Cardiovascular and renal benefits of dry bean and soybean intake

James W Anderson, Belinda M Smith, and Carla S Washnock

ABSTRACT Dry beans and soybeans are nutrient-dense, fiber-rich, and are high-quality sources of protein. Protective and therapeutic effects of both dry bean and soybean intake have been documented. Studies show that dry bean intake has the potential to decrease serum cholesterol concentrations, improve many aspects of the diabetic state, and provide metabolic benefits that aid in weight control. Soybeans are a unique source of the isoflavones genistein and daidzein, which have numerous biological functions. Soybeans and soyfoods potentially have multifaceted health-promoting effects, including cholesterol reduction, improved vascular health, preserved bone mineral density, and reduction of menopausal symptoms. Soy appears to have salutary effects on renal function, although these effects are not well understood. Whereas populations consuming high intakes of soy have lower prevalences of certain cancers, definitive experimental data are insufficient to clarify a protective role of soy. The availability of legume products and resources is increasing, incorporating dry beans and soyfoods into the diet can be practical and enjoyable. With the shift toward a more plant-based diet, dry beans and soy will be potent tools in the treatment and prevention of chronic disease. Am J Clin Nutr 1999;70(suppl):464S–74S.

KEY WORDS Soy, legumes, cardiovascular disease, cholesterol, diabetes, renal function, isoflavones

INTRODUCTION

Dry beans and soybeans are unique foods because of their rich nutrient content. These legumes contain complex carbohydrates, vegetable protein, dietary fiber, oligosaccharides, phytochemicals (especially the isoflavones in soy), and minerals. Their complex carbohydrates and dietary fiber contents contribute to their low glycemic indexes, which benefit diabetic individuals (1) and reduce the risk of developing diabetes (2). Soy protein is now recognized as a “complete” protein, with a protein digestibility–corrected amino acid score of 1, equivalent to the gold standard, egg albumin (3). Substituting vegetable for animal protein may reduce urinary calcium excretion and reduce the risk of osteoporosis (4). The dietary fiber components include both soluble and insoluble fibers, which offer many health benefits (5). The importance of oligosaccharides as prebiotics and their role in colon function is being widely recognized (6). The isoflavones genistein and daidzein are unique to soybeans and have numerous biologic functions (7). Finally, the minerals in beans are readily available, which is important in reducing the risks of osteoporosis (8) and hypertension (9).

NUTRIENT AND NONNUTRIENT PROFILE OF DRY BEANS AND SOYBEANS

Some of the major nutrients provided by dry beans and soybeans are shown in Table 1. Dry beans provide more complex carbohydrates than do soybeans. Both types of beans have limited amounts of simple carbohydrates. The oligosaccharides—raffinose, stachyose, and verbascose—in dry beans and soybeans (10) give legumes some of their notoriety because they are not hydrolyzed in the small intestine and are fermented to short-chain fatty acids (SCFAs) and gas in the colon (14). Recent research indicates that oligosaccharides are important prebiotics and favorably alter the bacterial flora of the colon (6). Because of their potential health benefits, soy oligosaccharides are available as commercial sweeteners in Japan (15). Some investigators attribute the notable longevity of rural Japanese individuals to their intake of soyfoods containing generous amounts of soy oligosaccharides (16). The role of the oligosaccharides found in beans and soybeans in the promotion of bifidobacteria development in the colon is still under study (3).

Dry beans are inexpensive sources of plant protein with potential to be used worldwide as substitutes for animal-protein sources. The protein content of most beans (uncooked) averages 20–25% by wt, whereas the protein content of soybeans is ~36% by wt (11). Although dry beans are rich in essential amino acids, they fall short in methionine and tryptophan content, requiring the consumption of larger amounts of protein to meet the nutritional requirements for these essential amino acids (10). In contrast, soy-protein foods are equivalent in quality to animal protein sources. Isolated soy protein has the same protein digestibility–corrected amino acid score as do casein and egg protein, which is 1.0 (3).

The fat content of dried beans averages only 1% by wt, with unsaturated fatty acids predominating (11). Soybeans are richer sources of fat (~18–20% by wt; 11, 17) and contain saturated, monounsaturated, and polyunsaturated fatty acids (15%, 23%, and 58% of total fat, respectively). The polyunsaturated fatty acids in soybean are linoleic acid (18:2n–6; 51% of total fat) and α-linolenic acid (18:3n–3; 7%) (17). The effects of linoleic and α-linolenic acids on eicosanoid synthesis are still under active study (15).

