See corresponding article on page 412.

Whole grains and protection against coronary heart disease: what are the active components and mechanisms?[1,2]

James W Anderson and Tammy J Hanna

The potential protective effect of whole-grain consumption against coronary heart disease (CHD) has challenged investigators and clinicians for > 20 y (1). Whole-grain foods are emerging as a dietary constituent that delivers significant health benefits. Several observational studies have provided strong support for a beneficial role of whole-grain intake in reducing the risk of CHD (2–4). In addition, whole-grain intake is associated with a reduced risk of developing diabetes (5), hypertension (6), and some types of cancer (7).

The recent interest in dietary fiber has perhaps clouded the importance of whole foods, such as whole grains, that reside at the base of the Food Pyramid (8). Whole grains provide complex carbohydrates, resistant starch, dietary fiber, minerals, vitamins, phytochemicals, and other substances (3, 4). The phytochemical components of whole grains can serve as both antioxidants and phytoestrogens (9). Whereas the serum lipid effects of whole-grain foods and dietary fiber have attracted great interest (10), whole-grain foods affect several risk factors for CHD. Whole grains rich in soluble fiber decrease serum total cholesterol and LDL-cholesterol concentrations, whereas wheat bran appears to have a specific triacylglycerol-lowering effect. Soy foods are perhaps the most extensively studied foods and current evidence suggests that both soy protein and soy isoflavones exert favorable effects on serum lipid concentrations (11). The phytoestrogens from whole grains and soy may convey these important hypotriglyceridemic effects.

On the basis of available evidence largely related to soy isoflavones, one can postulate that whole grains may reduce risk of CHD through favorable effects on lipids, their antioxidant properties, antithrombotic and decreased platelet-aggregating effects, and favorable effects on vascular reactivity. In addition, whole-grain, low-glycemic-index foods enhance insulin sensitivity, thus reducing the adverse cardiovascular effects of insulin resistance. These effects will be summarized.

Whole-grain foods are a rich source of antioxidants, including vitamins, trace minerals, phenolic acids, lignans, and phytoestrogens. Vitamin E and selenium are particularly concentrated in whole grains. Other trace minerals such as copper, zinc, and manganese are also found in the outer layer of grains. In addition, phytic acid, traditionally considered an antinutrient, may also function as an antioxidant. In particular, phytic acid has the ability to form chelates with a variety of metals, suppressing damaging iron-catalyzed redox reactions (12). Overall, whole grains are a potent source of numerous antioxidant compounds that may help to inhibit oxidative damage.

In addition to their antioxidant properties, whole grains may also reduce the risk of CHD through antithrombotic and decreased platelet-aggregating effects. Coagulation and fibrinolysis control the formation and resolution of fibrin and may affect risk of atherogenesis and thrombogenesis. Many have suggested that diet may serve an important role in the primary and secondary prevention of CHD through modifications in coagulation and fibrinolysis. In particular, diets low in fat and high in fiber result in a permanent increase in plasma fibrinolytic activity and a biphasic decrease in factor VIIc (13). These changes favorably affect cardiovascular disease risk.

Although the estrogen-like properties of whole-grain phytoestrogens have been discussed, the vascular effects have not been characterized. Whole grains are a source of lignans, particularly, enterodiol, enterolactone, and matairesinol, which are diphenolic compounds having a structure similar to that of estrogenic compounds and that have been shown to be weakly estrogenic (12). The phytoestrogens from whole grains share properties with soy isoflavones, which promote favorable vascular responses to stress. In a preliminary trial, 22 young adult rhesus monkeys with preexisting diet-induced atherosclerosis were subjected to 6 mo of dietary intervention. Dietary soy isoflavones were found to enhance the response to acetylcholine of atherosclerotic arteries in female monkeys. In addition, subsequent research by the same group also found that soy isoflavones promote endothelium-modulated dilation and inhibit constrictor responses to collagen infusion by inhibiting platelet aggregation or platelet release of vasoconstrictors (14). In this manner, the phytochemical component of whole grains may be affecting CHD risk through changes in vascular health.

The effects of whole-grain foods on insulin resistance are of great potential importance in reducing the risk of CHD. The insulin resistance syndrome afflicts as many as 80 million US residents and is an important forerunner of type 2 diabetes (15). Dietary glycemic index has been shown to be positively associated with risk of both diabetes (5) and CHD (4). Whole-grain intake addresses several CHD risk factors associated with the insulin

[1] From the Metabolic Research Group, VA Medical Center and University of Kentucky, Lexington.

