Soluble Fibers Prevent Insulin Resistance in Hamsters Fed High Saturated Fat Diets

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America and other developed countries are experiencing an obesity and type II diabetes epidemic. In 2002 6.3% of the U.S. population (3) was estimated to be diabetic, with type II diabetics making up 90–95% of those diagnosed with diabetes. Metabolic syndrome is a group of characteristics that usually precedes diabetes. Characteristics include obesity, insulin resistance, high blood pressure, abdominal obesity, high blood cholesterol, and high blood fasting glucose and insulin. It is believed that cellular damage to the pancreatic cells that produce insulin and other tissues occurs during the period in which metabolic syndrome characteristics are expressed, and eventually the individual develops diabetes. Type II diabetes (or adult-onset diabetes), which was once rarely found in young people, is also becoming increasingly common in school children.

The research presented here shows that some soluble fibers can overcome the adverse metabolic effects of diets high in saturated fats. Barley is one of the few food sources containing significant amounts of soluble fiber and may help to prevent insulin resistance and resulting type II diabetes. Barley and other sources of soluble fiber may also delay the onset of diabetes in individuals who are already insulin resistant and help to prevent elevated blood glucose. Because elevated blood glucose is associated with diabetes, it is often negatively associated with cereal foods, a source of glucose, by consumers. Barley and oats, however, are two of the best food sources of soluble dietary fiber. Most fruits, vegetables, and other cereal grains contain predominantly insoluble dietary fiber.

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Insulin Resistance and High Saturated Fat Diets

Our research using the Syrian hamster suggests that saturated fats may be a direct cause of insulin resistance and elevated blood glucose, as well as symptoms such as high blood pressure, elevated cholesterol, and other characteristics of metabolic syndrome. However, the harmful effects of saturated fats can be overcome in the presence of soluble fibers, including beta-glucan from barley. The male Syrian hamster has been used extensively to study lipid metabolism because it has many similarities to humans.

In this study hamsters were fed a diet with calories from fat similar to the average American diet. The fat component of the diet was either 5% (low fat [LF]) or 20% (high fat [HF]). The percentage of fat energy in the HF diet was calculated to be 37.3%, compared with the 33–37% mean fat intake of U.S. males 19–50 years of age (1984–1995) (1). The fat composition was the same for both LF and HF diets: 75% butterfat and 25% corn oil. The predominant fatty acids were oleic (25%), palmitic (22%), linoleic (17%), and stearic (10%). The remainder of the diets contained 20% casein, 7.7% dietary fiber, corn starch, vitamins, and minerals.

The hamsters were fed for 4 weeks, and a standard method of determining whole-body insulin resistance, the euglyce-mic insulinemic clamp, was used to determine insulin resistance. During this procedure a constant flow of insulin is administered to the animal through a flexible plastic catheter. Insulin causes glucose uptake by the muscles and other peripheral tissues and lowers the level of blood glucose. The level of glucose is monitored through a second catheter. If the blood glucose concentration drops below the original level, more glucose is administered through a second catheter. The rate of glucose through the second catheter is a measure of insulin resistance. Higher uptake by the peripheral tissues and greater glucose administration is a sign of good insulin sensitivity. Conversely, decreased uptake and sluggish uptake by peripheral tissues is a sign of insulin resistance.

The study was approved by the Animal Care and Use Committee, Western Regional Research Center (Albany, CA) and followed the Guide for the Care and Use of Laboratory Animals (Committee on Care and Use of Laboratory Animals 1985).

Impact of Soluble Fiber on Insulin Resistance

The euglycemic insulinemic clamp data is shown in Table I. The hamsters fed the LF diet serve as a reference for a good glucose infusion rate or insulin sensitivity. Compared with hamsters fed the LF diet, the hamsters fed a HF diet had approximately 50% of the glucose infusion rate. The movement of glucose from the blood to peripheral tissues, such as liver, muscle, adipose, and others, had decreased. The hamsters fed HF diets containing barley or the semisynthetic soluble cellulose hydroxypropylmethylcellulose (HPMC) had significantly higher glucose administration rates than hamsters fed the HF diet. The glucose infusion rate of hamsters fed HF + barley was intermediate between that of the LF and HF fed animals.