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TABLE 1
Nutrition profile of dry beans and soybeans, expressed per 100 g dry wt

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dry beans</th>
<th>Soybeans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex carbohydrates (g)</td>
<td>56</td>
<td>21</td>
</tr>
<tr>
<td>Simple carbohydrate (g)</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Stachyose (mg)</td>
<td>1848</td>
<td>3300</td>
</tr>
<tr>
<td>Raffinose (mg)</td>
<td>336</td>
<td>1600</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>22</td>
<td>36</td>
</tr>
<tr>
<td>Total fat (g)</td>
<td>1</td>
<td>19</td>
</tr>
<tr>
<td>Saturated fat (g)</td>
<td>0.3</td>
<td>2.8</td>
</tr>
<tr>
<td>Monounsaturated fat (g)</td>
<td>0.11</td>
<td>4.4</td>
</tr>
<tr>
<td>Polysaturated fat (g)</td>
<td>0.55</td>
<td>11.2</td>
</tr>
<tr>
<td>Ratio of α-linolenic to linoleic acid (mg)</td>
<td>0.252:0.301</td>
<td>1.3:9.9</td>
</tr>
<tr>
<td>Insoluble fiber (g)</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Soluble fiber (g)</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>154</td>
<td>276</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>172</td>
<td>280</td>
</tr>
<tr>
<td>Potassium (mg)</td>
<td>1140</td>
<td>1797</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>6.4</td>
<td>16</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>2.5</td>
<td>4.8</td>
</tr>
</tbody>
</table>

†From references 3, 10–13.

Soy isoflavones have many important biochemical effects that may mediate some of the health benefits outlined above (29). Genistein is a potent inhibitor of protein-tyrosine kinase, which may attenuate the growth of cancer cells (22, 30, 31). However, these isoflavones also have potent antioxidant effects, preventing the oxidation of lipid particles and reducing their contribution to atherosclerotic progression (32, 33).

The amount of isoflavones in soy products varies with type of soybean, geographic area of cultivation, and processing (34–36). Products that contain most of the bean, such as mature soybeans, roasted soybeans, soy flour, and textured soy protein are excellent sources of isoflavones and provide ≈5.1–5.5 mg total isoflavones/g soy protein. Green soybeans (3.3 mg/g) and tempeh (3.1 mg/g) are intermediate sources of isoflavones. Tofu, isolated soy protein, and some types of soy milk provide ≈2 mg isoflavones/g soy protein. Alcohol-extracted products, such as soy-protein concentrate, have lower amounts of isoflavones with values ≤0.3 mg isoflavones/g soy protein. A preliminary aggregation of data for the genistein and total isoflavone content of commonly available soy products from published sources (29, 33, 36–38) and from unpublished sources made available to us from manufacturers and investigators is shown in Table 2.

ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

Coronary artery disease

Accounting for more than half the deaths in the United States and costing more than $120 billion annually, cardiovascular disease is a major medical and public health concern in the United States, (39), in other Western countries, and in developing countries all over the world (40). Dietary interventions to reduce heart disease risk (41, 42) include attention to consumption of types of fatty acids (43), dietary fiber (44), isoflavones (45), and antioxidants (46). Dry beans and soyfoods contribute to all these areas.

Fatty acids

Dry beans are essentially fat-free and act to displace fat from the diet. Many soyfoods have moderate amounts of oil that is predominantly unsaturated. Linoleic acid (51%) is the predominant fatty acid of soyfoods and has specific actions on eicosanoid synthesis and metabolism, lipid peroxidation, and platelet aggregation, some of which may be detrimental (43). Soyfoods also provide α-linolenic acid (7%), an n-3 fatty acid not commonly found in plant foods, which has specific effects on eicosanoid synthesis and metabolism and appears to have favorable effects on platelet reactivity (43). Although effects of the individual fatty acids in soy are not documented, the low saturated-fat content makes soyfoods a good choice for a heart-healthy diet.

Dietary fiber

Dietary fiber has major protective effects against atherosclerotic cardiovascular disease (5, 44, 47, 48). Epidemiologic data suggest that intake of complex carbohydrates and dietary fiber is inversely related to coronary artery disease (5, 44, 47, 49). Dietary fiber intake also slows development of atherosclerosis in animal models (47, 50). Whereas soluble fiber clearly decreases serum cholesterol and LDL-cholesterol concentrations (5, 51), the inverse relation between dietary fiber intake and coronary artery disease appears to be independent of serum cholesterol concentrations (5, 52), and seems more closely related to cereal
TABLE 2
Protein and isoflavone contents of selected soy products

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving size</th>
<th>Protein content</th>
<th>Isoflavone content</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Weight g</td>
<td>Volume</td>
<td>g/100 g</td>
</tr>
<tr>
<td>Mature soybeans, uncooked</td>
<td>46.5</td>
<td>1/4 cup</td>
<td>37.0</td>
</tr>
<tr>
<td>Roasted soybeans</td>
<td>43</td>
<td>1/4 cup</td>
<td>35.2</td>
</tr>
<tr>
<td>Soy flour</td>
<td>21</td>
<td>1/4 cup</td>
<td>37.8</td>
</tr>
<tr>
<td>Textured soy protein, dry</td>
<td>30</td>
<td>1/4 cup</td>
<td>6.0</td>
</tr>
<tr>
<td>Green soybeans, uncooked</td>
<td>128</td>
<td>1/2 cup</td>
<td>16.6</td>
</tr>
<tr>
<td>Soymilk</td>
<td>228</td>
<td>1 cup</td>
<td>4.4</td>
</tr>
<tr>
<td>Tempeh, uncooked</td>
<td>114</td>
<td>4 oz</td>
<td>17.0</td>
</tr>
<tr>
<td>Tofu, uncooked</td>
<td>114</td>
<td>4 oz</td>
<td>15.8</td>
</tr>
<tr>
<td>Soy protein isolate, dry</td>
<td>28</td>
<td>1 oz</td>
<td>92.0</td>
</tr>
<tr>
<td>Soy concentrate, dry</td>
<td>28</td>
<td>1 oz</td>
<td>63.6</td>
</tr>
</tbody>
</table>