[2] Reprints not available. Address correspondence to JW Anderson, Medical Service, 111C, 2250 Leestown Road, Lexington, KY 40511. E-mail: jwandersmd@aol.com.

resistance syndrome—hyperinsulinemia, hyperglycemia, hypertrigylceridemia with low HDL cholesterol, and hypertension.

Liu et al (4) have presented convincing data that support the hypothesis that increasing the consumption of whole-grain foods may protect against CHD. However, as the authors concede, a major limitation of observational studies is that even strong associations do not ensure causal relations. Prospective, controlled clinical trials are required to assess strong links between dietary components and disease states, but they are difficult to perform because it is almost impossible to provide control foods that are similar enough to the study foods to ensure blinding of investigators and volunteers. Long-term clinical trials with specific foods have not been done; therefore, this evidence is not available.

Thus, studies strongly suggest that the regular consumption of whole grains significantly reduces the risk of CHD (2–4). The estimated risk reduction with the highest measured intake of whole-grain intake is ≈28% (risk ratios of 0.70–0.74). Therefore, it may be prudent for health-care professionals to recommend to those individuals who may be at increased risk of CHD to follow the US Department of Agriculture Food Guide Pyramid recommendation to consume 6–11 servings of grains/d (8). From the work of Liu et al and previous publications, it appears that consumption of 2–3 servings of whole grains/d may have significant benefits in the prevention of cardiovascular disease. Recommending that an individual incorporate moderate amounts of whole grains, including dark bread, whole-grain breakfast cereals, popcorn, cooked oatmeal, or brown rice in their diet may have important implications in the prevention of Western diseases.

REFERENCES

1. Morris JN, Marr JW, Clayton DG. Diet and heart: a postscript. Br Med J 1977;2:1307–14.
2. Rimm EB, Stampfer MJ, Ascherio A, et al. Vegetable, fruit, and cereal intake and risk of coronary heart disease among men. JAMA 1996;275:447–51.
3. Jacobs DR, Meyer KA, Kushi LH, Folsom AR. Whole-grain intake may reduce risk of ischemic heart disease death in postmenopausal women: the Iowa Women's Health Study. Am J Clin Nutr 1998;68:248–57.
4. Liu S, Stampfer MJ, Hu FB, et al. Whole-grain consumption and risk of coronary heart disease: results from the Nurses' Health Study. Am J Clin Nutr 1999;70:412–9.
5. Salmeron J, Manson JE, Stampfer MJ, Colditz G, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 1997;277:472–7.
6. Ascherio A, Rimm EB, Giovannucci EL, et al. A prospective study of nutritional factors and hypertension among US men. Circulation 1992;86:1475–84.
7. Adlercreutz H. Western diet and Western diseases: some hormonal and biochemical mechanisms and associations. Scand J Clin Lab Invest Suppl 1990;201:3–23.
8. US Department of Agriculture, US Department of Health and Human Services. Nutrition and your health: dietary guidelines for Americans. Washington, DC: US Government Printing Office, 1995.
9. Slavin JL. Epidemiological evidence for the impact of whole grains on health. Crit Rev Food Sci Nutr 1994;34:427–34.
10. Anderson JW. Dietary fibre, complex carbohydrates and coronary heart disease. Can J Cardiol 1995;11:55G–62G.
11. Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of effects of soy protein intake on serum lipids in humans. N Engl J Med 1995;333:276–82.
12. Slavin J, Jacobs D, Marquart L. Whole-grain consumption and chronic disease: protective mechanisms. Nutr Cancer 1997;27:14–21.
13. Markmann P, Sandstrom B, Jespersen J. Favorable long-term effect of a low-fat/high-fiber diet on human blood coagulation and fibrinolysis. Arterioscler Thromb 1993;13:505–11.
14. Williams JK, Clarkson TB. Dietary soy isoflavones inhibit in-vivo constrictor responses of coronary arteries to collagen-induced platelet activation. Coron Artery Dis 1998;9:759–64.
15. Kruszynska YT, Mulford MI, Baloga J, Yu JG, Olefsky JM. Regulation of skeletal muscle hexokinase II by insulin in nondiabetic and non-insulin-dependent diabetic subjects. Diabetes 1998;47:1107–13.

The American Journal of Clinical Nutrition