

A Review of the Effects of Barley β -Glucan on Cardiovascular and Diabetic Risk

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Cardiovascular disease (CVD), primarily in the form of heart disease and stroke, causes more deaths in North America than any other disease and is observed in both men and women, irrespective of race or ethnicity (1). Deaths caused by CVD and coronary heart disease (CHD) can be correlated with metabolic syndrome, a condition that is increasingly prevalent and now affects approximately 25% of the U.S. adult population (11). This condition is characterized by a cluster of metabolic dysfunctions that may include abdominal obesity (waist circumference >40 in. in males and >35 in. in females), atherogenic dyslipidemia (elevated triglyceride levels [≥ 150 mg/dL], small LDL particles, and low HDL cholesterol levels [< 40 mg/dL in males and < 50 mg/dL in females]), elevated blood pressure ($\geq 130/\geq 85$ mm Hg), insulin resistance, and glucose intolerance (≥ 110 mg/dL) (27). When unchecked, metabolic syndrome often progresses to diabetes, a disease of tremendous public health concern and an independent risk factor for CHD and other forms of CVD (21,27).

Modifying risk factors offers the greatest potential for reducing CVD incidence, morbidity, disability, and mortality. Diet can play a key role in modifying several major risk factors, including high blood pressure, high cholesterol, and excessive body weight. Additionally, in individuals with metabolic syndrome dietary interventions that positively influence lipids, glucose metabolism, and body weight may help prevent or delay the development of diabetes and CVD.

There is mounting evidence supporting a role for dietary fiber, especially viscous soluble fibers, in prevention and management of CVD, diabetes, and related conditions. Fiber can have beneficial effects on several cardiovascular risk factors, including body



weight, blood pressure, and blood cholesterol levels. Soluble fibers in particular, including pectin from fruits and β -glucans found in oats and barley, can lower total and LDL cholesterol levels (6,10), improve blood glucose regulation (16), and promote satiety (24,31). Soluble fiber intake may also prevent the increase in triglycerides and reduction of HDL cholesterol that sometimes occur with diets rich in carbohydrates (especially from refined grains) (23).

Major health organizations are increasingly recognizing the cardiovascular benefits of high fiber intake. The American Heart Association (AHA) dietary guidelines assert that a healthy diet including a variety of high-fiber foods is the foundation for achieving and maintaining cardiovascular health (19). The National Cholesterol Education Program's (NCEP) ATP III guidelines, which identify LDL cholesterol as the primary target of cholesterol-lowering therapy, recognize the beneficial role of dietary fiber, specifically soluble fibers, in improving blood cholesterol levels

and reducing CHD risk. These guidelines recommend a diet that includes 20–30 g of dietary fiber and at least 5–10 g of soluble fiber per day. Higher soluble fiber intakes of 10–25 g/day are recommended for additional reductions in LDL cholesterol. These recommendations are supported by research showing that, on average, an increase in soluble fiber intake of 5–10 g/day is accompanied by a 5% reduction in LDL cholesterol (27).

CVD-Related Health Benefits of Fiber

Epidemiological observational studies demonstrate a strong association between higher fiber intake and lower cardiovascular (CV) risk in both men and women. Data from 68,782 women in the Nurses' Health Study revealed that those with the highest total dietary fiber intake (quintile median 22.9 g/day) had a 47% lower risk for major CV events than women with the lowest fiber intake (quintile median 11.5 g/day) (38). Another large study looked at 39,876 female health professionals. Those who had the highest fiber intake (quintile median 26.3 g/day) had a 35% lower incidence of total CVD and 54% fewer heart attacks than women who had the lowest fiber intake (quintile median 12.5 g/day) (20). In a study of 43,757 male health professionals, the incidence of heart attack and fatal coronary disease was 41% and 55% lower, respectively, for those with the highest fiber intake (quintile median 28.9 g/day) compared with those with the lowest intake (quintile median 12.4 g/day). In this study, a 10-g increase in dietary fiber corresponded to a 19% decrease in risk of heart attack (32).

Soluble fiber intake is more strongly associated with decreased CV risk than insoluble fiber. In the Nurses' Health Study, an increase in soluble fiber intake of 5 g/day led to a 25% decrease in CHD, whereas the same increase in insoluble fiber intake led to a 12% decrease in CHD (37). Of 9,776 adults who participated in the NHANES I Follow-up Study (4), those with the highest soluble fiber intake (quartile median 5.9 g/day) had 15% fewer CHD events and 10% fewer CVD events than those with the lowest soluble fiber intake (quartile median 0.9 g/day).