1 Values are representative and presented for illustrative purposes; values were obtained from the published literature and from analyses we obtained for selected products. The isoflavone content varies widely among soybean varieties and from product to product depending on the manufacturing process and source of soy protein—these estimates are our best calculation of isoflavone values provided by currently available products. The following references provide more detailed information about the different isoflavones in specific products: 28, 33, 35–37.

fiber intake (which predominately reflects insoluble wheat fiber) than to fruit and vegetable sources of soluble fiber (48, 53).

In a thorough literature review of clinical studies in humans, Glore et al. (51) reported that soluble fiber produced significant reductions in total serum cholesterol concentrations and LDL-cholesterol concentrations in 88% and 84%, respectively, of the studies reviewed. Most clinical studies in humans have used either high-fiber foods or fiber supplements (5). Many studies have documented the hypocholesterolemic effects of dry beans (10). Metabolic-ward studies suggest that dry-bean intake has the potential to decrease serum cholesterol concentrations of hypercholesterolemic subjects by ≈10% (10). Soy-fiber supplementation has a modest hypocholesterolemic effect in animals (20, 47) and humans (5, 19). Because most of the studies with soy protein have used isolated soy protein that does not contain soy fiber, the hypocholesterolemic effects of soy protein were unrelated to soy-fiber intake (23).

The hypocholesterolemic effects of foods rich in soluble fiber such as dry beans and oat bran have usually been attributed to their fiber content (5, 54–56). One perplexing issue relates to their differing effects on bile acid excretion. Whereas hypocholesterolemic effect of oat bran intake is related to a significant increase in bile acid excretion and fecal bile loss (55, 57, 58, 59), bean intake does not increase fecal bile acid excretion (55). Psyllium appears to exert most of its cholesterol-lowering effects through an increase in fecal bile acid excretion (60). Dry bean intake, however, appears to decrease bile acid excretion (55), making this an unlikely mechanism for producing hypocholesterolemia.

Thus, our current concepts about hypocholesterolemic mechanisms for fiber-rich foods and fiber supplements seem oversimplified. Soybeans, with or without their fiber, appear to decrease serum cholesterol concentrations through their protein or isoflavone contents (23). The vegetable protein content of oat bran may contribute to its hypocholesterolemic effects but its β-glucan content appears to be the major factor (59). Purified or isolated soluble fibers such as oat gum, guar gum, and psyllium appear to increase fecal bile acid loss, which decreases serum cholesterol concentrations (58, 60).

For almost 20 y the SCFA hypothesis has suggested that fermentation of dietary fiber in the colon generates SCFAs, which inhibit cholesterol synthesis (61). Although this hypothesis has been downplayed, it has not been disproved (61). Our studies with oat bran (62) and dry beans (61) documented the postprandial increase in serum acetate concentration that serves as a surrogate marker for propionate reaching the liver. Our in vitro studies indicated that propionate, in physiologic concentrations, inhibits hepatic cholesterol synthesis (63). Thus, the soluble fiber in dry beans and the oligosaccharide components of dry beans and soybeans are fermented in the colon and generate SCFAs, which may hinder hepatic cholesterol synthesis.

In addition to mechanistic effects of the fiber content of dry beans and soybeans on bile acid absorption and metabolism and SCFA synthesis and metabolism, they could influence fasting and postprandial serum lipoprotein concentrations by 1) altering gastric emptying, which could alter the kinetics of lipid absorption; 2) influencing intestinal transit time, which could be rate-limiting for postprandial serum lipoprotein concentrations; 3) modifying pancreatic secretion or pancreatic enzyme activity, which could affect nutrient absorption rates and extent of absorption in the small intestine; 4) acting on micelle formation, which could affect lipolysis and absorption; 5) varying intestinal motility, which could influence rates and quantities of lipids absorbed; 6) changing transport barriers such as the unstirred layer, which could decrease lipid absorption; 7) modifying lymphatic flow rates, which could regulate rates of entry of lipoproteins into the peripheral circulation; or 8) influencing secretion rates of insulin or other pancreatic or intestinal hormones, which could affect hepatic lipid and lipoprotein synthesis and secretion rates (60).

The specific effects of soluble fiber and oligosaccharides from legumes on these proposed mechanisms for cholesterol reduction have not been critically examined.

**Legume protein**

Soybeans and dry beans may exert a major cholesterol-lowering effect through their vegetable protein content. In experimental animal models feeding a variety of different plant proteins is associated with lower serum cholesterol concentrations than with feeding a variety of different animal proteins (64, 65). Legume proteins appear to have specific hypocholesterolemic effects. Clinical studies using soy protein for cholesterol reduction date
back to 1967, when Hodges et al (66) showed the cholesterol-lowering properties of soy in male prison inmates. More than 40 studies have found soy to be effective at reducing cholesterol when added to or replacing animal protein in the diet (23).

