endocrine responses as triggers of appetite, and the degree to which they can be modified by fibre and glycaemic-index changes.

Although the studies demonstrating differences in insulin sensitivity are few, a growing number of studies demonstrate



**Fig. 2.** Cumulative *ad libitum* food intake 1–5 h after lunch in obese boys fed breakfasts and lunches with different glycaemic index (GI). Source: Ludwig *et al.* 1999; published with the consent of the author.

beneficial effects of viscous soluble fibre–low glycaemic-index diets on risk factors associated with the insulin resistance-associated diseases. There are also studies demonstrating improved serum lipids, carbohydrate tolerance and glycaemic control with insoluble (wheat) fibre (Bosello *et al.* 1980), but the majority of studies have failed to find significant effects in acute and short-term studies. A picture therefore emerges indicating a broad range of risk-reduction benefits for viscous fibre–low-GI diets without demonstrated changes in insulin sensitivity (Table 1). On the other hand, insoluble cereal fibre in whole-grain foods

**Table 1.** Fibre and low glycaemic-index (GI) effects

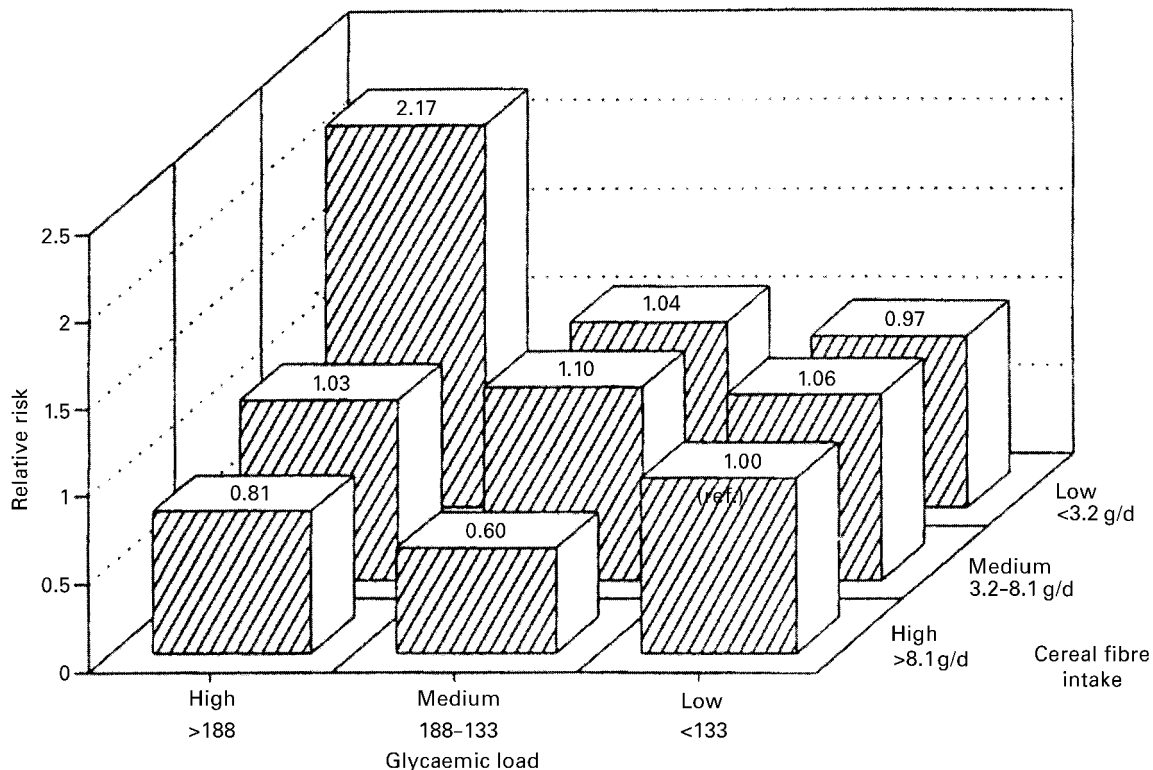
Study	Low-GI foods	Soluble fibre	Insoluble fibre
<b>Controlled studies</b>			
Reduced glycaemic response	+	+	–
Reduced serum lipids	+	+	–
Reduced clotting factors	+	+	?
<b>Epidemiological studies</b>			
Reduced risk of diabetes	+	?	+
Reduced risk of CHD	+	?	+

may be associated with increased insulin sensitivity in the context of high-fibre, high-carbohydrate diets, but with less clear acute benefits on glucose and lipid metabolism when insoluble fibre is taken without dietary change.