We have shown previously (5) that beta-glucan isolated from oats is more effective in lowering plasma cholesterol in hamsters than the same amount of beta-glucan in an enriched oat flour. Although beta-glucans in whole grains and flours are higher molecular weight polymers and potentially more bioactive, they are not fully extractable by cold or hot water (2). Extraction temperature also has an effect on polymer molecular weight, with the cold extracts having higher molecular weights. The physiological effect of foods containing beta-glucans in cell wall-containing fractions may be diminished relative to the fiber extract, because water, time, and temperature determine the rate and amount of the polymer diffused out of cell walls and into the stomach or intestinal lumen. Food processing conditions, therefore, affect the biological activity of beta-glucans consumed in flour or grain forms.

The dietary fiber in the LF and HF diets was an insoluble microcrystalline cellulose. Animals on the HF diet had significantly lower glucose administration rates than those on the LF diet. In a subsequent study, hamsters fed 20% corn oil alone did not develop signs of insulin resistance, such as fat infiltration of tissues. Abdominal adiposity, another symptom of metabolic syndrome in humans, was lower in animals fed soluble fibers, although overall body weight gain was not different for the 4-week time period. Plasma insulin was lower in the HF + HPMC fed animals but was not lower in the HF + barley fed animals. Barley, the source of soluble beta-glucans, was fed as a flour. Because beta-glucans are located in the cell wall and must diffuse out during passage through the digestive system, lower activity would be expected. We have seen similar differences between extracts of beta-glucans and flours containing beta-glucans in studies of cholesterol lowering by soluble fibers.

The data show that carbohydrate levels in the diet have little or no effect on increasing insulin resistance. All the HF diets contained the same amount and type of carbohydrate. The LF diet, our reference for good glucose disposal and high insulin sensitivity, contained, by necessity, a higher amount of carbohydrate to make up the difference in amounts of fat between the LF (5% fat) and HF (20% fat) diets.

Rivellese and Lilli (4) recently reviewed the adverse effects of saturated fats on insulin sensitivity. Some of the effects include the down regulation of the glucose transport protein, GLUT4, and subsequent decrease of glucose transport into muscle and impairment of glycogen synthesis. When glucose is absent or available at lower levels, cells metabolize fat for energy, which

Table I. Effects of diet on insulin resistance, abdominal adiposity, and plasma insulin

Parameter	Low Fat	High Fat (HF)	HF + Barley	HF + HPMC[a]
Glucose rate[b] (μmol/kg/min)	106 ± 8.5	55 ± 6.4	85 ± 5.8	109 ± 3.5
Abdominal fat pad (mg)	2,133 ± 164	2,990 ± 379	2,570 ± 228	1,750 ± 221
Plasma insulin (pmol/L)	76.3 ± 10	121.4 ± 22	111.0 ± 14	47.9 ± 4

[a] Hydroxypropylmethylcellulose.
[b] Glucose clamp.

is thought to generate more free radicals and result in cellular damage. In addition to restoring insulin sensitivity, barley is a good source of both water- and fat-soluble antioxidants, which help to suppress free radicals and prevent cell damage.

In addition to measuring insulin resistance, blood parameters, and abdominal fat weight, we also examined the cell structure of liver, skeletal muscle, pancreas, adipose, and heart muscle tissues using transmission electron microscopy (TEM). All tissues from HF fed animals had fat vacuoles that were not present in the animals fed either the LF diet or soluble fiber in the form of barley, HPMC, or psyllium (Fig. 1). Damage to nuclear membranes was observed in some tissues. Insulin normally stored as granules in the beta cells of the pancreas were depleted in the HF + insoluble cellulose fed animals. Animals fed HF and soluble fibers (barley, psyllium, or HPMC) experienced some restoration of insulin storage. Adipose cell size was increased in the HF + insoluble cellulose fed animals.