Our meta-analysis critically reviewed 38 controlled clinical studies examining the effects of intake of soy protein, either textured or isolated, on serum lipid concentrations (23). Soy-protein intake averaged 47 g/d in these studies. Of the 38 studies, 34 (89%) reported a net decrease in serum cholesterol concentrations with soy-protein intake. Soy protein exerted a favorable effect on all lipoprotein risk factors compared with animal-protein control diets in the following manner: serum cholesterol concentrations were 0.59 mmol/L (23 mg/dL; 9.3%) lower (P < 0.001); LDL-cholesterol concentrations were 0.56 mmol/L (21.7 mg/dL; 12.7%) lower (P < 0.001); triacylglycerol concentrations were 0.15 mmol/L (13.3 mg/dL; 10.5%) lower (P < 0.001); and HDL-cholesterol concentrations were 0.03 mmol/L (1.2 mg/dL; 2.4%) higher (P > 0.05). Changes in serum cholesterol and LDL-cholesterol concentrations were significantly (P < 0.001) related to baseline serum cholesterol concentrations as follows: persons with serum cholesterol < 5.17 mmol/L (200 mg/dL) had 7.7% lower LDL-cholesterol values than the control subjects, whereas persons with serum cholesterol values > 8.67 mmol/L (335 mg/dL) had 24.0% lower LDL-cholesterol values than did the control subjects.

The mechanisms by which soy protein or other vegetable proteins decrease serum lipoprotein concentrations are still under study. Earlier animal studies (67) suggested that the amino acid composition of soy protein, compared with that of animal protein, played a major role. Recent studies suggest that a 7S globulin is absorbed and affects LDL-receptor activity (68). Because data are not available to separate the effects of soy protein from the effects of soy isoflavones, an integrated discussion of their hypocholesterolemic action is included in the next section. In addition to their hypocholesterolemic effects soy isoflavones appear to have additional cardioprotective effects, as discussed in the next section.

Isoflavones

The hypocholesterolemic mechanisms of soyfoods are still under investigation and the constituents of soy responsible for these serum lipid effects are under discussion (23, 68, 69, 70). As discussed above, small peptide components, individual amino acid ratios, nonprotein components such as isoflavones, or a combination of factors may alter lipoprotein metabolism. Possible mechanisms that have been studied in animals and humans include enhancement of bile acid excretion, reduced cholesterol metabolism, increased thyroid hormones, and reduced insulin-to-glucagon ratios (23, 71).

Lovati et al (68) suggested that LDL-cholesterol degradation is enhanced by peptides formed from the hydrolysis of the 7S globulin by the liver. Huff et al (72) showed an increased turnover rate of VLDL apolipoprotein B in men fed soy protein diets compared with animal protein diets. Lovati et al (73) reported that soy-protein diets stimulated up-regulation of LDL-receptors and observed an 8-fold increase in LDL-cholesterol degradation compared with animal-protein diets.

Soy isoflavones, structurally similar to estrogens (22), interact with estrogen receptors and may decrease serum cholesterol concentrations by similar mechanisms (22). Anthony et al (69) reported that monkeys fed isoflavone-rich soy-protein-isolate diets had significantly better serum lipid values (lower total cholesterol and higher HDL-cholesterol concentrations) than monkeys fed isoflavone-poor soy-protein-isolate diets. Whereas the administration of the antiestrogen tamoxifen is accompanied by an increase in serum triacylglycerol concentrations, soy-protein administration is associated with a decrease in serum triacylglycerol concentrations.

Other cardiac benefits of soy intake, independent of cholesterol reduction, have been identified and investigated. In vitro studies of vascular cell cultures have shown that the isoflavone genistein inhibits atherosclerotic lesion development by inhibiting cell adhesion, altering growth factor activity, and inhibiting cell proliferation (74, 75). Clarkson et al (76) used monkeys with experimental atherosclerosis as a model to examine the effects of estrogen administration on vascular dilatation in vivo. Using a similar animal model they also showed that an isoflavone-rich soy-protein-isolate diet has a favorable effect on dilatation of coronary arteries similar to that of estrogen administration (24, 77).

Thrombin formation and platelet activation are inhibited by genistein in vitro (78). Clinical studies in humans, however, did not show a significant effect from diets rich in isoflavones from soy-protein isolates (79). Two studies documented the beneficial effects of estrogen therapy on the thrombolytic activity of blood in humans; the effects appear to be mediated through reductions in plasminogen activator inhibitor concentrations in blood (80, 81). Whereas soy isoflavones may have similar effects, further studies are required to determine whether dietary soy protein and its isoflavones have significant effects on thrombosis and platelet aggregation in humans.