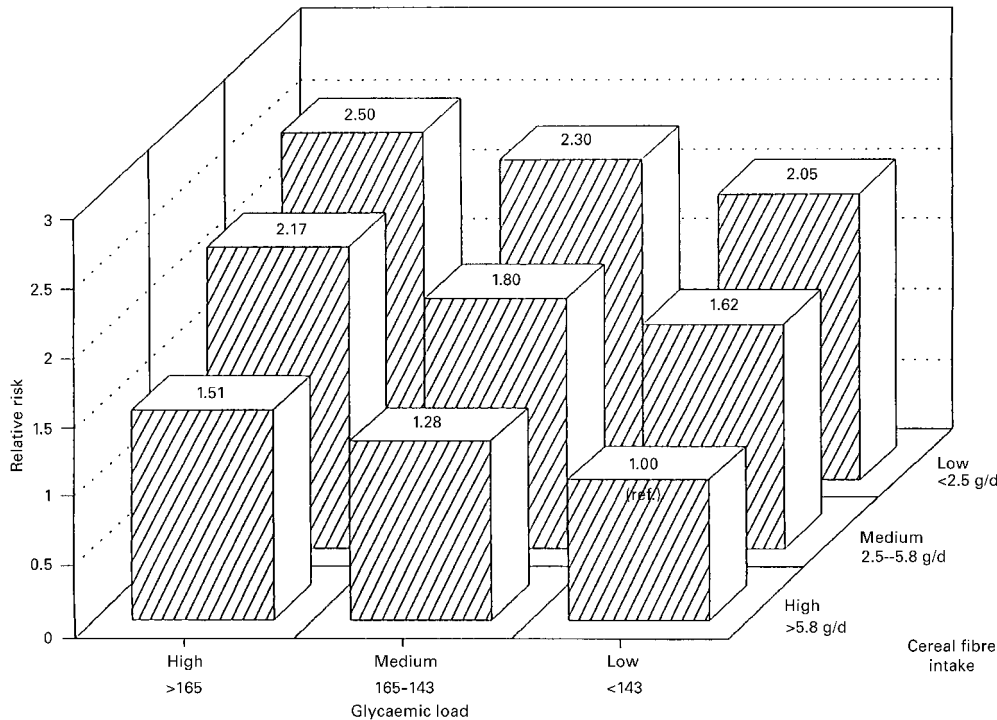
**Epidemiological studies**

Viscous soluble fibre consumption has not been shown to have benefits in epidemiological studies, probably because it is not separated from non-viscous soluble fibres in the majority of data, and because, in general, intake levels are low in western populations where the epidemiological studies are carried out (Table 1).

In contrast, slow-release carbohydrate foods in low glycaemic-index diets have been shown to reduce the risk of diabetes (Salmeron *et al.* 1997a, b) (Figs. 3 and 4). This may relate to a decreased insulin demand by consumption of minimally refined forms of grains. Similar effects have been

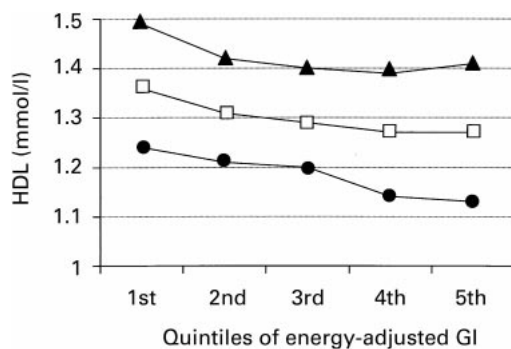


**Fig. 3.** Relative risk of non-insulin-dependent diabetes mellitus by different levels of cereal fibre intake and glycaemic load in women. Source: Salmeron *et al.* 1997b; published with the consent of the author.



**Fig. 4.** Relative risk of non-insulin-dependent diabetes mellitus by different levels of cereal fibre intake and glycaemic load in men. Source: Salmeron *et al.* 1997a; published with the consent of the author.

seen with low glycaemic-index foods in relation to heart disease in the Nurses' Study (Liu *et al.* 1999). The greatest effect on CHD risk reduction with low glycaemic-index intake is seen at the highest BMI and, thus in the presumably more insulin-resistant individuals, further suggesting an interaction between glycaemic index and insulin resistance (Liu *et al.* 1998). The higher HDL levels may be the lipid changes that are responsible in part for the reduced risk of heart disease associated with low glycaemic-index diets (Luscombe *et al.* 1999). It is also possible that higher HDL levels may be a reflection of reduced insulin resistance. Both a survey of British adults ( $n=2200$ ) (Frost *et al.* 1999) and NHANES III data ( $n=30\,908$ ) (Ford & Liu 1999; Fig. 5) indicate that higher HDL levels are seen



**Fig. 5.** Mean concentration of HDL according to quintiles of energy-adjusted glycaemic index (GI): squares, adults aged 20+; triangles, women; circles, men. The Third National Health and Nutrition Examination Survey (NHANES III) (30 908 subjects),  $P < 0.00001$ . Source: Ford & Liu, 1999; published with the consent of the author.

associated with low glycaemic-index diets. Another reason may relate to clotting factor improvements.