To increase our understanding of the metabolic differences, a microarray analysis of liver tissue from animals fed the LF, HF, or HF + HPMC diets was conducted. A microarray chip containing approximately 8,000 different genes was used to identify differences in genes expression. The results were consistent with the hypothesis that saturated fat is directly involved in insulin resistance. The key enzyme for converting saturated fat into unsaturated fat was expressed at a higher level in the animals fed the HF + insoluble cellulose diet compared with the animals fed the HF + HPMC diet. Enzymes in the fat oxidation pathway also were elevated in the animals fed HF + insoluble cellulose.

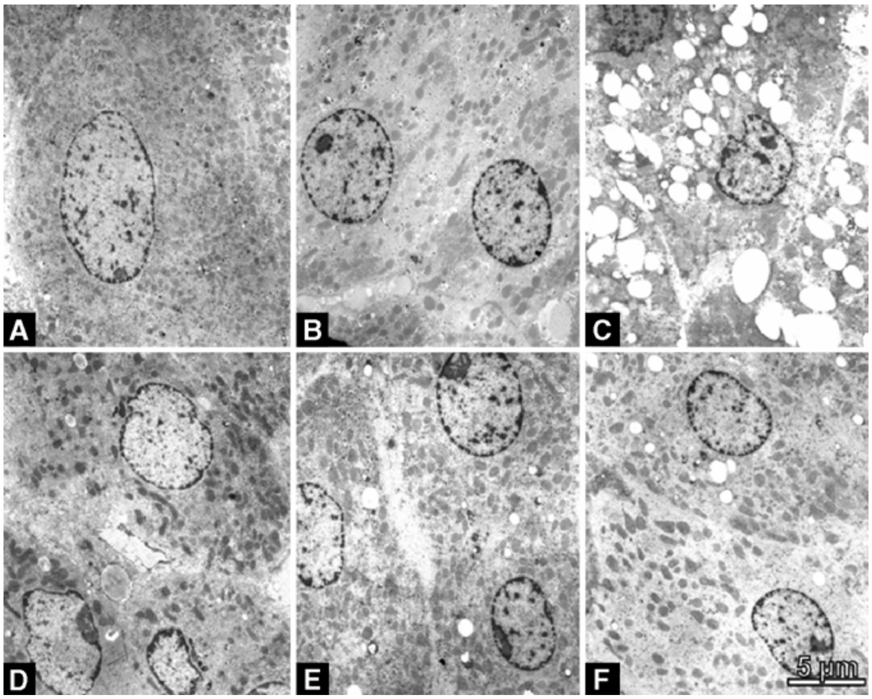

Fig. 1. Transmission electron micrograph of liver tissue from hamsters fed **A,** low-fat (LF), **B,** corn oil only, **C,** high-fat (HF), **D,** HF + psyllium, **E,** HF + barley, and **F,** HF + hydroxypropylmethylcellulose (HPMC) diets. Liver tissue from hamsters fed a HF diet (**C**) contains fat vacuoles and irregular nuclei not seen in livers from animals fed a LF diet (**A**) or HF + soluble fiber diets (**D–F**).

Conclusions

In this study, we found that saturated fat, not carbohydrates, in the diets of test animals caused insulin resistance. Insulin resistance even in diets containing high levels of saturated fats could be reversed, however, by substituting soluble fibers for insoluble fibers. In animals that were insulin resistant, the liver, and possibly other tissues, metabolized more fat. Fat oxidation is thought to result in permanent damage to tissues, ultimately resulting in diabetes. In addition to reducing insulin resistance and perhaps preventing or delaying the onset of diabetes, barley also contains antioxidants that may help retard cell damage by free radicals.

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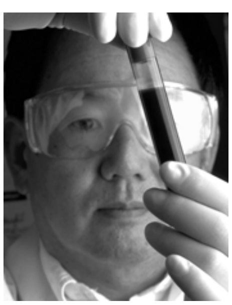

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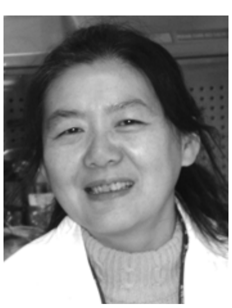

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Acknowledgments

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