Antioxidants

Soy isoflavones have antioxidant properties (32). Because LDL oxidation has a central role in the pathogenesis of atherosclerosis (74, 82), these soy isoflavones may have protective effects against atherogenesis in humans. LDL oxidation initiates a cascade of events that includes accelerated platelet aggregation, injury to arterial endothelial cells, and, in the subendothelium, the production of cytokines, adhesion factors, growth factors and other molecules that facilitate development of foam cells and fatty streaks. In vitro studies suggest that genistein and daidzein inhibit LDL oxidation in the subendothelium of vessels in a similar manner to that of vitamin E (83). In vitro studies indicate that genistein inhibits LDL oxidation in vitro (A Chait, unpublished observations, 1996). Our studies in rats indicate that feeding an isoflavone-rich soy-protein isolate significantly inhibits LDL oxidation after LDLs are isolated from the serum (JW Anderson, unpublished observations, 1998). These studies suggest that soy isoflavones are transported in LDLs and act like vitamin E to inhibit in vivo oxidation.

Kazanazawa et al (33) administered soycreme, a high-fat soy beverage derived by a special process, to healthy subjects and patients 6 mo after they had a stroke. Serum cholesterol concentrations were reduced and in vitro analysis showed that the soycreme suppressed LDL peroxidation and reduced LDL particle size in healthy subjects and patients with cerebrovascular disease. Of additional interest, estrogens also appear to have weak antioxidant effects on ex vivo oxidation of LDLs (84). In aggregate, the available studies indicate that soy isoflavones have antioxidant effects in vitro. However, conflicting reports make in vivo effects somewhat unclear.

Stroke

The third leading cause of death and the leading cause of serious disability, stroke, affects almost 4 million persons in the
United States each year (39). Ischemic strokes account for $\approx 85\%$ of strokes in North America and Europe (85). The roles of dyslipidemia and nutrition in primary and secondary prevention of strokes are much less conclusive than in heart disease. The pathogenesis of coronary artery disease events appears to involve development of an atherosclerotic plaque, plaque rupture, and thrombosis, with endothelial dysfunction playing a contributory role (86). In sharp contrast, the development of ischemic strokes involves large-vessel atherothrombotic disease, small-vessel atherothrombotic disease, and embolic disease (87). Although the atherosclerotic process and thrombus formation are similar in coronary and cerebral vessels, many other factors (such as atrial fibrillation) may contribute to an acute stroke. Nevertheless, lifestyle modifications provide a measure of protection from cerebral vascular disease and stroke. The incidence of stroke is generally lower in vegetarians in Western countries, which may be due to diet components or associated lifestyle factors (88). Fruit and vegetables are rich sources of potassium, antioxidant vitamins, and fiber. In an 11-y prospective study of middle-aged Californians, high potassium intake was protective against stroke independent of other diet variables and blood pressure (89).

Emerging evidence indicates that the severity of atherosclerotic disease of the carotid vessels is strongly correlated with the severity of the dyslipidemia, especially high LDL-cholesterol and low HDL-cholesterol concentrations (90). Recent clinical trials showed that improving serum lipoprotein profiles results in decreased risk of cerebral vascular events (91). Thus, lifestyle guidelines to decrease serum LDL-cholesterol and triacylglycerol concentrations and increase serum HDL-cholesterol concentrations appear as applicable to stroke prevention as to coronary artery disease prevention. An appropriate guideline seems to be to reduce saturated fat and cholesterol intakes and to increase intakes of dietary fiber, antioxidant, and phytochemicals from plant-based foods. Thus, heart-healthy dietary guidelines for stroke prevention should include bean and soy products.

**OBESITY**

Obesity is a complex disease with serious medical consequences (92). About 35% of American adults are considered to be obese (93) and obesity is exceeded only by smoking as a cause of preventable death (42). Dietary intervention for the purpose of weight loss is a challenge, and there has been limited success in maintaining long-term losses (94). Dietary fiber offers adjunctive benefits to hypoenergetic diet regimens. High-fiber foods, such as beans, deliver more bulk with less energy (95, 96). They take longer to eat and produce a feeling of fullness in the intestine (97). They may also influence satiety by altering concentrations of hormones such as cholecystokinin and insulin (95).

Studies suggest that protein is more satiating than carbohydrate or fat (98–101). Careful clinical studies examining the effects of high-protein diets compared with high-carbohydrate diets on weight loss of obese individuals, however, have not been reported. The observations of enhanced postmeal satiety associated with protein compared with other nutrients could suggest that increasing legume-protein intake may have weight-loss benefits. The potential renal toxicity of increased animal-protein intake (102–105) makes it disadvantageous for obese individuals to consume diets high in animal protein, especially because these individuals are more likely to have diabetes, glucose intolerance, or hypertension. Because soy protein appears to increase the workload of the kidneys to a much smaller extent than does animal protein (104, 105), soy protein may have advantages in the treatment of obese individuals. Concern about the high fat content of many soyfoods warrants careful instruction in the use of lower fat or fat-free versions of products, including textured soy protein, tofu, meat analogues, and soymilk.

**DIABETES**

Dry beans and soyfoods offer benefits in the prevention of diabetes and in the clinical management of established diabetes. Legume intake reduces the risk of developing diabetes in the same way it protects against obesity because legumes are high in fiber, low in fat, and have low glycemic indexes. Obesity is the major risk factor for diabetes and accounts for $\approx 70\%$ of the variance in the prevalence of this common disease (106). As outlined in the previous section, high-fiber and, potentially, high-protein foods assist in weight loss and management, thereby exerting diabetes-preventive effects. In several careful studies, investigators observed a significant inverse association between total dietary fiber intake and risk of type 2 diabetes (2, 107, 108). Additional observations suggest that foods with low glycemic indexes such as legumes were protective whereas foods with high glycemic indexes had a positive correlation with risk (2, 107).