Epidemiological observational studies also demonstrate a strong association between higher intakes of fiber or whole grains and lower risk of metabolic syndrome and its risk factors. In one study, researchers followed 4,999 Swedish men and women and demonstrated relationships between food patterns, independent of specific nutrients, and specific components of metabolic syndrome. Food patterns rich in high-fiber bread provided favorable effects, whereas patterns high in refined bread had adverse effects (37).

Although observational investigations provide promising data about fiber and cardiovascular health, there are well-recognized limitations to these studies. Problems include selection biases, differing composition of study populations, inaccuracies of self-reported dietary intake, limited information about fiber sources, and difficulty identifying and controlling for confounding factors. Additionally, the role played by food synergies, or the way in which nutrients act together to influence metabolism and the risk of some chronic diseases, is difficult to strategically evaluate. For example, although CVD risk appears to be lower with consumption of whole grains than with consumption of refined grains, it is possible that the phytochemicals located in the fiber matrix, in addition to or instead of the fiber itself, may be responsible for

some or all of the reduced risk. To understand the role of soluble fiber and pathways by which food synergies work, it seems necessary to evaluate purified soluble fiber in combination with larger units, namely foods or food patterns (15). Experimental animal and randomized controlled human trials can be used to overcome many of these limitations and estimate the health effects of various sources of soluble fibers, including β -glucan from barley.

Health Benefits of Barley Foods and Barley Soluble Fiber

Although the majority of human studies examining the effects of β -glucan have used oat sources, a number of randomized controlled clinical trials have investigated the cholesterol-lowering effects of barley foods rich in β -glucan. In 1991 a crossover clinical trial demonstrated that a 4-week diet enriched with barley foods was more effective at lowering cholesterol in 21 men with high cholesterol than a diet with similar wheat foods. Compared with the wheat foods period (1.5 g of β -glucan per day), the barley foods period (8 g of β -glucan per day) resulted in significantly lower total (6%) and LDL (7%) cholesterol levels (26). One study evaluated the lipid responses in 11 men after they ate low-fat test meals with one of three pasta types: a low-fiber wheat pasta (0.3 g of β -glucan), a barley

pasta naturally high in β -glucan (5.2 g of β -glucan), or a barley pasta enriched with β -glucan (5 g of β -glucan). Four hours after the barley meals, total cholesterol levels dropped below fasting levels; no significant change in cholesterol occurred after eating the wheat pasta meal (5).

Not all studies involving barley β -glucan have shown significant reductions in lipid parameters, however. In a crossover study of 18 men with mildly high cholesterol, the addition of a β -glucan-enriched form of barley (8.1–11.9 g of β -glucan per day) to diets with 38% of the calories from fat did not result in significant changes in blood lipid measurements. Only small, non-significant reductions in total (1.3%) and LDL (3.8%) cholesterol were recorded (18).

Some researchers have suggested that components of barley other than β -glucan have lipid-lowering properties. Lupton and coworkers (22) treated 79 mildly hypercholesterolemic subjects with cellulose, barley bran flour (primarily insoluble fiber), or barley oil added to the NCEP Step 1 diet. The barley bran flour group showed significant reductions in total, LDL, and HDL cholesterol. The barley oil group showed significant reductions in total and LDL cholesterol but showed no change in HDL cholesterol. Although a significant reduction in energy, dietary cholesterol, and fat consumption did occur in both the flour and oil

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groups, changes in lipid values were greater than expected from diet changes alone. Most experts agree that the lipid-altering properties of barley are due primarily to soluble β -glucan fiber.

The benefits of barley foods may go beyond lowering cholesterol. Results of some recent studies are especially relevant due to the rise in the prevalence of metabolic syndrome and prediabetes. Soluble fiber delayed glucose absorption in the gut and decreased postprandial blood glucose in healthy patients and diabetics. A linear decrease in glycemic index with increasing β -glucan content was found for test meals with equivalent available carbohydrate fed to eight healthy adults (7). A pearl barley meal decreased hepatic glucose output and improved glucose tolerance in 10 healthy adults but did not produce a difference in plasma insulin levels (34). In a study of 15 diabetics, postmeal glucose was significantly reduced after consumption of barley breads compared with wheat bread (35). In a trial involving 11 males with type II diabetes (29), incorporation of barley bread (5 g of β -glucan per day) into the diet improved glycemic response. Insulin response increased, and some subjects reduced their dose of oral hypoglycemics.