Perhaps more surprising is the linked association of insoluble fibre with diabetes and CHD risk in cohorts studied (Table 1). Since 1979 studies have repeatedly shown that fibre, and cereal fibre in particular, results in a reduced risk of CHD (Rimm *et al.* 1994). It has been estimated that an additional 5 g of cereal fibre per day will reduce the risk of CHD by 37% (Wolk *et al.* 1999). Recent data from the Nurses' Study also suggest that increased intake of whole grains may protect against CHD (Liu *et al.* 1999). Interestingly, the lower risk associated with higher whole-grain intake was not fully explained by its contribution to intakes of dietary fibre, indicating that other component(s) of whole grains, separate from fibre, may also act to reduce the risk of CHD. Moreover, both the Nurses' Study (Salmeron *et al.* 1997b) and the Health Professionals Study (Salmeron *et al.* 1997a) showed an independent and inverse relation between cereal fibre and risk of type 2 diabetes (Figs 3 and 4).

#### Cereal fibre and increased vegetable protein intake

In the absence of an effect of cereal fibre on glycaemic control, serum lipids, or other risk factors for diabetes or CHD, the question remains as to the possible mechanism. When wheat fibre is given as wheat bran in experimental studies, it becomes important to balance the protein intake on the control phase with additional fibre-free sources of protein (Table 2). In epidemiological studies this results in a higher protein:starch ratio on a high wheat-fibre diet compared to a low-fibre diet, due to the higher ratio in

**Table 2.** Protein in wholemeal/whole-grain foods and bran

Food	Contents per 100 g				
	Calories (kcal)	Fat (g)	Protein (g)	CHO (g)	Protein/CHO (%)
<i>Breads</i>					
White bread	235	1.9	8.4	49.3	17
Wholemeal bread	215	2.5	9.2	41.6	22
<i>Cereals</i>					
Cornflakes	360	0.7	7.9	85.9	9
Allbran	261	3.4	14.0	46.6	30
<i>Bran</i>					
Wheat bran	206	5.5	14.1	26.8	53

Source: McCance & Widdowson, 1991. CHO, carbohydrate.

**Table 3.** Effects of breakfast of starch-free (SF) bread (high in soy protein and monounsaturated fatty acids) in eight type 2 diabetic patients

Parameter	Bread	Before	After	P
F-blood glucose	Ordinary	11.6 ± 3.1	11.8 ± 2.5	NS
	SF	13.3 ± 3.5	10.2 ± 2.0	< 0.006
HbA1c (%)	Ordinary	8.6 ± 1.4	8.4 ± 1.4	NS
	SF	9.0 ± 1.4	8.1 ± 1.5	< 0.02
S-cholesterol	Ordinary	5.7 ± 0.8	5.8 ± 0.7	NS
	SF	5.8 ± 0.6	5.5 ± 0.5	= 0.05

Source: Stilling *et al.* 1999: data published with the consent of the author.

wheat bran. This effect is even reflected, although to a much more limited extent, in wholemeal or whole-grain breads (Table 2). The same is true for breakfast cereals and other foods where wheat bran or wholemeal flour is used in place of white flour. It is therefore possible in studies where either white or bran cereal products are eaten that the effects observed may in part be related to protein, although other components of whole grains including specific protein fractions or other fibre-associated compounds may also be responsible.

Protein breads have been shown to improve carbohydrate tolerance, and over 3-month periods to reduce HbA1c in type 2 diabetic subjects (Stilling *et al.* 1999; Table 3). In hyperlipidaemic subjects gluten (wheat protein) reduces serum triglyceride levels (Jenkins *et al.* 1999), and in the Nurses' Study increased protein intake was associated with reduced risk of ischaemic heart disease (Hu *et al.* 1999). Soy proteins have attracted recent attention for their ability to reduce serum lipids and act as antioxidants (Lichtenstein 1998) possibly related to their flavonoid content, and consumption of soy in China and Japan has been proposed as one reason for the longevity and freedom from many western diseases.

### Conclusions

There is limited evidence to suggest that fibre (soluble or insoluble) or low-GI foods reduce insulin resistance. However, in reviewing the literature, whole-grain foods and low glycaemic-index foods are emerging as dietary constituents that appear to reduce the likelihood of disease complications by reducing risk factors for the insulin-resistant diseases.

Although a reason for the effects of viscous fibre and low glycaemic-index foods is evidently based on slowing the rate of absorption and creating a late reservoir in the small intestine, the mechanism of action of insoluble (cereal) fibre remains obscure. It is suggested that, despite its lack of effect in acute studies, the protein content of wheat bran may in part be responsible for some of the beneficial effects seen in cohort studies. Beneficial effects may also be attributable to other components of the whole grain. It is therefore justified to focus on the interaction of vegetable protein with starchy foods, in addition to the effect of fibre, the nature of the starch, degree of gelatinization and particle size.

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