In addition to contributing to weight loss and management, dietary fiber intake improves glycemic control (109), enhances sensitivity to insulin (110, 111), and favorably affects serum lipid concentrations (51, 55). Beans in particular are slowly digested and take longer to digest, with shorter carbohydrate digestion and glycemic responses among healthy subjects to 5 different legumes—chick peas, pigeon peas, black beans, mung beans, and white beans—varied, but were all significantly lower than those to white bread (112). Soybeans, in particular, have a low glycemic index (1). They are rich in phytates, soluble fiber, and tannins, all of which correlate inversely with carbohydrate digestion and glycemic response (21). In subjects with glucose intolerance, soy-fiber supplementation improved glucose tolerance and insulin response (19).

**CANCER**

One-third of all cancers are thought to be related to diet (18, 113). A major protector against cancer appears to be a diet high in fiber, low in fat, with generous intakes of vegetables and fruit rich in phytochemicals and antioxidants (18, 113–118). Whereas intake of most categories of vegetables (raw, allium, cruciferous, green vegetables, carrots, and tomatoes) for which there is a strong inverse relation to cancer risk, there is an equivocal relation to cancer risk with intake of legumes (dry beans, lentils, and peas). A summary of studies showed that 70–85% of studies showed an inverse relation between vegetable intake and cancer risk (average: $81\%$) whereas 39% showed an inverse relation between legume intake and cancer risk (113). On the other hand, the percentage of studies suggesting a positive relation of cancer risk with vegetables ranged from 5% to 20% (average: 13%); the percentage of studies suggesting a positive risk of cancer with legumes was 44% (113). This summary of studies indicates that the evidence currently available does not permit a definitive statement regarding the relation of dry beans with cancer risk.

The evidence indicating that soyfood intake has a protective effect against various types of cancer is stronger than that for dry beans (113–119). Populations with high intakes of soyfoods—such
as in China, Japan, and other Asian countries—usually have lower prevalences of cancers of the breast, uterus, prostate, and colon (113, 117). Because of the strong experimental evidence of the effects of isoflavones (31, 32, 75, 120–124), they are postulated to exert cancer preventive effects in humans. Isoflavone concentrations in serum and urine are 10–100-fold higher in Asian women than in American women; this supports the potential protective role of these phytochemicals (7, 27). Recently, Ingram et al (125) reported a substantial reduction in breast cancer risk among women with high intakes (as estimated by urinary excretion) of phytoestrogens. Adlercreutz et al (7) reviewed the evidence suggesting that isoflavones have hormone-like cancer protection that influences growth factor action, malignant cell proliferation, cell differentiation, and angiogenesis. Most clinical studies have not specifically examined the relation of soyfood intake and cancer risk, so definitive data are not available (113). Thus, at the present time epidemiologic data are moderately supportive of a protective role of soyfoods against certain types of cancers. The in vitro and animal data have identified important mechanisms by which genistein and other isoflavones may prevent the transformation of healthy cells into premalignant cells, slow cell proliferation, and attenuate angiogenesis. Clinical trials in prostate cancer are in progress (126) and clinical trials in breast cancer are under consideration (22).

KIDNEY DISEASE

The relation between excess protein intake and reduced kidney function has long been recognized and is considered when making dietary recommendations, especially to persons at risk of diabetic nephropathy (103). The “Brenner hypothesis” states that excessive protein intake causes hyperfiltration and glomerular hypertension, which results in the progressive deterioration of kidney function and leads to nephropathy (103). Recently, we put forth the “soy protein and diabetes kidney disease hypothesis,” suggesting that substituting soy protein for animal protein will protect against development of kidney disease in diabetic individuals and be effective in reversing or slowing the progression of established kidney disease in diabetic individuals (104). Limited evidence suggests that protein from dry beans may also have renal protective effects, but more investigation of this area is required (127). This section will review evidence supporting our hypothesis that substituting soy protein, or perhaps other vegetable protein, for animal protein has protective or restorative benefits for diabetic individuals with or at risk of nephropathy.

Protein intake and kidney function

After a large protein meal, blood flow to the kidneys increases significantly (104, 105). In healthy subjects, an increase in renal blood flow of 10% occurred after a large protein meal, whereas an increase of 33% occurred in subjects with chronic renal disease. Beef meals increase renal blood flow and glomerular filtration rates more than do chicken or fish meals. Soy protein does not affect renal blood flow or glomerular filtration rates (104). The mechanisms responsible for these changes are not understood and are still under investigation (103).

Protein-restricted diets remain the mainstay in nutrition management of chronic renal disease. Most recent clinical studies indicate that dietary protein restriction can slow progression of renal disease in nondiabetic or diabetic patients (128). In a comprehensive meta-analysis of the effects of protein-restricted diets on the progression of renal disease, data suggested that these diets reduced the risk of renal failure or death in nondiabetic patients (129).