To further investigate the effects of barley β -glucan on CVD and diabetes-related risk factors, our group recently conducted a randomized, controlled study to evaluate whether a concentrated β -glucan extract added to food products could effectively lower LDL cholesterol in hyperlipidemic subjects with and without metabolic syndrome. Because the molecular weight of polymers influences viscosity and palatability, both high and low molecular weight (HMW and LMW, respectively) β -glucan extracts were tested at daily doses of 3 and 5 g. After a 4-week diet-stabilization phase, subjects consumed the β -glucan treatment twice per day via ready-to-eat juice and cereal. After 6 weeks of treatment, mean LDL cholesterol levels fell by 15% in the 5 g of HMW β -glucan per day group, 13% in the 5 g of LMW β -glucan per day group, and 9% in both of the 3 g of β -glucan per day groups. The 5 g/day dose was more effective than the 3 g/day dose, but molecular weight did not significantly influence the findings (30).

Human studies appear to confirm what was indicated by the epidemiological data: the soluble fiber fractions of certain grains do alter CVD and diabetic risk. However, there are inconsistencies in the human data, which may be due to a variety of causes, including dose of treatment, molecular weight of treatment, dietary control, sample size, and/or variation in types of barley foods and supplements. These questions require additional research for clarification.

Mechanisms of Action of Soluble Fibers

The process by which soluble fiber lowers serum cholesterol is not completely under-

stood, but there is evidence of two probable mechanisms: 1) decreased absorption of cholesterol and bile acids in the gastrointestinal tract, leading to increased hepatic uptake of the LDL particle; and 2) microbial fermentation of intestinal contents, yielding products that may alter cholesterol biosynthesis. Recent research supports this hypothesis. Addition of barley β -glucan increased the viscosity of small intestinal digesta in animals (8,36), which correlated with decreased digestibility of lipids and decreased plasma total and LDL cholesterol in chicks (36). The ability of germinated barley foodstuffs to trap bile salts in vitro also has been demonstrated (2,17). Addition of barley β -glucan to diets of rats resulted in greater bile acid excretion compared with the control group and an increase in the activity of an enzyme (CYP7A1) involved in the synthesis of bile acids from cholesterol (39). A 50% decrease in HMG CoA reductase, a key enzyme in cholesterol synthesis, was found in chickens fed a barley diet enriched with β -glucan (28). This effect can be explained by short chain fatty acid production in the gut resulting from β -glucan fermentation (3,13,25). Experimental diets containing 500 g of barley meal (7–12 g of β -glucan per 100 g) significantly increased the amount and location of neutral sterols in the guts of rats, especially when higher concentrations of macromolecular β -glucans were present in the diet. Composition and transport of bile acids were also affected, as well as the microbial conversion of cholesterol to coprostanol, cholestanone, and coprostanone (9).

The molecular weight of the β -glucan seems to play a role in its effect on steroid excretion and the decrease of plasma lipids. It is well known that the molecular weight of polymers is one of the principal properties determining their viscosity. Similarly, the viscosity of barley flour slurries is affected by the content of soluble β -glucans, β -glucanase activity, and the molecular weight of the β -glucans. There has been only one previous study reporting a dietary intervention using β -glucans extracted from oats with molecular weight modifications (12). Studies have shown that as fiber viscosity decreases (as molecular weight decreases), so do many of the potential health benefits (12,14). The efficacy of low molecular weight β -glucan is still in question but is being tested. In our clinical trial mentioned above, we observed that a LMW concentrated barley β -glucan significantly improved LDL cholesterol.

The mechanism by which barley β -glucan and other soluble fibers improve markers of glucose and insulin metabolism is poorly understood. The leading theory is that soluble fibers increase the viscosity of the intestinal contents, causing reduced postprandial insulin and glucose levels. Over time, lower ambient insulin levels improve cellular insulin sensitivity, resulting in improved glucose metabolism. Additional work

is needed to understand how soluble fibers improve diabetic risk and control.

Conclusions

Recent guidelines strongly recommend increased total and soluble fiber consumption for general and cardiovascular health. High soluble fiber consumption protects against CHD, and there is strong evidence that soluble fiber decreases total and LDL cholesterol (6,27,33). ATP III guidelines for reducing LDL cholesterol recommend that most individuals should use intensive therapeutic lifestyle changes before initiating drug therapy. Increased soluble fiber consumption as part of these lifestyle changes is suggested to augment LDL cholesterol-lowering drug therapy and/or reduce the dose of medications.

Barley β -glucan fiber has been shown to reduce total and LDL cholesterol and improve glucose metabolism in different populations in various studies. Therefore, barley foods and functional foods containing extracted barley β -glucan should be considered safe and effective options for improving lipids in moderately dyslipidemic men and women.

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