Wheat Bran, Whole Grain, and Food Synergy

This issue of *Diabetes Care* contains an article by Jenkins et al. (1) with a surprising, perhaps counter-intuitive result. The authors studied 23 type 2 diabetic volunteers in a randomized cross-over design with 3 months consumption of wheat bran contributing 19 g fiber per day, compared with 3 months consumption of refined grain with 4 g fiber per day. The wheat bran supplement had no discernible effect on body weight, fasting blood glucose, HbA_{1c}, serum lipids, apolipoproteins, blood pressure, serum uric acid, clotting factors, homocysteine, C-reactive protein, magnesium, calcium, iron, or ferritin. The only statistically significant finding was unanticipated: there was a small increase in LDL oxidation associated with wheat bran. The study was conducted meticulously by investigators well known for their important findings in the effect of foods on human metabolism. We applaud both the execution and the publication of this article.

Despite the applause, all studies have potential flaws, and limitations of this study deserve comment. One remarkable flaw is that 44 of the 67 people who began the study dropped out. There is no way to fully assess whether these dropouts might have biased the findings. In our experience, asking participants to stay with a study for two 3-month periods is very ambitious. According to Dr. Jenkins (personal communication, 14 June 2002), this difficult protocol was carried out without any payment to the participants. Our assumption is that the failure to provide any financial compensation to participants is telling and likely accounts for the high dropout rate. However, it is our opinion that desire to be compensated for research participation is largely unrelated to metabolic outcomes.

Another weakness in the study design is that the participants chose their own diets, except for the breads and cereals supplemented with wheat bran. The failure to provide all meals to participants during the study period will increase variance of study outcomes but is unlikely to entirely wash out metabolic changes. It is hard to imagine, for example, participants eating foods that cancelled out the additional wheat bran in the treatment diet.

We also doubt that the failure of wheat bran to affect several metabolic parameters is the play of chance. A sample size of 23 participants, who all consumed both wheat bran and a refined wheat diet, is larger than many other feeding and food supplement studies. Other studies have found metabolic changes with smaller sample sizes, among these is one carried out by our research group (2) in which 11 participants were fed all food for 6 weeks, with whole grain (including substantial amounts of whole wheat) compared with refined grain foods. In our study, the whole grain diet showed improvements in fasting insulin and other markers of insulin resistance.

We therefore accept the wheat bran study of Jenkins et al. as a negative study. So what is going on? There is no question that wheat bran is high in many phytochemicals, some identified and some not (3). If the study is not fatally flawed, and isolated wheat bran has little metabolic effect, then how does that fit in with copious findings reporting healthful effects of cereal fiber and whole grain foods (2,4)? Note that the phrase "cereal fiber and whole grain foods" means mostly commercially available whole wheat, rolled oats, and brown rice in the feeding study (2) and commercially available whole wheat, wheat bran, rolled oats, and whole rye in the prospective studies of incidence of clinical end points (4).

Wheat bran may, in fact, have limited effectiveness. Mixed, but most often null, results have been reported in metabolic studies of wheat bran and lipid profile (4). For example, another study by Jenkins et al. (5) found no difference in blood lipids among healthy adults eating crushed corn flakes (a refined grain product) versus wheat bran. Blood lipid profile improved significantly with hard red spring wheat bran and nonsignificantly with corn bran but not with soft white wheat bran (6). In contrast to wheat bran, blood lipids improve using brans high in soluble fiber, such as oat bran (4,7). Glucose and insulin profile was not improved among healthy men using hard red spring wheat bran or soft white wheat bran, but it was improved using corn bran (8). Two other studies found improved glycemic profile with wheat bran consumption (9,10). Failure of the 2-year Diet and Reinfarction Trial (DART) to reduce mortality among ~1,000 postmyocardial infarction men who were randomized to advice to increase cereal fiber intake (11) is consistent with lack of effect of wheat bran. Fiber intake was low, only ~17 g/day in those advised to increase fiber. Although the reports do not explicitly break out dietary source of fiber, it is clear that as much as half of the fiber came from wheat bran (12).

We view the Jenkins et al. study as a contribution to the understanding of food synergy, the proposition that food constituents in a food, or foods in a food pattern, act on health in an additive or more than additive fashion. To study food synergy, a top-down approach has been proposed (13), namely a series of studies in which a health effect is identified for a whole food or food pattern, followed by study of progressively smaller parts of the food or dietary pattern. The point is to study subunits of foods or food patterns and perhaps specific phytochemicals or nutrients that are effective, with an ultimate goal to discover parts of the whole that work together to have a favorable health effect. The DART study (11) is interesting from the viewpoint of food synergy. Among the eight randomized groups in DART, the second lowest mortality occurred in the group that received advice to make all recommended changes: increase fish, reduce fat, and increase fiber. This suggests that cereal fiber, even if substantially from wheat bran, is effective in conjunction with other changes. The idea that it is healthful to consume whole wheat and other whole grains together with other plant foods, such as legumes, fruits, and vegetables, is supported by a variety of studies, often characterized as "high fiber diets." For example, Jang et al. (14) found favorable alteration in several metabolic parameters in men with coronary artery disease, including some with type 2 diabetes, with consumption of a powder that was largely brown rice, whole barley, and Job's tears but also contained small quantities of black beans, sesame, and other vegetables.

The Jenkins et al. study might be seen as one in a series of top-down studies. The logic would be as follows. Pereira et al. (2) studied mixed whole grains and found improved insulin resistance in overweight, hyperinsulinemic, nondiabetic participants. One may conclude that mixed whole grains have an effect. Vuksan et al. (5) found that lipid profile was favorably influenced by a partly destarched, high-fiber, high-protein test supplement that had been formed by amylolytic digestion of starch from wheat in the manufacture of ethanol. Therefore, although the description of the test product is sketchily described, a reduced-starch whole-grain product is effective. It is not clear, however, whether the amylolytic digestion affected the bran or germ in any way. Cara et al. (15) found improved lipid profile among healthy hypercholesterolemic adults using wheat germ for 4 weeks. One may conclude from this study that a part of the wheat kernel is effective. Now, Jenkins et al. report no effect of wheat bran in type 2 diabetic men and women. Interestingly, we find very few studies specifically of whole wheat, so there is little information about the effects of whole wheat, as opposed to mixed whole grains or mixed whole grains with legumes and other plant foods. Of course, the different study samples (including normal, obese, hyperinsulinemic, diabetic, and hyperlipidemic adults) and designs (including randomized controlled cross-over feeding, supplement, and uncontrolled observation) may make mutual interpretation of the above studies inadvisable. A coordinated series of top-down studies would be very helpful in sorting out what grains and what parts of grains work to improve health.

Despite the negative study of Jenkins et al. reported in this issue of *Diabetes Care*, the case for consumption of diverse whole grain foods is fairly strong. More research is needed on individual grains and their parts. For public health policy, prudence requires continued recommendation to eat whole grain foods as part of an otherwise phytochemical-rich diet.

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