Soy protein and renal function

Meal studies indicate that soy protein does not alter postprandial renal blood flow or glomerular filtration rates, whereas animal protein significantly increases these indexes (105, 130, 131). Longer-term intakes of soy-protein diets were associated with lower renal blood flow, glomerular filtration rate, and fractional clearance of albumin than were those of animal-protein diets (104). Of interest in this area, vegan and lactoovovegetarian subjects without renal disease had lower glomerular filtration rates and less urinary albumin excretion than did omnivores; however, the vegans also had lower protein intakes, on average, than did the omnivorous subjects (104).

Long-term studies also indicate that soy-protein intake protects kidneys, whereas excessive animal-protein intake may be harmful to kidneys. In animal models of kidney disease, rats fed soy protein had much slower progression of renal disease than did rats fed casein (132). Human studies have not been optimally controlled but suggest that substituting soy protein for animal protein decreases proteinuria in individuals with chronic glomerular disease (133–136). In a study of diabetic individuals with nephropathy, Jibani et al (127) noted that a vegetarian diet significantly decreased proteinuria compared with their baseline omnivorous diet.

Diabetic nephropathy

In diabetic individuals, long-standing hyperglycemia leads to chronic renal vasodilatation, glomerular hyperfiltration, cellular injury, glomerulosclerosis, mesangial proliferation, and, finally, proteinuria and uremia (102). Hypertension, almost universal in persons with type 2 diabetes, accelerates this process (135). Many individuals with type 1 and type 2 diabetes have higher renal blood flow and glomerular filtration rates and lower renal vascular resistance than nondiabetic individuals (136, 137). Only one-third of diabetic individuals develop nephropathy, and it is likely that those that do have a genetic predisposition for this condition (138). Hyperfiltration may be an early indicator that diabetic individuals are at high risk of developing nephropathy (138).

Several investigators (139–141) have examined the hemodynamic responses of diabetic individuals to various types of protein meals. The results of these studies are conflicting. These disparate results may relate to heterogeneity in the nature of diabetes, to the insulin and glucagon responsiveness of different subjects, to renal hormone production, and to the extent of autonomic dysfunction (141).

Dietary protein restriction appears to slow the progression of diabetic nephropathy (129, 142). In a carefully controlled, random-allocation, parallel study in diabetic individuals, a low-protein diet was associated with a decline in glomerular filtration rate and a slight decrease in proteinuria with nephropathy compared with the usual diabetic diet (143). A meta-analysis also concluded that protein-restricted diets slowed the progression of diabetic nephropathy (129).

Thus, the pathogenesis of diabetic nephropathy is complex and multifactorial. The acute effects of animal- compared with vegetable-protein meals in diabetic and control subjects are unclear. Chronic protein restriction appears to slow the progression of diabetic nephropathy. The available, clinical studies,
TABLE 3
Practical applications of dry beans and soybeans

<table>
<thead>
<tr>
<th>Food and serving size</th>
<th>Taste, texture and application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry beans (120 g; 1/2 cup cooked)</td>
<td>Mild taste, absorbs other flavors. Use in soups, salads, stews, dips, and casseroles; used in many ethnic recipes.</td>
</tr>
<tr>
<td>Whole soybeans (120 g; 1/2 cup cooked)</td>
<td>Can be cooked as regular beans, in soups, salads, stews, dips, casseroles and many ethnic recipes.</td>
</tr>
<tr>
<td>Roasted soybeans (120 g; 1/2 cup cooked)</td>
<td>A crunchy snack, similar to peanuts. Available in oil-or dry-roasted. Also known as soy nuts.</td>
</tr>
<tr>
<td>Soymilk (240 g; 1 cup)</td>
<td>Lactose free, available plain or flavored. Used in much the same way as cow milk.</td>
</tr>
<tr>
<td>Isolated soy protein (30 g; 1 oz)</td>
<td>Found in many commercially prepared products. The powder can be added to almost any recipe or beverage.</td>
</tr>
<tr>
<td>Soy flour (45 g; 3.5 oz)</td>
<td>Roasted soybeans ground into a fine powder, found as full fat or defatted. Substitute up to one-quarter of the regular flour in baked goods with soy flour. Adds moisture to product. Stir before using.</td>
</tr>
<tr>
<td>Textured soy protein (240 g; 1 cup)</td>
<td>Compressed soy flour; the protein fiber changes the structure. Rehydrate with 7/8 cup boiling water to 1 cup textured soy protein. Replace part or all of the meat in any recipe.</td>
</tr>
<tr>
<td>Concentrates (90–120 g; 3–4 oz)</td>
<td>In packaged convenience foods, eg, frozen burgers, sausages, meat analogs, and soy cheese.</td>
</tr>
<tr>
<td>Tofu (120 g; 4 oz)</td>
<td>The result of curdling hot soymilk with a coagulant. Absorbs flavor of other ingredients. Available in firm, soft, and silken tofu. Use in stir-fries, soups, casseroles, shakes, and pies.</td>
</tr>
<tr>
<td>Miso (30 g; 2 tbs)</td>
<td>Made from a combination of soybeans, grain, salt, and a mold culture. Aged in vats for 1–3 y. Used as a condiment to flavor soups, sauces, and dressings.</td>
</tr>
<tr>
<td>Tempeh (120 g; 4 oz)</td>
<td>Fermented soybean cake with a smoky or nutty taste. Grill or add to sauces and casseroles. Mix with mayonnaise to make sandwich spread.</td>
</tr>
</tbody>
</table>

though inadequately controlled, suggest that substituting vegetable protein for animal protein has a favorable effect on diabetic nephropathy. Diabetic individuals with nephromegaly and hyperfiltration appear to have more resistance to protein restriction or substitution for animal protein than do diabetic individuals with normal kidney size and glomerular filtration rates. Further research is required to examine our hypothesis that substituting soy protein for animal protein will protect against the development of kidney disease in diabetic individuals and will be effective in reversing or slowing the progression of established kidney disease in diabetic individuals. Because of the extensive evidence of detrimental effects of excess protein intake (144) and of the beneficial effects of restricting protein and substituting vegetable for animal protein, it seems prudent to recommend that diabetic individuals moderate their protein intake and select vegetable protein instead of animal protein when practical (145).

OTHER HEALTH CONSIDERATIONS

Osteoporosis

Osteoporosis is a major health problem in the United States; it affects ≈20 million women, causes > 1.5 million fractures/y, and costs ≤$10 billion annually (146, 147). Soy isoflavones are proposed to preserve bone mineral density (148, 149). Animal studies (149, 150) support the potential benefits of soy isoflavones on bone mineral density and preliminary human studies (151) also support the potential role of soy isoflavones in increasing bone mineral density in postmenopausal women.

Menopausal symptoms

The reduction in estrogen production in middle-aged women results in the symptoms commonly associated with menopause. Several preliminary studies of the effects of soy isoflavone administration on menopausal symptoms suggest a benefit but are inconclusive (27, 152–154).

The recent study by Brzezinski et al (28) provides more persuasive information. One hundred forty-five postmenopausal women were randomly assigned to consume phytoestrogen-rich or control diets for a 12-wk period. Women following the phytoestrogen-rich diet consumed ≈3 servings of soyfoods daily, providing ≥60 mg total isoflavones/d (these values were estimated from Table 2 because information provided by the authors was incomplete). Serum concentrations of isoflavones did not change significantly in women on the control diet but daidzein concentrations increased 12-fold and genistein concentrations increased 22-fold with the phytoestrogen-rich diet. Of interest, menopausal symptomatology scores decreased by 50% (P < 0.005), hot flash scores decreased by 54% (P < 0.05), and vaginal dryness score decreased by 60% (P < 0.005) in the phytoestrogen-rich diet group. The placebo effects of treatment were shown in this study because these 3 indexes also decreased in the control group but only significantly so for the menopausal symptomatology scores, with a decrease of 48% (P < 0.05).

PRACTICAL CONSIDERATIONS

The focus of healthy eating is in the bottom tier of the food pyramid, which includes grains rich in fiber, and in the second tier, which includes vegetables and beans. Dry beans and soybeans also are good sources of quality protein and can be substituted for animal protein sources. Dry beans bring complex carbohydrates with low glycemic indexes and a favorable mixture of soluble and insoluble fibers to the table, and soybeans provide high-quality protein and unique isoflavones.

Ideal candidates for increased soy intake are persons with family histories of coronary artery disease or osteoporosis. Men with family histories of prostate cancer or borderline elevations of prostate antigen should consider increasing their soy-protein intake on a regular basis.
intake. We recommend that most persons have some soyfoods weekly because small daily amounts of isoflavones, analogous to a baby aspirin, may have protective effects. Persons with coronary heart disease or osteoporosis would appear to derive clear benefits from increased intake of soy protein.

Women who are unwilling or unable to take estrogen replacement therapy should consider soy-protein intake to reduce their risk of osteoporosis, menopausal symptoms, and atherosclerotic cardiovascular disease. The use of soy protein by women with breast cancer is still under rigorous investigation. Although soy isoflavones may have an antiestrogen effect similar to that of tamoxifen, they may also have estrogenic activities that are detrimental to women with histories of breast cancer with estrogen-positive receptors (22).

The amount of soy protein that should be recommended for use to achieve “therapeutic effects” is unknown. Also, further research is required to determine the safety of isoflavones in pharmaceutical doses. Animal studies suggest that small amounts of isoflavones have favorable effects on lipoprotein oxidation and cholesterol reduction. Much more work is required to determine the minimum amount needed to have a specific beneficial health effect.

Information about the isoflavone content of various soy products is provided in Table 2. Whereas 30 g soy protein/d may be required to obtain a significant hypocholesterolemic effect (23), intake of significantly smaller amounts of isoflavone-rich foods may provide distinct health benefits as well.

A guide to using dry beans and soyfoods in practical ways is provided in Table 3. In our experience, most consumers can find ways of incorporating soy products into their daily diets. The health advantages far outweigh the slight inconvenience involved in changing shopping habits and eating patterns.

REFERENCES